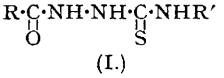
408. *Compounds Related to Thiosemicarbazide. Part III.* 1-*Benzoyl*-S-*methyl*isothiosemicarbazides.

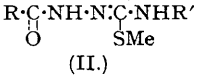
By Eric Hoggarth.

1-Benzoylthiosemicarbazides form *S*-methyl derivatives which readily cyclise with loss of methanethiol to give 2-amino-5-phenyl-1 : 3 : 4-oxadiazoles. The 1-benzoyl-*S*-methyl*iso*-thiosemicarbazides have been subjected to treatment with acids and bases under conditions similar to those used with the parent compounds (Part II), and the constitution of the products has been established.

1-Benzoylthiosemicarbazides (Part II, this vol., p. 1163) (I; R = Ph or *p*-MeO·C_6H_4, R′ = H) in alcoholic solution reacted with methyl iodide to give the hydriodides of the corresponding 1-*benzoyl*-S-*methyl*iso*thiosemicarbazides* (II). The free *S*-methyl*iso*thiosemicarbazides were more conveniently prepared in N-sodium hydroxide, and with this variation the *compounds* (II;



(I.)

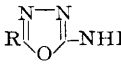


(II.)

R = *p*-NO_2·C_6H_4 or *p*-C_6H_4Cl, R′ = H), (II; R = Ph, R′ = Me, Pr^i, or Ph), and (II; R = *p*-MeO·C_6H_4, R′ = Me) as well as the foregoing, were prepared. These *S*-methyl derivatives were crystalline solids whose melting points, determined in the usual way (with slow heating), were in some cases higher than those of the parent compounds. The reason for this unusual behaviour is that on heating, methanethiol is readily lost with formation of 2-amino-5-

phenyl-1 : 3 : 4-oxadiazoles (III). If the *S*-methyl compounds are placed in a hot bath they melt with vigorous effervescence and resolidify. An analogous ready elimination of methanethiol has been described by Arndt and Tscherscher (*Ber.*, 1923, **56**, 1984) for the *S*-methyl ether of phenylguanylthiosemicarbazide, NHPh·C(:NH)·NH·NH·C(SMe):NH. For comparison, 2-amino-5-phenyl-1 : 3 : 4-oxadiazole (III; R = Ph, R′ = H) was prepared as described by Fehrenbach and Stollé (*J. pr. Chem.*, 1929, **122**, 289), and their method was extended to the preparation of the *compounds* (III; R = *p*-MeO·C_6H_4 or *p*-C_6H_4Cl, R′ = H).

The cyclisation reactions of 1-benzoyl-*S*-methyl*iso*thiosemicarbazides, like those of the parent 1-benzoylthiosemicarbazides (Part II), are greatly influenced by the nature of the agent used. The ease with which methanethiol is lost, however, is usually reflected in the isolation of appreciable amounts of the corresponding amino-oxadiazole. When heated with syrupy phosphoric acid (preferably with the addition of some phosphoric oxide) the compounds (II; R = Ph, *p*-MeO·C_6H_4, or *p*-C_6H_4Cl, R′ = H) gave, in addition to the amino-oxadiazoles (III), the corresponding benzoic acids and a third type of substance which was insoluble in both acids and alkalis. The best yields of the neutral compounds were obtained at rather lower temperatures than used in the initial experiments, and as a rule some unchanged *S*-methyl*iso*thiosemicarbazides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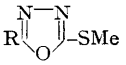
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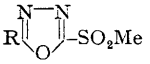
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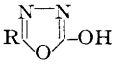
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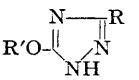
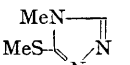

(VII.)


(VIII.)

were then isolated in place of the amino-oxadiazoles. Increasing the reaction time gave tarry products. Unlike the 1-benzoylthiosemicarbazides which are dehydrated by phosphoric or sulphuric acid to give the same products, the compound (II; R = Ph, R′ = H) gave only benzoic acid with 95% sulphuric acid. The neutral compounds have been shown to be 2-*methylthio*-5-*phenyl*-1 : 3 : 4-*oxadiazoles* (IV; R = Ph, *p*-MeO·C_6H_4 or *p*-C_6H_4Cl), and this unexpected elimination of the nitrogen atom was confirmed by showing that the three compounds (II; R = Ph, R′ = H, Me, or Pr^i) gave the same neutral compound (IV; R = Ph), and both (II; R = *p*-MeO·C_6H_4, R′ = H or Me) gave (IV; R = *p*-MeO·C_6H_4).

The cyclisation of *S*-methyl*iso*thiosemicarbazides having a terminal methyl group was complicated by the occurrence of another new compound. In the case of (II; R = Ph, R′ = Me) the acid-soluble fraction has been shown to be a mixture of two compounds with very similar properties. These are 2-*methylamino*-5-*phenyl*-1 : 3 : 4-*oxadiazole* (III; R = Ph, R′ = Me) and 5-*methylthio*-3-*phenyl*-4-*methyl*-4 : 1 : 2-*triazole* (VIII). The constitution of the latter was settled by comparison with the product of the methylation of the parent thiol (Part II). In the case of (II; R = Ph, R′ = Pr^i) unchanged starting material (only) was found in the acid-soluble fraction. Further proof of the constitution of the methylthio-oxadiazoles has been found in their oxidation to sulphones (V; R = Ph, *p*-MeO·C_6H_4, or *p*-C_6H_4Cl). The oxidation of the first two examples (with permanganate) was normal, but the *p*-chloro-compound gave also appreciable amounts of *p*-chlorobenzoic acid. The sulphones have labile methanesulphonyl groups. They dissolve in cold N-sodium hydroxide, giving salts of 2-*hydroxy*-5-*phenyl*-1 : 3 : 4-*oxadiazoles* (VI; R = Ph, *p*-MeO·C_6H_4, or *p*-C_6H_4Cl) and react readily with amines. Compound (V; R = Ph) with *iso*propylamine gave the *amino-oxadiazole* (III; R = Ph, R′ = Pr^i) which confirms the assigned structures. Reaction with 2-diethylaminoethylamine took place (exothermically) at 70—80°, and the following *compounds* were prepared: (III; R = Ph, *p*-MeO·C_6H_4, or *p*-C_6H_4Cl, R′ = $[CH_2]_2$·NEt_2).

On heating with sodium ethoxide solution, 1-benzoyl-*S*-methyl*iso*thiosemicarbazides gave, in addition to the amino-oxadiazoles, 5-*ethoxy*-3-*phenyl*-1 : 2 : 4-*triazoles* (VII; R = Ph, *p*-MeO·C_6H_4, or *p*-C_6H_4Cl, R′ = Et). The constitution of the ethers (VII) was established by acid hydrolysis to 5-hydroxy-3-phenyl-1 : 2 : 4-triazoles (VII; R = Ph, *p*-MeO·C_6H_4, or *p*-C_6H_4Cl, R′ = H). Young and Witham (*J.*, 1900, **77**, 226) prepared (VII; R = Ph, R′ = H) by oxidation of benzaldehyde semicarbazone with ferric chloride. This and the two other *hydroxy-triazoles* were prepared by this alternative route for comparison, and it has been shown that considerable quantities of the corresponding azines (not noted by Young and Witham) are formed as by-products. The by-products of this reaction were examined to ascertain whether or not 2-amino-5-phenyl-1 : 3 : 4-oxadiazoles were also formed in analogy with the oxidation of benzaldehyde thiosemicarbazones to aminothiadiazoles. No acid soluble material was found. The use of sodium methoxide in place of the ethoxide with (II; R = *p*-MeO·C_6H_4, R′ = H) gave the *methoxy-triazole* (VII; R = *p*-MeO·C_6H_4, R′ = Me) which was hydrolysed to the same hydroxy-triazole as was the corresponding ethoxytriazole.

Comparison of the behaviour of the *S*-methyl ethers of 1-benzoylthiosemicarbazides with that of the parent compounds is complicated by the ready formation of 2-amino-oxadiazoles by the former. However, both give triazole derivatives with sodium alkoxide solutions, and the formation of oxadiazole derivatives from the ethers under acid conditions corresponds to the formation of 2-amino-5-phenyl-1 : 3 : 4-thiadiazoles by the parent compounds. Breakdown to the benzoic acids, noted in the parent series only with the *p*-methoxybenzoyl compounds, is more generally encountered with the ethers.

Experimental.

After initial experiments, all crystallisations of *S*-methyl*iso*thiosemicarbazides were made by adding the vacuum-dried crude product to hot solvent, filtering rapidly, and chilling the filtrate slightly before leaving it to crystallise. This is necessary to avoid loss of methanethiol, especially in the case of 1-benzoyl-4-phenyl-*S*-methyl*iso*thiosemicarbazide.

1-*Benzoyl*-S-*methyl*iso*thiosemicarbazide* (II; R = Ph, R′ = H).—(*a*) 1-Benzoylthiosemicarbazide (6·5 g.) in alcohol (250 c.c.) at 60° was shaken in a stoppered bottle with a solution of methyl iodide (5·5 g.) in alcohol (30 c.c.) and set aside for 12 hours. The hydriodide obtained by evaporation under reduced pressure was dissolved in water (250 c.c.), filtered (charcoal), and made just alkaline with sodium carbonate. The solid (6·5 g.) was collected and crystallised from ethyl acetate (containing a little alcohol), giving the *product* as large highly-refractive prisms or needles (3·9 g.), m. p. 233° (decomp.) (melting with vigorous effervescence and resolidification in a bath at 180°) (Found: C, 51·5; H, 5·3; N, 19·8; S, 15·8. $C_9H_{11}ON_3S$ requires C, 51·7; H, 5·3; N, 20·1; S, 15·3%).

(*b*) 1-Benzoylthiosemicarbazide (9·8 g.) in N-sodium hydroxide (50 c.c.) was shaken for 20 minutes with methyl iodide (3·5 c.c.) in alcohol (10 c.c.), and the solid collected and crystallised as above, giving stout refractive needles (7·8 g.), m. p. 233—234° (decomp.).

1-p-*Methoxybenzoyl*-S-*methyl*iso*thiosemicarbazide* (II; R = *p*-MeO·C_6H_4, R′ = H).—(*a*) 1-*p*-Methoxybenzoylthiosemicarbazide (11·0 g.) in 2-ethoxyethanol (700 c.c.) at 50° reacted with methyl iodide (7·8 g.) in alcohol (50 c.c.) to give the S-*methyl*iso*thiosemicarbazide* (10·0 g.), which crystallised from methyl alcohol in colourless needles (5·0 g.), m. p. 244° (decomp.) (melts with effervescence and resolidification in a bath at 200°) (Found: C, 50·5; H, 5·6. $C_{10}H_{13}O_2N_3S$ requires C, 50·2; H, 5·4%).

(*b*) 1-*p*-Methoxybenzoylthiosemicarbazide (22·0 g.) in N-sodium hydroxide (100 c.c.) reacted with methyl iodide (15·6 g.) in alcohol (20 c.c.) as in (*b*) above, giving the *S*-methyl*iso*thiosemicarbazide (22·0 g.) which crystallised from methyl alcohol in colourless needles (17·1 g.), m. p. 244° (decomp.).

The following were prepared by method (*b*): p-*nitrobenzoyl*-S-*methyl*- (II; R = *p*-NO_2·C_6H_4, R′ = H), golden-yellow plates (from alcohol), m. p. 176° (decomp.) (solidifies and remelts at 206°) (Found: C, 42·1; H, 3·7; S, 12·7. $C_9H_{10}O_3N_4S$ requires C, 42·5; H, 3·9; S, 12·6%), 1-p-*chlorobenzoyl*-S-*methyl*- (II; R = *p*-C_6H_4Cl, R′ = H), colourless needles (from ethyl acetate), m. p. 248—252° (decomp.) (Found: C, 44·6; H, 4·2; S, 12·9. $C_9H_{10}ON_3SCl$ requires C, 44·4; H, 4·1; S, 13·2%), 1-*benzoyl*-4 : S-*dimethyl*- (II; R = Ph, R′ = Me), colourless needles (from ethyl acetate), m. p. 140° decomp.) (Found: C, 53·7; H, 5·6; S, 14·3. $C_{10}H_{13}ON_3S$ requires C, 53·8; H, 5·8; S, 14·3%), 1-*benzoyl*-S-*methyl*-4-iso*propyl*- (II; R = Ph, R′ = Pr^i), colourless needles (from alcohol–ethyl acetate), m. p. 145° (decomp.) (Found: C, 57·8; H, 6·8; S, 13·1. $C_{12}H_{17}ON_3S$ requires C, 57·4; H, 6·8; S, 12·8%), 1-p-*methoxybenzoyl*-4 : S-*dimethyl*- (II; R = *p*-MeO·C_6H_4, R′ = Me), colourless needles (from ethyl acetate containing a little alcohol), m. p. 166° (decomp.) (Found: C, 52·2; H, 6·2. $C_{11}H_{15}O_2N_3S$ requires C, 52·2; H, 5·9%), and 1-*benzoyl*-4-*phenyl*-S-*methyl*-iso*thiosemicarbazide* (II; R = R′ = Ph), colourless refractive needles (from ethyl acetate–alcohol), m. p. 205—207° (decomp.) (Found: C, 63·1; H, 5·4; S, 11·2. $C_{15}H_{15}ON_3S$ requires C, 63·2; H, 5·3; S, 11·2%). In the last case, concentration of the crystallisation liquors gave the (sulphur-free) oxadiazole, m. p. 212° (Found: C, 70·4; H, 4·6. $C_{14}H_{11}ON_3$ requires C, 70·8; H, 4·6%) (see below).

2-*Amino*-5-*phenyl*-1 : 3 : 4-*oxadiazole* (III; R = Ph, R′ = H).—1-Benzoyl-*S*-methyl*iso*thiosemicarbazide (1·0 g.) was heated in an oil-bath at 200°. Methanethiol was rapidly evolved and after 10 minutes the residue was cooled and crystallised from alcohol, giving sheaves of colourless needles (0·65 g.), m. p. 242°, not depressed by admixture with a specimen prepared by the method of Fehrenbach and Stollé (*loc. cit.*) (Found: C, 59·8; H, 4·1. Calc. for $C_8H_7ON_3$: C, 59·6; H, 4·3%).

2-*Amino*-5-p-*methoxyphenyl*-1 : 3 : 4-*oxadiazole* (III; R = *p*-MeO·C_6H_4, R′ = H).—(*a*) *p*-Methoxybenzoyl-*S*-methyl*iso*thiosemicarbazide (1·2 g.) was heated for 0·25 hour at 190° and then by crystallisation from alcohol gave the *oxadiazole* as colourless needles (0·85 g.), m. p. 248—249° (Found: C, 56·8; H, 5·0. $C_9H_9O_2N_3$ requires C, 56·6; H, 4·7%).

(*b*) *p*-Methoxybenzoylthiosemicarbazide (5·6 g.), litharge (35·0 g.), and alcohol (750 c.c.) were heated under reflux for 24 hours and then filtered. The solvents were removed in a vacuum, and the residue was crystallised from alcohol giving colourless needles (1·6 g.), m. p. 248° not depressed by the compound prepared as in (*a*) (Found: C, 56·4; H, 4·9%).

2-*Amino*-5-p-*chlorophenyl*-1 : 3 : 4-*oxadiazole* (III; R = *p*-C_6H_4Cl, R′ = H).—(*a*) 1-*p*-Chlorobenzoyl-*S*-methyl*iso*thiosemicarbazide (1·0 g.) was heated for 0·25 hour at 200°; the residue, crystallised from alcohol, gave the *product* as large highly-refractive pale yellow prisms (0·5 g.), m. p. 274° (Found: C, 49·0; H, 2·9. $C_8H_6ON_3Cl$ requires C, 49·1; H, 3·1%).

(*b*) 1-*p*-Chlorobenzoylthiosemicarbazide (2·8 g.), alcohol (350 c.c.), and litharge (18·0 g.) gave, as in (*b*) (preceding compound), pale yellow prisms (0·7 g.), m. p. 272—274°, not depressed by the compound prepared as in (*a*) (Found: C, 49·1; H, 3·2%).

The following were obtained from the *S*-methyl*iso*thiosemicarbazides by heating for 0·25—0·5 hour at 135—140°. 2-*Methylamino*- (III; R = Ph, R′ = Me), colourless glistening plates (from benzene), m. p. 154° (Found: C, 62·5; H, 5·1. $C_9H_9ON_3$ requires C, 61·8; H, 5·1%), 2-iso*propylamino*- (III; R = Ph, R′ = Pr^i), colourless needles (from benzene), m. p. 139° (Found: C, 64·8; H, 6·2. $C_{11}H_{13}ON_3$

requires C, 65·0; H, 6·4%), and 2-*anilino*-5-*phenyl*-1 : 3 : 4-*oxadiazole* (III; R = R′ = Ph), large colourless needles, m. p. 210°, from alcohol (Found : C, 71·1; H, 4·7%).

2-*Methylthio*-5-*phenyl*-1 : 3 : 4-*oxadiazole* (IV; R = Ph).—(*a*) A mixture of syrupy phosphoric acid (20 c.c.) and phosphoric oxide (*ca.* 5·0 g.) was stirred and heated in a bath at 120°, while 1-benzoyl-S-methyl*iso*thiosemicarbazide (4·1 g.) was added during 0·5 hour. Benzoic acid, m. p. 120°, sublimed. Stirring and heating were continued for 0·5 hour, the residue diluted with ice–water, and the oil extracted with ether. The aqueous acid liquid gave, on being basified at 0—5°, a solid which was collected and crystallised from ethyl acetate, giving 1-benzoyl-S-methyl*iso*thiosemicarbazide as large colourless prisms (0·4 g.), m. p. 236° (Found : C, 51·4; H, 5·0%). In other experiments (heating at 125—130°) this acid liquor gave 2-amino-5-phenyl-1 : 3 : 4-oxadiazole, which crystallised from alcohol in colourless needles (0·4 g.), m. p. 242° (Found : C, 59·9; H, 4·2%). The ethereal extracts were shaken with 10% sodium carbonate solution, and the alkaline washes made acid, giving benzoic acid (0·5 g.), m. p. 121° (from water). The residual ethereal solution was dried and distilled, giving 2-*methylthio*-5-*phenyl*-1 : 3 : 4-*oxadiazole* as a colourless oil, b. p. 180—182°/20 mm., setting to a mass of colourless prisms (2·5 g.), m. p. 38°. From light petroleum (b. p. 40—60°) long colourless needles, m. p. 39°, were obtained on cooling to 0° (Found : C, 56·3; H, 4·0; N, 14·5; S, 16·5. $C_9H_8ON_2S$ requires C, 56·25; H, 4·2; N, 14·6; S, 16·7%). When the above experiment was repeated with 95% sulphuric acid (22·0 c.c.) in place of the phosphoric acid–phosphoric oxide, only benzoic acid (2·2 g.; m. p. 120°) was isolated. A smaller yield of methylthio-oxadiazole (1·5 g.) was obtained with syrupy phosphoric acid alone.

(*b*) 1-Benzoyl-4 : S-dimethyl*iso*thiosemicarbazide (6·6 g.) and phosphoric acid (30 c.c.), as in (*a*), gave benzoic acid (0·5 g.), m. p. 121°, and 2-methylthio-5-phenyl-1 : 3 : 4-oxadiazole (0·8 g.), m. p. 38°. The precipitate obtained on basifying the phosphoric acid liquors (3·5 g.) was crystallised slowly from benzene–light petroleum (b. p. 60—80°), whereupon small colourless needles separated. The mother-liquor was carefully decanted and the residue repeatedly crystallised from the same solvent mixture, giving 2-methylamino-5-phenyl-1 : 3 : 4-oxadiazole (0·9 g.), m. p. 153° (Found : C, 61·6; H, 5·1%). The original benzene–light petroleum liquor was allowed to crystallise further, giving a mixture of large colourless plates and more small needles. The plates were separated by hand (1·6 g.) and recrystallised, giving 5-*methylthio*-3-*phenyl*-4-*methyl*-4 : 1 : 2-*triazole* (1·4 g.), m. p. 138° (Found : C, 58·6; H, 5·0. $C_{10}H_{11}N_3S$ requires C, 58·5; H, 5·4%). This triazole was also obtained by treating the parent thiol (0·9 g.) in alcohol (7·0 c.c.) at 60° with methyl iodide (0·8 g.) in alcohol (3·0 c.c.) in a closed vessel. After 12 hours, ether (10·0 c.c.) was added, the hydriodide collected and decomposed with N-sodium hydroxide, the solid dissolved in N-hydrochloric acid, filtered (charcoal), and precipitated with sodium hydroxide. The solid (0·6 g.; m. p. 136°) was crystallised from benzene–light petroleum, giving large colourless plates (0·4 g.), m. p. 136—137° (Found : C, 58·6; H, 5·3%).

(*c*) 1-Benzoyl-S-methyl-4-*iso*propyl*iso*thiosemicarbazide (4·4 g.), phosphoric acid (20 c.c.), and phosphoric oxide (5·0 g.) gave, as in (*a*), 2-methylthio-5-phenyl-1 : 3 : 4-oxadiazole (0·5 g.), m. p. 38° (Found : C, 56·5; H, 4·2%), and benzoic acid (0·4 g.). Neutralisation of the acid mother-liquors gave unchanged starting material (2·6 g.), m. p. 142° (after crystallisation from ethyl acetate containing a little alcohol) (Found : S, 12·6%).

2-*Methylthio*-5-p-*methoxyphenyl*-1 : 3 : 4-*oxadiazole* (IV; R = *p*-MeO·C_6H_4).—(*a*) 1-*p*-Methoxybenzoyl-S-methyl*iso*thiosemicarbazide (10·0 g.) was added to a mixture of phosphoric acid (40 c.c.) and phosphoric oxide (10·0 g.) at 110—115° (at 120° much charring took place) during 0·5 hour. After a further 0·25 hour at 115° some effervescence took place and the mixture was at once poured on ice. The precipitate was collected, washed with water, suspended in 10% sodium carbonate solution, and filtered. The filtrate, on acidification, gave *p*-anisic acid (2·6 g.), which crystallised from water in colourless needles, m. p. 182°. The insoluble residue was crystallised from light petroleum (b. p. 60—80°), giving 2-*methylthio*-5-p-*methoxyphenyl*-1 : 3 : 4-*oxadiazole* as colourless needles (2·2 g.), m. p. 100—101° (Found : C, 54·0; H, 4·4; N, 12·5; S, 14·3. $C_{10}H_{10}O_2N_2S$ requires C, 54·1; H, 4·5; N, 12·6; S, 14·4%). Basifying the phosphoric acid liquors gave 1-*p*-methoxybenzoyl-S-methyl*iso*thiosemicarbazide which crystallised from alcohol in long colourless needles (2·1 g.), m. p. 246° (Found : C, 50·5; H, 5·4%).

(*b*) 1-*p*-Methoxybenzoyl-4 : S-dimethyl*iso*thiosemicarbazide treated, as in (*a*), gave the same methylthio-oxadiazole, m. p. 100° (Found : C, 53·9; H, 4·3%).

2-*Methylthio*-5-p-*chlorophenyl*-1 : 3 : 4-*oxadiazole* (IV; R = *p*-C_6H_4Cl).—1-*p*-Chlorobenzoyl-S-methyl*iso*thiosemicarbazide (4·9 g.), phosphoric acid (20·0 c.c.), and phosphoric oxide, allowed to react at 120° as in method (*a*) for the *p*-methoxybenzoyl compound, gave the *methylthio-oxadiazole* which crystallised from light petroleum (b. p. 60—80°) as large colourless plates (1·5 g.), m. p. 119° (Found : C, 47·5; H, 3·0. $C_9H_7ON_2ClS$ requires C, 47·8; H, 3·1%). 1-*p*-Chlorobenzoyl-S-methyl*iso*thiosemicarbazide was isolated from the acid liquors and crystallised from ethyl acetate, giving colourless needles (1·0 g.), m. p. 254° (Found : C, 44·7; H, 4·3; S, 13·2%).

2-*Methanesulphonyl*-5-*phenyl*-1 : 3 : 4-*oxadiazole* (V; R = Ph).—2-Methylthio-5-phenyl-1 : 3 : 4-oxadiazole (6·5 g.) in acetic acid (50 c.c.) was stirred while potassium permanganate (11·0 g.) in water (170 c.c.) was added during 1 hour, the temperature being kept at 30—35°. After stirring for a further hour, the reaction liquid was cooled to 0° and decolorised with sulphur dioxide, and the solid collected. After being dried in a vacuum over phosphoric oxide, the *sulphone* crystallised from light petroleum (b. p. 80—100°) containing a little benzene as colourless needles (5·5 g.), m. p. 133—134° (Found : C, 48·5; H, 4·0; S, 14·3. $C_9H_8O_3N_2S$ requires C, 48·2; H, 3·6; S, 14·3%).

2-*Methanesulphonyl*-5-p-*methoxyphenyl*-1 : 3 : 4-*oxadiazole* (V; R = *p*-MeO·C_6H_4).—Crystallised from benzene, this *product* formed flat colourless needles, m. p. 184° (Found : C, 47·3; H, 4·0; S, 12·3. $C_{10}H_{10}O_4N_2S$ requires C, 47·2; H, 3·9; S, 12·6%).

2-*Methanesulphonyl*-5-p-*chlorophenyl*-1 : 3 : 4-*oxadiazole* (V; R = *p*-C_6H_4Cl).—2-Methylthio-5-*p*-chlorophenyl-1 : 3 : 4-oxadiazole (6·9 g.) was oxidised in acetic acid (100 c.c.) with potassium permanganate (9·0 g.) in water (150 c.c.) as above. After removal of manganese dioxide at 0°, the white solid was collected and triturated with ice-cold 5% sodium carbonate solution. The alkaline filtrate was treated with hydrochloric acid, and the precipitated *p*-chlorobenzoic acid (0·5 g.) crystallised from benzene, giving colourless glistening needles, m. p. 238—240° not depressed by an authentic sample (Found : C,

53·4; H, 3·2. Calc. for $C_7H_5O_2Cl$: C, 53·7; H, 3·2%). The residue insoluble in sodium carbonate solution was dried in a vacuum and crystallised from benzene, giving the *oxadiazole* as colourless felted needles (4·9 g.), m. p. 160° (Found: C, 42·1; H, 2·9; S, 12·6. $C_9H_7O_3N_2ClS$ requires C, 41·7; H, 2·7; S, 12·4%). The *p*-chlorobenzoic acid is not formed by the action of the sodium carbonate, as direct crystallisation gave a mixture of the sulphone and the acid, separated in part by hand picking.

2-Hydroxy-5-phenyl-1 : 3 : 4-oxadiazole (VI; R = Ph).—2-Methanesulphonyl-5-phenyl-1 : 3 : 4-oxadiazole (1·0 g.) was ground with N-sodium hydroxide (10 c.c.), filtered (charcoal), and treated with concentrated hydrochloric acid. The solid was collected and crystallised from water, giving the *hydroxy*-compound as long silky needles (0·65 g.), m. p. 135—136° (Found: C, 59·5; H, 3·9. $C_8H_6O_2N_2$ requires C, 59·3; H, 3·7%).

Similar experiments and crystallisation from benzene–light petroleum (b. p. 60—80°) gave *2-hydroxy-5-p-methoxyphenyl-* (VI; R = *p*-MeO·C_6H_4), colourless flat needles, m. p. 184° (Found: C, 56·0; H, 4·1. $C_9H_8O_3N_2$ requires C, 56·3; H, 4·2%), and *2-hydroxy-5-p-chlorophenyl-1 : 3 : 4-oxadiazole* (VI; R = *p*-C_6H_4Cl), colourless, flat, glistening needles, m. p. 226—227° (Found: C, 48·6; H, 2·6. $C_8H_5O_2N_2Cl$ requires C, 48·9; H, 2·5%).

2-isoPropylamino-5-phenyl-1 : 3 : 4-oxadiazole (III; R = Ph, R′ = Pr^i).—2-Methanesulphonyl-5-phenyl-1 : 3 : 4-oxadiazole (1·1 g.) and *iso*propylamine (0·6 g.; dried over sodium) were heated in a sealed tube for 0·5 hour at 100°. The residue was dissolved in N-hydrochloric acid (100 c.c.), filtered (charcoal), and treated with sodium hydroxide, giving a solid which was collected and dried in a vacuum (0·7 g.) and then melted at 136—137°. Crystallisation from benzene gave long colourless needles (0·5 g.), m. p. 138—139° not depressed by admixture with the compound as prepared above (Found: C, 64·9; H, 6·1%).

2-2′-Diethylaminoethylamino-5-phenyl-1 : 3 : 4-oxadiazole (III; R = Ph, R′ = $[CH_2]_2$·NEt_2).—Powdered 2-methanesulphonyl-5-phenyl-1 : 3 : 4-oxadiazole (3·3 g.) was cautiously added to dry 2-diethylaminoethylamine (2·7 g.; dried over sodium) at 80° during 10 minutes, so that the temperature did not rise above 100°. After a further 10 minutes, the melt was cooled and dissolved in 10% acetic acid and filtered (charcoal); sodium hydroxide precipitated an oil, which was extracted with ether, dried (Na_2SO_4), and distilled, giving the *amine* as a colourless oil, b. p. 192—194°/0·01 mm., setting to a crystalline mass (3·1 g.), m. p. 40—42°. From light petroleum (b. p. 40—60°), colourless leaflets separated on cooling in ice, m. p. 48° (Found: C, 64·9; H, 7·3; N, 21·4. $C_{14}H_{20}ON_4$ requires C, 64·6; H, 7·7; N, 21·5%). The *picrate* separated from alcohol in yellow needles, m. p. 176°, which on recrystallisation gave deep orange prisms, m. p. 178° (Found: C, 48·9; H, 4·6. $C_{14}H_{20}ON_4,C_6H_3O_7N_3$ requires C, 49·1; H, 4·7%).

The following were prepared from the corresponding sulphones in similar experiments. *2-2′-Diethylaminoethylamino-5-p-methoxyphenyl-1 : 3 : 4-oxadiazole* (III; R = *p*-MeO·C_6H_4, R′ = $[CH_2]_2$·NEt_2) crystallised in colourless needles or leaflets from benzene–light petroleum (b. p. 60—80°), m. p. 107° (Found: C, 62·1; H, 7·5. $C_{15}H_{22}O_2N_4$ requires C, 62·1; H, 7·6%), and gave a *picrate* golden-yellow needles (from alcohol), m. p. 175—176° (Found: C, 47·1, 46·9; H, 5·1, 4·6. $C_{15}H_{22}O_2N_4,C_6H_3O_7N_3,H_2O$ requires C, 46·9; H, 5·0%). *2-2′-Diethylaminoethylamino-5-p-chlorophenyl-1 : 3 : 4-oxadiazole* (III; R = *p*-C_6H_4Cl, R′ = $[CH_2]_2$·NEt_2) crystallised in large colourless glistening plates, m. p. 99° (Found: C, 56·6; H, 6·1. $C_{14}H_{19}ON_4Cl$ requires C, 57·0; H, 6·4%).

5-Ethoxy-3-phenyl-1 : 2 : 4-triazole (VII; R = Ph, R′ = Et).—1-Benzoyl-*S*-methyl*iso*thiosemicarbazide (8·4 g.) was heated under reflux with a solution of sodium (1·5 g.) in alcohol (200 c.c.) for 3 hours, the solvent removed under reduced pressure, and the residue shaken well with ice and water and filtered off. The residue (2·8 g.; m. p. 238—240°) was crystallised from alcohol, giving 2-amino-5-phenyl-1 : 3 : 4-oxadiazole as colourless sheaves of needles (1·5 g.), m. p. 242—243° (Found: C, 59·8; H, 4·6%). The alkaline mother-liquors were cooled strongly, made just acid with acetic acid, the precipitate allowed to harden, collected, and dissolved in hot N-sodium hydroxide (100 c.c.). After filtration (charcoal), an excess of strong hydrochloric acid was added to the cold solution until the first-formed precipitate was dissolved. The solution was again filtered (charcoal) and made just alkaline (potassium hydrogen carbonate), and the triazole was collected, dried in a vacuum, and crystallised from light petroleum (b. p. 100—120°), giving clumps of large glistening needles (1·0 g.), m. p. 116—117° (Found: C, 63·8; H, 5·8; N, 22·0. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·8; N, 22·2%).

5-Ethoxy-3-p-methoxyphenyl-1 : 2 : 4-triazole (VII; R = *p*-MeO·C_6H_4, R′ = Et).—1-*p*-Methoxybenzoyl-*S*-methyl*iso*thiosemicarbazide (9·1 g.) gave, as in the preceding experiment, 2-amino-5-*p*-methoxyphenyl-1 : 3 : 4-oxadiazole (3·35 g.), m. p. 250° (Found: C, 56·6; H, 4·8%), and the *ethoxy-triazole* which crystallised from benzene in small colourless rectangular plates (2·8 g.), m. p. 146° (Found: C, 59·9; H, 6·1; N, 19·5. $C_{11}H_{13}O_2N_3$ requires C, 60·3; H, 5·9; N, 19·2%). This ethoxy-triazole was much less soluble in dilute hydrochloric acid than was the 3-phenyl analogue.

5-Ethoxy-3-p-chlorophenyl-1 : 2 : 4-triazole (VII; R = *p*-C_6H_4Cl, R′ = Et).—1-*p*-Chlorobenzoyl-*S*-methyl*iso*thiosemicarbazide (4·9 g.) and a solution of sodium (0·75 g.) in alcohol (100 c.c.) gave 2-amino-5-*p*-chlorophenyl-1 : 3 : 4-oxadiazole (0·7 g.), m. p. 270° (Found: C, 49·3; H, 3·3%), and the *ethoxy-triazole* which crystallised from benzene in clumps of colourless needles (1·6 g.), m. p. 148° (Found: C, 53·3; H, 4·5. $C_{10}H_{10}ON_3Cl$ requires C, 53·7; H, 4·5%). The ethoxy-triazole was not sufficiently soluble in dilute acid to be purified in the way used above and was, probably for this reason, difficult to crystallise.

5-Methoxy-3-p-methoxyphenyl-1 : 2 : 4-triazole (VII; R = *p*-MeO·C_6H_4, R′ = Me).—This *compound* was obtained in the same way as the corresponding ethoxy-compound, by use of sodium methoxide and crystallised from benzene in large colourless prisms, m. p. 164° (Found: C, 58·3; H, 5·3. $C_{10}H_{11}O_2N_3$ requires C, 58·5; H, 5·4%).

5-Hydroxy-3-phenyl-1 : 2 : 4-triazole (VII; R = Ph, R′ = H).—(*a*) 3-Ethoxy-5-phenyl-1 : 2 : 4-triazole (0·9 g.) was heated under reflux with concentrated hydrochloric acid (25 c.c.) for 0·5 hour. After initial dissolution, crystals quickly separated and after cooling were collected, washed with water, and crystallised from alcohol, giving colourless needles (0·5 g.), m. p. 324° (Young and Witham, *loc. cit.*, give m. p. 321—322°) (Found: C, 59·7; H, 4·6. Calc. for $C_8H_7ON_3$: C, 59·6; H, 4·3%). This compound (0·3 g.), fused sodium acetate (0·3 g.), and acetic anhydride (4·0 c.c.) were heated under reflux for 5 minutes and then poured into water and the acetyl derivative crystallised from alcohol, giving large colourless needles

(0·2 g.), m. p. 248° (Young and Witham give m. p. 248°) (Found : C, 59·3; H, 4·7; N, 21·1. Calc. for $C_{10}H_9O_2N_3$: C, 59·1; H, 4·4; N, 20·7%).

(*b*) Benzaldehyde semicarbazone (5·5 g.), alcohol (25 c.c.), water (0·5 c.c.), and ferric chloride (anhydrous; 5·5 g.) were heated in a sealed tube at 135—140° for 2 hours, cooled, and diluted with water (200 c.c.). The solid was collected and stirred with N-sodium hydroxide for 0·5 hour. The filtrate was made acid (hydrochloric acid), and the solid collected, washed, and crystallised from alcohol, giving colourless needles of the hydroxy-triazole (1·1 g.), m. p. 324° not depressed by the compound as prepared above (Found : C, 59·4; H, 4·4%). The acetate, prepared as previously, crystallised from alcohol in colourless needles, m. p. 248°. The insoluble material left after the initial extraction with sodium hydroxide solution was stirred with N-hydrochloric acid. Nothing was extracted and the residue of benzaldehyde azine was crystallised from alcohol in yellow plates (1·0 g.), m. p. 90° not depressed by admixture with an authentic sample.

5-*Hydroxy*-3-p-*methoxyphenyl*-1 : 2 : 4-*triazole* (VII; R = *p*-MeO·C_6H_4, R′ = H).—(*a*) 3-Ethoxy-5-*p*-methoxyphenyl-1 : 2 : 4-triazole (1·0 g.) gave, by acid treatment, the *hydroxy-triazole* which was crystallised from 2-ethoxyethanol and then from acetic acid, giving small colourless leaflets (0·85 g.), m. p. 334° (Found : C, 56·7; H, 4·7. $C_9H_9O_2N_3$ requires C, 56·5; H, 4·7%). The *acetate* was formed as above and crystallised from alcohol giving fine hair-like needles, m. p. 226° (Found : C, 56·5; H, 4·8. $C_{11}H_{11}O_3N_3$ requires C, 56·65; H, 4·7%). The hydroxy-triazole (0·3 g.), m. p. 334° (Found : C, 56·5; H, 4·8%), was also obtained by the action of acid on 3-methoxy-5-*p*-methoxyphenyl-1 : 2 : 4-triazole (0·5 g.).

(*b*) Oxidation of *p*-methoxybenzaldehyde semicarbazone (9·7 g.) with ferric chloride (8·5 g.) in alcohol (50 c.c.) and water (1·0 c.c.), as described for the benzylidene compound, gave the hydroxy-triazole which crystallised from acetic acid in colourless leaflets (2·1 g.), m. p. 336° (Found : C, 56·3; H, 4·7%). The acetate crystallised from alcohol in fine colourless needles, m. p. 226° (Found : C, 56·4; H, 4·9%). *p*-Methoxybenzaldehyde azine, which crystallised from xylene in yellow needles (1·4 g.), m. p. 170° not depressed by an authentic sample, was also isolated.

5-*Hydroxy*-3-p-*chlorophenyl*-1 : 2 : 4-*triazole* (VII; R = *p*-C_6H_4Cl, R′ = H).—(*a*) 3-Ethoxy-5-*p*-chlorophenyl-1 : 2 : 4-triazole (0·9 g.) gave, with acid, the *hydroxy-triazole* which was crystallised from acetic acid in long silky needles (0·5 g.), m. p. 402—404° (Found : C, 49·0; H, 3·1. $C_8H_6ON_3Cl$ requires C, 49·1; H, 3·1%).

(*b*) Oxidation of *p*-chlorobenzaldehyde semicarbazone (1·9 g.) with ferric chloride (1·5 g.) in alcohol (10 c.c.) and water (1·0 c.c.) gave the hydroxy-triazole, which crystallised from acetic acid in colourless needles (0·3 g.), m. p. 406° (Found : C, 49·2; H, 2·8%), and *p*-chlorobenzaldehyde azine which crystallised from alcohol in golden leaflets (0·6 g.), m. p. 208° (Pascal, and Normand, *Bull. Soc. chim.*, 1911, **9**, 1061, give m. p. 211°) (Found : C, 60·4; H, 3·7. Calc. for $C_{14}H_{10}N_2Cl_2$: C, 60·6; H, 3·6%).

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