105. *The Conversion of Sucrose into Pyridazine Derivatives. Part II. 4-Amino-2-phenyl-6-methyl-3-pyridazone, 4-Amino-2-(p-nitrophenyl)-6-methyl-3-pyridazone, and their Sulphanilamido-derivatives.**

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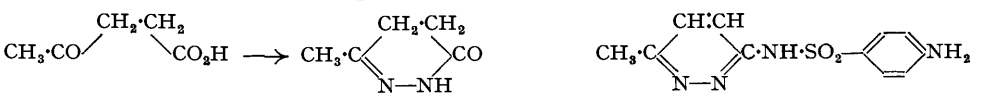
The preparations of the sulphanilamido-derivatives of the new amino-pyridazones named in the title are described. The constitutions of some of the intermediates are established.

Sulphanilamide derivatives having a diazine substituent on the N^4 group have come into prominence in recent years, owing largely to the fact that treatment of certain diseases by their aid seems to be accompanied by a particularly small degree of toxic effect. The diazines used, however, in the manufacture of these sulphanilamide derivatives are variously substituted pyrimidines and pyrazines; pyridazine derivatives seem to have been largely neglected.

We have therefore embarked on a study of the sulphanilamide and other derivatives of this type of compound. In Part I (this vol., p. 239) we described the preparation of 3-sulphanilamido-6-methylpyridazine and the intermediates required in its synthesis from lævulic acid, and showed that it possessed striking bacteriostatic power, so much so that against certain organisms it possessed greater activity than sulphathiazole.



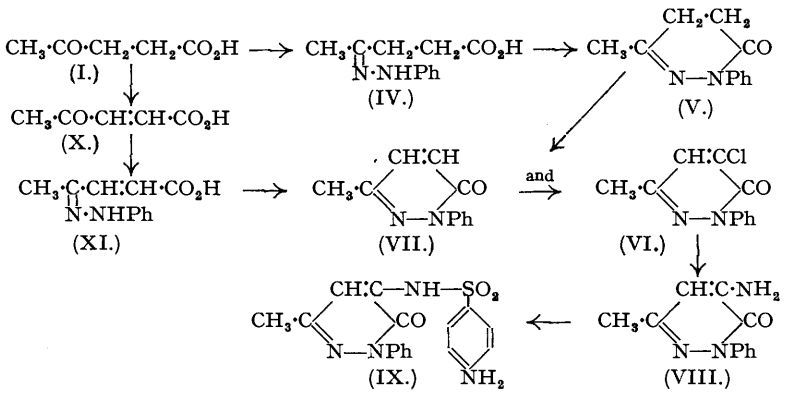
(I.) (II.) (III.)

The essential step in the synthesis of this compound was the condensation of lævulic acid (I) with hydrazine to form 6-methyl-3-pyridazinone (II) which, after several further transformations was converted into 3-sulphanilamido-6-methylpyridazine (III). Now we have prepared sulphanilamide derivatives from the condensation products of phenylhydrazine or *p*-nitrophenylhydrazine with lævulic acid.

Lævulic acid (I) when treated with phenylhydrazine yielded the corresponding phenylhydrazone (IV). On heating this at 160°, ring closure was effected, and the product was 2-phenyl-6-methyl-3-pyridazinone (V). This compound was prepared by Fischer (*Annalen*, 1886, **236**, 147) who referred to it as the anhydride of lævulic acid phenylhydrazone. On being treated with phosphorus pentachloride, this was converted into a mixture of 2-phenyl-6-methyl-3-pyridazone (VII) and 4-chloro-2-phenyl-6-methyl-3-pyridazone (VI), the latter in 60% yield and the former in very small yield. Ach (*ibid.*, 1889, **253**, 47), who first carried out this

* Patent applied for.

transformation, reported equal amounts. The yield of 4-chloro-2-phenyl-6-methyl-3-pyridazone could be further augmented, since it could be obtained by treating 2-phenyl-6-methyl-3-



pyridazone with phosphorus pentachloride. This experiment indicates that the mechanism of the reaction between (V) and phosphorus pentachloride is such that first a dehydrogenation occurs at C_4 and C_5 and subsequently chlorination takes place on C_5 to give (VI).

That the constitution of the pyridazone derivative obtained from 2-phenyl-6-methyl-3-pyridazinone was indeed represented by (VII), *i.e.*, with an unsaturated linkage between C_4 and C_5, has been proved by the fact that it is also obtained by cyclisation of the phenylhydrazone (XI) of β-acetylacrylic acid (X) which, of course, must possess αβ-unsaturation.

The conversion of 4-chloro-2-phenyl-6-methyl-3-pyridazone, proof of the constitution of which was afforded by Ach (*loc. cit.*), into *4-amino-2-phenyl-6-methyl-3-pyridazone* (VIII) was easily effected in 88% yield by treatment with methyl-alcoholic ammonia at 125—130°.

This amine formed only a *monohydrochloride*, and on acetylation with acetic anhydride and sodium acetate, it gave *4-acetamido-2-phenyl-6-methyl-3-pyridazone*, which did not form salts. On treating 4-amino-2-phenyl-6-methyl-3-pyridazone with *p*-acetamidobenzenesulphonyl chloride in pyridine solution 4-(p-*acetamidobenzenesulphonamido*)-*2-phenyl-6-methyl-3-pyridazone* was obtained which, on treatment with either 10% aqueous sodium hydroxide or with 2N-hydrochloric acid, was transformed into *4-sulphanilamido-2-phenyl-6-methyl-3-pyridazone* (IX), and this was reacetylated by means of acetic acid and acetic anhydride. Alternatively, the sulphanilamide derivative was obtained by condensation of the amine (VIII) with *p*-nitrobenzenesulphonyl chloride to form 4-(p-*nitrobenzenesulphonamido*)-*2-phenyl-6-methyl-3-pyridazone*, followed by its catalytic hydrogenation over Raney nickel.

The new sulphanilamide derivative was only slightly soluble in water (5·5 mg. per 100 c.c. of solution), but even so compares favourably in this property with sulphapyrazine and sulphathiazole. The results of the bacteriostatic tests on this sulphonamide (IX), carried out under the auspices of the Medical Research Council, are shown in Table I. It is seen that this compound, although it did not possess the outstanding bacteriostatic action of 3-sulphanilamido-6-methylpyridazine, did nevertheless show considerable activity.

TABLE I.

	Horse blood medium.	Synthetic medium.	Hartley's broth medium.					
Compound.	*Streptococcus hæmolyticus.*	*Escherichia coli.*	*Streptococcus hæmolyticus.*	*Escherichia coli.*	*Proteus vulgaris.*	*Pseudomonas aeruginosa.*	*Staphylococcus adreus.*	*Clostridium welchii.*
4-Sulphanilamido-2-phenyl-6-methyl-3-pyridazone	1·0	0·1	20	3	50	50	100	20
Sulphathiazole	0·3	0·03	15	5	10	5	100	5

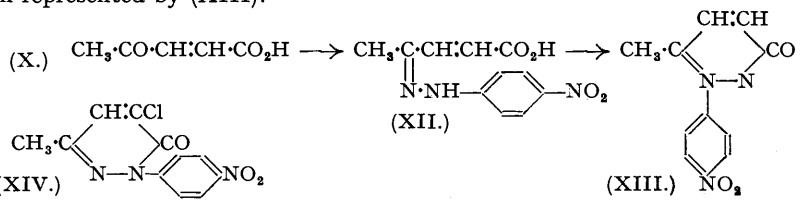
The figures represent mg. of compound per 100 c.c. of solution necessary to prevent growth of the organism.

4-Sulphanilamido-2-(p-nitrophenyl)-6-methyl-3-pyridazone was prepared from 2-(*p*-nitrophenyl)-6-methyl-3-pyridazinone by a series of reactions similar to those described above, *i.e.*,

by the condensation of lævulic acid with *p*-nitrophenylhydrazine, and also by an alternative procedure involving the nitration of 2-phenyl-6-methyl-3-pyridazinone according to the method of Fischer and Ach (*Annalen*, 1889, **253**, 59).

2-(*p*-Nitrophenyl)-6-methyl-3-pyridazinone, on treatment with an excess of phosphorus pentachloride at 160°, yielded 2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone* (XIII) and 4-*chloro*-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone* (XIV) although the yield of the former was only about 4% of the theoretical. The reaction is completely analogous to that which takes place when 2-phenyl-6-methyl-3-pyridazinone is treated with an excess of phosphorus pentachloride.

The constitutions of the products (XIII) and (XIV) were proved as follows. β-Acetylacrylic acid (X) was converted into its *p*-nitrophenylhydrazone (XII). This when cyclised by heating gave a product identical with the halogen-free substance obtained from the reaction of phosphorus pentachloride with 2-(*p*-nitrophenyl)-6-methyl-3-pyridazinone; this must therefore have the constitution represented by (XIII).



Moreover, 2-phenyl-6-methyl-3-pyridazone (VII), the structure of which has been similarly proved by an analogous reaction, on nitration also yielded (XIII). Similarly 4-chloro-2-phenyl-6-methyl-3-pyridazone (VI), the structure of which had been proved by Ach (*Annalen*, 1889, **253**, 47) yielded on nitration a product identical with (XIV). Since in (XIII) and (XIV), the *p*-nitrophenyl grouping is pre-fixed, these results indicate that the rest of the molecule of (XIII) must have a structure similar to (VII), and that of (XIV) a structure similar to (VI).

4-Chloro-2-(*p*-nitrophenyl)-6-methyl-3-pyridazone, on treatment at 120—130° with methyl alcohol saturated at 0° with ammonia gas, was converted into 4-*amino*-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*, which, in contrast to 4-amino-2-phenyl-6-methyl-3-pyridazone, did not form a salt. It was readily acetylated with acetic anhydride to form 4-*acetamido*-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*.

When the amino-derivative was condensed with *p*-acetamidobenzenesulphonyl chloride in dry pyridine solution, it yielded 4-(p-*acetamidobenzenesulphonamido*)-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*. This product was deacetylated by treatment with 10% aqueous sodium hydroxide solution to yield the free *sulphonamide*, reacetylated with dilute acetic acid and acetic anhydride. Both the acetyl derivative and the free sulphonamide had a very small solubility in water, that of the free sulphonamide being 0·8 mg. per 100 c.c. of solution at 15°. The sulphonamide was tested bacteriostatically against *Staphylococcus aureus*. It appeared to show some inhibitory effect on the growth of this organism, but it seemed that its solubility was too small to allow the attainment of a sufficiently concentrated solution for use in chemotherapy.

Experimental.

Lævulic Acid Phenylhydrazone.—The acid (10·91 g.) was dissolved in water (10 c.c.), phenylhydrazine (10 c.c.; 10·2 g.), dissolved in glacial acetic acid (10 c.c.), was added, and the mixture warmed for a few minutes. On cooling, a solid separated which was filtered off, washed with a little water, and recrystallised from ethyl alcohol, forming white cubes, m. p. 109—110° (Fischer, *Annalen*, 1886, **236**, 146, gives m. p. 108°); yield, 15·54 g.(80·9%).

2-*Phenyl*-6-*methyl*-3-*pyridazinone.*—Lævulic acid phenylhydrazone (6·37 g.) was heated at 160—165° for 3 hours. Thereafter the product was recrystallised from ethyl alcohol–water, forming colourless plates, m. p. 107° (Fischer, *ibid.*, p. 147, gives m. p. 106°); yield, 3·25 g. (56·5%) (Found: C, 70·4; H, 5·9; N, 15·2. Calc. for $C_{11}H_{12}ON_2$: C, 70·2; H, 6·3; N, 14·9%). It had a solubility in water at 15° of 0·53 g. per 100 c.c. of solution.

Treatment of 2-*Phenyl*-6-*methyl*-3-*pyridazinone with Phosphorus Pentachloride.*—The pyridazinone (15 g.) and phosphorus pentachloride (75 g.) were intimately mixed and then heated at 160°. A vigorous evolution of hydrogen chloride ensued. The mixture was allowed to cool, ice-water added to decompose excess of phosphorus pentachloride, and the product repeatedly extracted with boiling water. The extract was filtered and set aside for 24 hours. Crystals of 4-chloro-2-phenyl-6-methyl-3-pyridazone which separated were collected; they recrystallised from ethyl alcohol in long, shining white needles, m. p. 135—136° (Ach, *Annalen*, 1889, **253**, 47, gives m. p. 136°); yield, 9·9 g. (55·9%) (Found: C, 60·0; H, 4·5; Cl, 15·4. Calc. for $C_{11}H_9ON_2Cl$: C, 59·9; H, 4·1; Cl, 16·1%).

After removal of this pyridazone, the filtrate was concentrated, and excess of aqueous sodium hydroxide added. The mixture was extracted with ether, and the extract dried ($MgSO_4$). After removal of the solvent, a yellow oil remained which crystallised. It recrystallised from ligroin in white cubes, m. p.

79—80°, and was 2-phenyl-6-methyl-3-pyridazone (Ach, *loc. cit.*, gives m. p. 81°); yield, 0·5 g. (3·3%) (Found: C, 60·6; H, 5·4; N, 14·6. Calc. for $C_{11}H_{10}ON_2$: C, 60·9; H, 5·3; N, 15·0%).

Treatment of 2-Phenyl-6-methyl-3-pyridazone with Phosphorus Pentachloride.—The pyridazone (0·55 g.) and phosphorus pentachloride (2·5 g.) were mixed intimately and then heated at 160°. A fairly vigorous evolution of hydrogen chloride occurred. After being cooled, ice-water was added to destroy excess of phosphorus pentachloride, and the product extracted repeatedly with boiling water. The solid which separated on cooling the extract, was filtered off; it recrystallised from ethyl alcohol in colourless needles, m. p. alone or in admixture with 4-chloro-2-phenyl-6-methyl-3-pyridazone 135—136°; yield, 0·40 g. (61·6%).

4-Amino-2-phenyl-6-methyl-3-pyridazone.—4-Chloro-2-phenyl-6-methyl-3-pyridazone (5·01 g.) was heated in an autoclave at 125—130° for 24 hours with methyl alcohol (300 c.c.) saturated at 0° with ammonia. After cooling, the mixture was filtered and evaporated to dryness. The solid residue was hydrolysed by heating with baryta (1·5 equivs.; 8·16 g. of barium hydroxide in 75 c.c. of water) for 2 hours at 80° (this and subsequent operations were carried out in an atmosphere of nitrogen), and the solution thereafter evaporated to dryness. The dry residue was extracted with chloroform, the extract dried ($MgSO_4$), and the solvent removed by distillation. The syrup remaining was crystallised by trituration with ethyl alcohol, and recrystallised from acetone–water in colourless needles, m. p. 169°; yield, 3·96 g. (88%) (Found: C, 65·5; H, 5·2. $C_{11}H_{11}ON_3$ requires C, 65·6; H, 5·5%). This *pyridazone* (0·1 g.) was dissolved in absolute ethyl alcohol (5 c.c.), and dry hydrogen chloride bubbled through the solution. The white *hydrochloride* which separated was collected, and recrystallised from ethyl alcohol–ether in colourless cubes, m. p. 176° (decomp.) (Found: C, 55·5; H, 5·4; Cl, 14·9. $C_{11}H_{12}ON_3Cl$ requires C, 55·5; H, 5·1; Cl, 15·3%).

4-Acetamido-2-phenyl-6-methyl-3-pyridazone.—4-Amino-2-phenyl-6-methyl-3-pyridazone (1·00 g.) was boiled under reflux for ½ hour with freshly fused and powdered sodium acetate (0·43 g.) and acetic anhydride (16 c.c.). After cooling, the mixture was poured into water and the solid (A) which separated was filtered off. The filtrate was neutralised with sodium hydrogen carbonate and extracted with chloroform. The extract was dried ($MgSO_4$), and the solvent removed by distillation. The solid remaining was combined with solid (A) and recrystallised from ethyl alcohol–chloroform in shining white plates, m. p. 265°; yield, 1·22 g. (quantitative) (Found: C, 64·4; H, 5·6; N, 16·9. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·4; N, 17·2%).

4-(N-Acetylsulphanilamido)-2-phenyl-6-methyl-3-pyridazone.—4-Amino-2-phenyl-6-methyl-3-pyridazone (1·8 g.) was dissolved in dry pyridine (20 c.c.), and *N*-acetylsulphanilyl chloride (1·1 mol.; 2·32 g.), also dissolved in dry pyridine (20 c.c.), was added. The mixture was stirred and kept at 45° for ½ hour. A solution of sodium hydroxide (0·35 g., 1 mol.) in water (120 c.c.) was added, and the pyridine removed by distillation under diminished pressure. The solid which separated was collected, and recrystallised from acetic acid–water in colourless cubes, m. p. 254°; yield, 1·64 g. (46%) (Found: C, 57·3; H, 4·8; N, 13·8. $C_{19}H_{18}O_4N_4S$ requires C, 57·3; H, 4·5; N, 14·1%).

4-Sulphanilamido-2-phenyl-6-methyl-3-pyridazone.—(a) 4-(*N*-Acetylsulphanilamido)-2-phenyl-6-methyl-3-pyridazone (0·169 g.) was heated under reflux for 45 minutes with 10% aqueous sodium hydroxide solution (10 c.c.). After cooling, the mixture was neutralised with dilute hydrochloric acid, and a white solid separated. This was collected, and recrystallised from ethyl alcohol–water in shining white plates, m. p. 178°; yield, theoretical [Found: C, 57·6; H, 4·6; N, 15·9; $-NH_2$ (by nitrite titration), 4·3. $C_{17}H_{16}O_3N_4S$ requires C, 57·3; H, 4·5; N, 15·7; $-NH_2$, 4·4%].

(b) The material (0·1427 g.) was boiled under reflux for one hour with 2N-hydrochloric acid (10 c.c.). On cooling, the mixture was neutralised with aqueous sodium hydroxide solution; the flocculent white solid which separated was collected. After recrystallisation from acetic acid–water it had m. p. 178° alone or in admixture with 4-sulphanilamido-2-phenyl-6-methyl-3-pyridazone; yield, 0·102 g. (78%).

Reacetylation.—This sulphanilamido-pyridazone (0·03 g.) was mixed with dilute acetic acid (2 c.c.) and acetic anhydride (2 c.c.). The mixture was kept overnight and then poured into water. The solid which separated was collected, and recrystallised from acetic acid–water in white cubes, m. p. 253—254° alone or in admixture with the above acetyl compound; yield, 0·017 g. (53%).

4-(p-Nitrobenzenesulphonamido)-2-phenyl-6-methyl-3-pyridazone.—4-Amino-2-phenyl-6-methyl-3-pyridazone (0·57 g.) was dissolved in dry pyridine (10 c.c.), *p*-nitrobenzenesulphonyl chloride (1·1 mols.; 0·682 g.), also dissolved in dry pyridine, was added, and the mixture kept at room temperature overnight. When this was poured into water containing sodium hydroxide (0·113 g.) a solid separated which was filtered off. Concentration of the filtrate yielded a further quantity of crystals. The combined products recrystallised from ethyl alcohol–water in colourless needles, m. p. 87°; yield, 0·25 g. (25%) (Found: C, 52·2; H, 3·2. $C_{17}H_{14}O_5N_4S$ requires C, 52·8; H, 3·6%).

Reduction.—This *compound* (0·25 g.) was dissolved in dry methyl alcohol (100 c.c.) and hydrogenated at room temperature over Raney nickel. The solution was filtered and evaporated to dryness. The residue was dissolved in hot ethyl alcohol–water and filtered (charcoal). On cooling, crystals were deposited, which were collected and recrystallised from ethyl alcohol-water in white plates, m. p. alone or in admixture with 4-sulphanilamido-2-phenyl-6-methyl-3-pyridazone 178°; yield, 0·07 g. (30·5%).

Lævulic Acid p-*Nitrophenylhydrazone.*—The acid (2·3 g.), dissolved in water (10 c.c.), was mixed with *p*-nitrophenylhydrazine (3·02 g.) dissolved in glacial acetic acid (3·02 c.c.), and the solution warmed. On cooling, a solid separated which recrystallised from ethyl alcohol–water in orange needles, m. p. 207—208° (Fischer and Ach, *Annalen*, 1889, **253**, 61, state that this hydrazone sinters and decomposes at about 190°); yield, 4·38 g. (89·4%) (Found: C, 53·0; H, 5·2. Calc. for $C_{11}H_{13}O_4N_3$: C, 52·6; H, 5·2%).

2-(p-Nitrophenyl)-6-methyl 3-pyridazinone.—The foregoing *p*-nitrophenylhydrazone (21 g.) was heated under diminished pressure on an oil-bath at the m. p. for 0·75 hour. The product, which crystallised on trituration with ethyl alcohol, was recrystallised from ethyl alcohol-water, affording yellow needles, m. p. 118°; yield, 12·7 g. (65·9%) (Found: C, 56·2; H, 4·7; N, 18·2. $C_{11}H_{11}O_3N_3$ requires C, 56·6; H, 4·7; N, 18·0%). This *compound* had a solubility in water at 15° of 0·1 g. per 100 c.c. of solution.

Treatment with phosphorus pentachloride. This pyridazinone (5·0 g.) and phosphorus pentachloride

(25 g.) were mixed intimately and heated to 160°, hydrogen chloride being evolved. The mixture was allowed to cool, and crushed ice added to destroy excess of phosphorus pentachloride. The product was extracted repeatedly with boiling ethyl alcohol–water and, on cooling, a yellow solid (A) separated. This recrystallised from acetone in white needles, m. p. 217—218°, and was shown to be 4-*chloro*-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*; yield, 2·0 g. (36%) (Found: C, 49·2; H, 3·2; Cl, 13·2. $C_{11}H_8O_3N_3Cl$ requires C, 49·7; H, 3·0; N, 13·3%).

The mother-liquors after separation of the solid (A) were concentrated, excess of aqueous potassium hydroxide was added, and the mixture extracted with ether. The extract was dried ($MgSO_4$), and the solvent removed by distillation. The solid (B) remaining recrystallised from acetone–water in white plates, m. p. 184—185. This compound was shown to be 2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*; yield, 0·18 g. (3·7%) (Found: C, 56·6; H, 4·1; N, 18·1. $C_{11}H_9O_3N_3$ requires C, 57·1; H, 3·9; N, 18·2%).

4-*Amino*-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*.—4-Chloro-2-(*p*-nitrophenyl)-6-methyl-3-pyridazone (0·62 g.) was heated in an autoclave at 120—130° for 24 hours with methyl-alcoholic ammonia (300 c.c.) (saturated at 0°). The resultant solution was filtered and evaporated to dryness. The residue was treated with baryta (1·5 equivs.; 0·3 g. of hydroxide in 50 c.c. of water) at 80° in an atmosphere of nitrogen, and the product, after being evaporated to dryness, was extracted with boiling chloroform. The extract, after being dried ($MgSO_4$), was evaporated to dryness, and the product recrystallised from ethyl alcohol in small yellow needles, m. p. 196°; yield, 0·25 g. (44·2%) (Found: C, 53·7; H, 4·4. $C_{11}H_{10}O_3N_4$ requires C, 53·7; H, 4·1%).

Acetyl derivative. The foregoing compound (0·1 g.), fused and powdered sodium acetate (0·04 g.), and acetic anhydride (5 c.c.) were boiled under reflux for ½ hour. After cooling, the mixture was poured into water, and the precipitate filtered off; it recrystallised from ethyl alcohol–water in colourless plates, m. p. 190—191°; yield, quantitative(Found: C, 53·8; H, 4·7. $C_{13}H_{12}O_4N_4$ requires C, 54·1; H, 4·2%).

4-(N-*Acetylsulphanilamido*)-2-(p-*nitrophenyl*)-6-*methyl*-3-*pyridazone*.—The above amine (1·27 g.) was dissolved in dry pyridine (25 c.c.), *N*-acetylsulphanilyl chloride (1·1 mols.; 1·35 g.), also dissolved in dry pyridine (10 c.c.), was added, and the mixture kept at 45° for ½ hour. A solution of sodium hydroxide (0·21 g.; 1 mol.) in water (100 c.c.) was added, and the pyridine distilled off under diminished pressure. The solid which separated was filtered off; it recrystallised from acetic acid–water in yellow needles, m. p. 238°; yield, 1·0 g.(45·4%) (Found: C, 51·4; H, 3·8. $C_{19}H_{17}O_6N_5S$ requires C, 51·5; H, 3·8%).

Hydrolysis. This *acetylsulphanilamido*-compound (0·30 g.) was boiled under reflux for 45 minutes with 10% aqueous sodium hydroxide solution (10 c.c.), and the mixture allowed to cool, and neutralised with dilute hydrochloric acid. The resulting *sulphanilamido*-compound was filtered off and recrystallised from ethyl alcohol–water in yellow plates, m. p. 190; yield, 0·12 g. (44·4%) [Found: C, 51·5; H, 3·3; $-NH_2$ (by nitrite titration), 3·8. $C_{17}H_{15}O_5N_5S$ requires C, 50·8; H, 3·7; $-NH_2$, 3·9%].

Reacetylation. The last compound (0·005 g.), dilute acetic acid (2 c.c.), and acetic anhydride (2 c.c.) were mixed, and the mixture kept overnight. When this was poured into water (100 c.c.), a solid separated, which recrystallised from acetic acid–water, m. p. 238° alone or in admixture with 4-(*N*-acetylsulphanilamido)-2-(*p*-nitrophenyl)-6-methyl-3-pyridazone; yield quantitative.

Nitration of 2-*Phenyl*-6-*methyl*-3-*pyridazinone*.—The pyridazinone (2·0 g.) and fuming nitric acid (14 c.c.) were mixed at 0° and kept for one hour. The mixture was poured into water, and the solid which separated was collected and recrystallised from ethyl alcohol in yellow needles, m. p. 117° alone or in admixture with 2-(*p*-nitrophenyl)-6-methyl-3-pyridazinone; yield, 1 g. (40%).

Nitration of 2-*Phenyl*-6-*methyl*-3-*pyridazone*.—The pyridazone (0·5 g.) was cooled to 0° in an ice-bath, fuming nitric acid (5 c.c.) added, and the mixture kept at 0° for an hour. On being poured into water, this yielded a solid which, after recrystallising from ethyl alcohol–water in colourless needles, had m. p. 184° alone or in admixture with 2-(*p*-nitrophenyl)-6-methyl-3-pyridazone; yield 0·56 g. (95%).

Nitration of 4-*Chloro*-2-*phenyl*-6-*methyl*-3-*pyridazone*.—This pyridazone (0·49 g.) was similarly nitrated; the resulting flocculent white solid recrystallised from ethyl alcohol–water in flocculent white needles, m. p. 218° alone or in admixture with 4-chloro-2-(*p*-nitrophenyl)-6-methyl-3-pyridazone; yield quantitative.

Nitration of 4-*Amino*-2-*phenyl*-6-*methyl*-3-*pyridazone*.—Similarly, from this pyridazone (0·61 g.) and fuming nitric acid (10 c.c.) was obtained a yellow solid which, recrystallised from absolute ethyl alcohol, had m. p. 196° alone or in admixture with 4-amino-2-(*p*-nitrophenyl)-6-methyl-3-pyridazone; yield, 0·43 g. (60·6%).

β-Acetylacrylic Acid Phenylhydrazone.—This hydrazone, prepared by the usual method and recrystallised from ethyl alcohol, formed yellow needles, m. p. 160° (Wolff, *Annalen*, 1891, **264**, 251, quotes m. p. 160°) (Found: C, 64·4; H, 5·9. Calc. for $C_{11}H_{12}O_2N_2$: C, 64·6; H, 5·9%).

Thermal decomposition. The hydrazone (1·0 g.) was heated at its m. p. for 2 hours. The residue was dissolved in ethyl alcohol, and the solution filtered (charcoal). After removal of solvent, the residue recrystallised from ligroin in white cubes, m. p. 79—80° alone or in admixture with 2-phenyl-6-methyl-3-pyridazone; yield, 0·5 g. (55%).

β-Acetylacrylic Acid p-*Nitrophenylhydrazone*.—This *hydrazone*, prepared by normal methods and recrystallised from ethyl alcohol–water, formed yellow needles, m. p. 220—221°; yield, 3·17 g. (39%) (Found: C, 52·8; H, 3·9; N, 16·8. $C_{11}H_{11}O_4N_3$ requires C, 53·0; H, 4·4; N, 16·9%).

Thermal decomposition. The *p*-nitrophenylhydrazone (2·13 g.) was heated in a vacuum at 180° for 4 hours. White crystals sublimed and were collected at the top of the flask; they recrystallised from ethyl alcohol–water in white needles, m. p. 183—184° alone or in admixture with 2-(*p*-nitrophenyl)-6-methyl-3-pyridazone; yield, 1·0 g. (50%).

Attempted Cyclisation of Ethyl β-Acetylacrylate Phenylhydrazone.—The phenylhydrazone (m. p. 117°; Bender, *Ber.*, 1888, **21**, 2493, gives m. p. 117°) (1·02 g.) was heated at 110° under diminished pressure for 3 hours. The product solidified on cooling, and was extracted with ligroin. The extract was evaporated to dryness, and the residue recrystallised from ligroin in white cubes, m. p. alone or in admixture with 2-phenyl-6-methyl-3-pyridazone, 79—80°; yield, 0·1 g. The residue remaining from the ligroin extraction was shown to be unchanged starting material (0·8 g.).

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