466. 2-*Amino*-1 : 3 : 4-*indotriazine. The Reaction between Isatin and Aminoguanidine.*

By Harold King and Jean Wright.

The aim of the investigation was the introduction of basic side-chains into 3-amino-1 : 2 : 4-indotriazine (I) (Rajagopalan, *Proc. Indian Acad. Sci.*, 1943, **18** *A*, 100) with a view to the production of potential antimalarials.

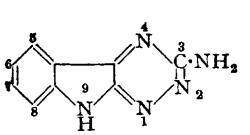
The product of Rajagopalan's reaction was not this indotriazine but *isatin* syn-β-*guanylhydrazone* (II) which could be cyclised in boiling aqueous solution to 2-*amino*-1 : 3 : 4-*indotriazine* (IV). An analogous compound was obtained from *N*-methylisatin. Attempts to attach side-chains to these substances were not successful.

Both parent *syn*-guanylhydrazones were converted in hot alkaline solution into *anti*-guanylhydrazones which could be cyclised to the above 2-aminoindotriazines by sublimation in a high vacuum at 250°. Hot acid treatment converted *isatin* anti-β-*guanylhydrazone* into the *syn*-form.

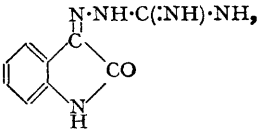
Diacetylisatin anti-β-*guanylhydrazone* on acid hydrolysis gave di-isatin azine (VI) whereas *acetyl*-N-*methylisatin* anti-β-*guanylhydrazone* gave *NN'*-dimethyl*iso*indigotin. These two symmetrical products with alcoholic phenylhydrazine yielded the phenylhydrazones of isatin and *N*-methylisatin respectively.

The *syn*- and *anti*-guanylhydrazones recorded in this communication appear to be the first examples of Hantzsch–Werner stereoisomerism in this type of compound.

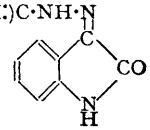
By the action of aminoguanidine on isatin in boiling glacial acetic acid solution Rajagopalan (*loc. cit.*) described the formation of a substance to which the constitution of a 3-aminoindotriazine (I) was attributed. As this seemed to be a readily accessible substance it occurred to us that it might be used as a basis for the synthesis of a series of potential antimalarials by the introduction of appropriate basic side-chains.



(I.)



(II.)



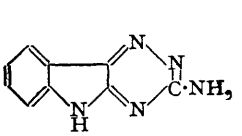
(III.)

On repetition, however, of Rajagopalan's preparation, a base was obtained to which the constitution of *isatin* syn-β-*guanylhydrazone* (II) is assigned. This base formed a characteristic *hydrochloride* and *nitrate* and when the hydrochloride was digested at 80° with excess of 0·5N-aqueous sodium hydroxide it was converted into an isomeric base to which the constitution *isatin* anti-β-*guanylhydrazone* (III) is attributed. Unlike the *syn*-base this base was a markedly crystalline substance and it formed a characteristic *hydrochloride* and *nitrate* different from the corresponding salts of the *syn*-base. When the hydrochloride of the *anti*-base was boiled in 16% aqueous hydrochloric acid solution the hydrochloride of the *syn*-base separated out. The base Rajagopalan had in hand was undoubtedly the crude *syn*-base and not the tricyclic structure claimed. The 3-aminoindotriazine formula, involving an attack by the ketone reagent on the α-position, which Rajagopalan assigned to his base is contrary to experience and it further involved the loss of a molecule of water, such as is not found to occur. The same doubt applies to the series of substituted 3-aminoindotriazines which De and Dutta (*Ber.*, 1931, **64**, 2605) claimed to have obtained by the action of aminoguanidine on substituted isatins in boiling glacial acetic acid solution.

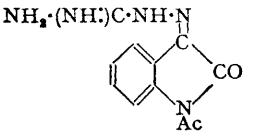
When, however, isatin *syn*-β-guanylhydrazone hydrochloride was boiled in dilute aqueous solution with excess of ammonia for several hours, it was converted with loss of water into a base $C_9H_7N_5$ to which the constitution 2-*amino*-1 : 3 : 4-*indotriazine* (IV) is assigned. Unlike the guanylhydrazones which are all yellow this base is almost colourless and the salts with mineral acids are pale yellow. Under similar conditions isatin *anti*-β-guanylhydrazone does not give this cyclic base but if it is heated to 250° in a high vacuum in a sublimation apparatus it slowly yields the aminoindotriazine as a crystalline sublimate. Attempts to condense this triazine with vinyl cyanide, with ethylene chloro- or bromo-hydrin or with dicyandiamide under a variety of conditions were unsuccessful.

When isatin *anti*-β-guanylhydrazone was boiled with acetic anhydride and pyridine it yielded *mono*- and *di-acetylisatin* anti-β-*guanylhydrazones*. The monoacetyl derivative is given the structure (V) since it is soluble in acid solution. When the diacetyl derivative was refluxed with 16% hydrochloric acid a very sparingly soluble maroon-coloured crystalline precipitate separated

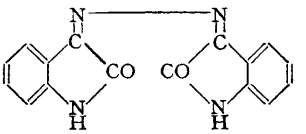
which has been identified as di-isatin azine (VI). The acetyl groups play some specific function in the process since, as already mentioned, the parent isatin *anti*-β-guanylhydrazone on boiling with 16% hydrochloric acid gave the *syn*-hydrochloride exclusively.



(IV.)



(V.)

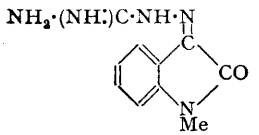


(VI.)

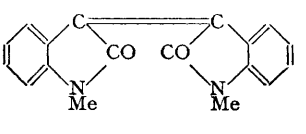
In this connection it is of interest that Marchlewski (*Ber.*, 1896, **29**, 1032) heated isatin β-semicarbazone with concentrated hydrochloric acid to 130° and obtained a substance difficultly soluble in all organic solvents which Borsche and Meyer (*Ber.*, 1921, **54**, 2849) suggested was di-isatin azine.

N-Methylisatin formed a precisely similar series of *syn*- and *anti*-β-guanylhydrazones and salts. Moreover when N-*methylisatin* anti-β-*guanylhydrazone* was acetylated it gave a *monoacetyl* derivative (VII) which on boiling with 16% hydrochloric acid gave not *N*-methylisatin azine but *NN'*-dimethyl*iso*indigotin (VIII) possibly through an intermediate azine.

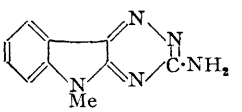
Di-isatin azine and *NN'*-dimethyl*iso*indigotin when digested with boiling alcoholic phenylhydrazine furnished isatin β-phenylhydrazone and *N*-methylisatin β-phenylhydrazone respectively.



(VII.)



(VIII.)



(IX.)

N-*Methylisatin* syn-β-*guanylhydrazone* could be cyclised in the usual way by boiling in dilute ammoniacal solution to form 2-*amino*-9-*methyl*-1 : 3 : 4-*indotriazine* (IX) identical with the product of methylation of 2-amino-1 : 3 : 4-indotriazine with methyl sulphate and sodium methoxide in methyl alcoholic solution. The same substance was also formed by heating *N*-methylisatin *anti*-β-guanylhydrazone to 250° in a high vacuum.

The finding of Hantzsch–Werner stereoisomerism of oxime type among guanylhydrazones does not appear to have been recorded previously. There are, however, many instances of such isomerism among the phenylhydrazones and semicarbazones but in very few instances has it been found possible to assign *syn*- and *anti*-structures to the two forms isolated. In the present instance the formation of a cyclic derivative from one of the guanylhydrazones in boiling aqueous solution appears to fix the constitution of the *syn*-form, the *anti*-form only furnishing the same cyclic aminoindotriazine under much more drastic conditions, namely heat and sublimation in a vacuum at 250°.

Experimental.

Isatin syn-β-*Guanylhydrazone* (II).—Isatin (14·7 g.) and aminoguanidine hydrogen carbonate (13·7 g.) in acetic acid (500 c.c.) were boiled for 30 minutes and the solution then poured into water (1200 c.c.). The solution was then concentrated under reduced pressure to a small volume (200 c.c.) and the hydrazone (17·8 g.) collected. The mother-liquors were diluted with water and again concentrated and gave a further crop (1·5 g.). The hydrazone so prepared has m. p. 205° (efferv.); it resolidifies and is then unmelted at 300°.

If the conditions given by Rajagopalan (*loc. cit.*) are followed, the only difference from the above being that after dilution with water the solution is basified with excess of aqueous ammonia, then the same product is obtained.

As this β-guanylhydrazone is very difficult to purify as the base, it is better to convert it into the hydrochloride.

Isatin syn-β-*guanylhydrazone hydrochloride*. The combined crops of guanylhydrazone (19·3 g.) were dissolved in the calculated amount of hot N-hydrochloric acid and on cooling the solution gave the *hydrochloride* (16·6 g.), m. p. 278° (efferv.). For analysis a portion was crystallised from 10 volumes of N-hydrochloric acid and separated in needles, m. p. 280° (efferv.) (Found: C, 42·0, 42·3; H, 4·7, 4·9; Cl, 13·8; H_2O, 7·2. $C_9H_9ON_5,HCl,H_2O$ requires C, 41·9; H, 4·7; Cl, 13·8; H_2O, 7·0%).

The *nitrate* was prepared from an aqueous solution of the hydrochloride by addition of ammonium nitrate solution. It separated in thin prisms or needles which when crystallised from 10 volumes of water had m. p. 228° (vigorous decomp.) (Found: loss at 100°, 6·4. $C_9H_9ON_5,HNO_3,H_2O$ requires H_2O, 6·3%. Found on dried solid: C, 40·7; H, 3·9; N, 31·0. $C_9H_9ON_5,HNO_3$ requires C, 40·6; H, 3·8; N, 31·6%).

The *base* separated as fine yellow needles when a dilute solution (1%) of the hydrochloride was treated with excess 2N-ammonia solution. From more dilute solution it sometimes separated in plates. It is sparingly soluble in water or in dry acetone but readily soluble in moist acetone. It can be crystallised with difficulty from moist acetone and is unmelted at 310° but it may show some sintering about 200° or more frequently near 235° (Found on air-dried solid: loss at 100°, 4·1. $C_9H_9ON_5,0{\cdot}5H_2O$ requires H_2O, 4·2%. Found on dried solid: C, 53·1; H, 4·8; N, 33·8. $C_9H_9ON_5$ requires C, 53·2; H, 4·4; N, 34·5%).

Isatin anti-*β-Guanylhydrazone* (III).—Isatin *syn*-*β*-guanylhydrazone hydrochloride (25·8 g.) was treated with 0·5N-sodium hydroxide solution (400 c.c.) and heated on the water-bath at about 80° for 2 hours. The *base* first precipitated changed to a well crystallised orange solid, yield 21·0 g., m. p. 246° (efferv.). If dried at 110° it melts at 260° (efferv.). When crystallised from 30 volumes of spirit it separated in tablets, m. p. 246—248° with vigorous effervescence followed by crystallisation in prisms which are unmelted at 300° (Found: C, 48·9; H, 4·8; N, 31·9; H_2O, 8·3. $C_9H_9ON_5,H_2O$ requires C, 48·8; H, 5·0; N, 31·7; H_2O, 8·2%).

The *hydrochloride* crystallises in soft orange-yellow woolly needles which collapse with partial liquefaction at about 200° and then effervesce about 270° (Found: C, 41·5; H, 5·0; H_2O, 6·9. $C_9H_9ON_5,HCl,H_2O$ requires C, 41·9; H, 4·7; H_2O, 7·0%). The *nitrate* crystallises from water as a felt of pale yellow or pale orange needles: both forms may separate simultaneously in different parts of the solution. It is soluble in 5 parts of hot water and has m. p. 162° (efferv.) (Found: C, 38·1; H, 4·3; N, 29·9; H_2O, 6·1. $C_9H_9ON_5,HNO_3,H_2O$ requires C, 38·0; H, 4·3; N, 29·6; H_2O, 6·3%).

Acetylation of Isatin anti-*β-Guanylhydrazone*.—The parent base (1·0 g.) was boiled with acetic anhydride (10 c.c.) and two drops of pyridine for 5 minutes and gave a crystalline solid (1·39 g.), m. p. 207—212°. This was dissolved in methyl ethyl ketone (60 c.c.) and the product crystallised twice more from the same solvent; yield 0·58 g., m. p. 220—221°. *Diacetylisatin* anti-*β-guanylhydrazone* crystallises in clusters of prisms and is soluble in 120 parts of boiling methyl ethyl ketone and in 8 parts of boiling acetic anhydride. It is not soluble in 16% aqueous hydrochloric acid (Found: C, 54·8; H, 4·6. $C_{13}H_{13}O_3N_5$ requires C, 54·3; H, 4·6%). Satisfactory nitrogen analyses by micro-Dumas could not be obtained.

The first methyl ethyl ketone crystallisation mother-liquor on concentration gave a solid, m. p. 229°, which on two further crystallisations from fresh methyl ethyl ketone gave *monoacetylisatin* anti-*β-guanylhydrazone* (V), 0·12 g., m. p. 236—237°, in rectangular elongated leaflets (Found: C, 53·6; H, 4·9. $C_{11}H_{11}O_2N_5$ requires C, 53·8; H, 4·5%). It is soluble in 16% aqueous hydrochloric acid to an orange-red solution.

Better yields of the diacetyl derivative can be obtained by boiling for 15 minutes instead of 5 and recrystallisation of the product from acetic anhydride with 10 minutes' boiling at each recrystallisation. The final product from acetic anhydride always gives a redder melt than the product from methyl ethyl ketone. More prolonged boiling leads to darker solutions and decreasing yields.

Action of 16% *Hydrochloric Acid on the Diacetyl Derivative*.—The diacetyl compound (5·0 g.) was boiled with 16% hydrochloric acid (100 c.c.) for 2 hours. The deep red solid which had separated was collected by filtering the hot solution, yield 1·64 g. It was recrystallised from pyridine or from glacial acetic acid (50 c.c.) and gave maroon-coloured needles (1·12 g.), m. p. 300° (decomp.) (Found: C, 66·3, 66·2; H, 3·5, 4·0; N, 18·5, 18·7. Calc. for $C_{16}H_{10}O_2N_4$: C, 66·2; H, 3·4; N, 19·3%). It was soluble in concentrated sulphuric acid to a green-brown solution and in 2N-sodium hydroxide giving a red solution. These properties agree with those of di-isatin azine (VI), and a specimen of di-isatin azine prepared from isatin and hydrazine sulphate by Schapiro's method (*Ber.*, 1929, **62**, 2133) had identical properties.

When the di-isatin azine from the diacetyl product was boiled with phenylhydrazine in alcohol for 2 hours it gave isatin *β*-phenylhydrazone identified by mixed m. p. with authentic isatin *β*-phenylhydrazone and by analysis (Found: C, 71·0; H, 4·5. Calc. for $C_{14}H_{11}ON_3$: C, 70·9; H, 4·6%).

When di-isatin azine was boiled with 20 parts of acetic anhydride and 5 drops of pyridine for 45 minutes needles of the NN′-*diacetyl* derivative separated (Found: C, 64·5; H, 3·9; N, 15·5. $C_{20}H_{14}O_4N_4$ requires C, 64·2; H, 3·7; N, 15·0%).

Action of 16% *Hydrochloride Acid on Isatin* anti-*β-Guanylhydrazone*.—The base (1·0 g.) was boiled with 16% hydrochloric acid for several hours during which period a crystalline solid began to separate and increased in quantity on cooling; yield 1·3 g., m. p. 280° (efferv.). A portion was recrystallised from dilute hydrochloric acid and separated in well-formed yellow prisms, m. p. 276° (decomp.). A mixture with isatin *syn*-*β*-guanylhydrazone hydrochloride also decomposed at the same temperature. It was dissolved in 20 parts of water and treated with concentrated ammonium nitrate solution. The nitrate separated in needles, m. p. 229°, with vigorous decomposition. The properties were precisely those of the *syn*-nitrate.

Isatin syn-*β-Guanylhydrazone-5-sulphonic Acid*.—Isatin *syn*-*β*-guanylhydrazone base was treated with dilute sulphuric acid and the yellow needles of the sulphate, unmelted at 300°, were collected and dried and then heated on a water-bath with sulphuric acid for 8 hours. On pouring into water the *sulphonic acid* separated and was purified by solution in dilute ammonia and precipitation with acetic acid. It separated in yellow needles, unmelted at 340° (Found in solid dried at 110°: C, 35·9; H, 3·8; N, 23·2. $C_9H_9O_4N_5S,H_2O$ requires C, 35·9; H, 3·7; N, 23·3%).

When isatin *anti*-*β*-guanylhydrazone (2 g.) was added to sulphuric acid (5 c.c.) and heated on the water-bath the deep yellow original solution became red and after 8 hours' heating the reaction mixture was worked up in the same way as in the preceding preparation. Yellow needles were obtained, unmelted at 340° (Found on solid dried at 110°: C, 36·1; H, 3·5; N, 23·4. Calc. for $C_9H_9O_4N_5S,H_2O$: C, 35·9; H, 3·7; N, 23·3%). Comparison of the properties of this sulphonic acid and of its sodium, ammonium, and calcium salts with those of the preceding acid showed that the two acids were identical.

N-*Methylisatin* syn-*β-Guanylhydrazone*.—*N*-Methylisatin (16·1 g.) and aminoguanidine hydrogen carbonate (13·7 g.) were boiled in glacial acetic acid (500 c.c.) for 30 minutes. The solution was poured into water, concentrated at 50° to a small volume, and excess of 2N-ammonia solution added. The yellow crystalline precipitate (22·0 g.) was collected, m. p. 210°. It was converted into a very sparingly

soluble *hydrochloride* in quantitative yield. A sample crystallised from a large volume of boiling water had m. p. 312° (Found: C, 47·0; H, 4·4; N, 27·5. $C_{10}H_{11}ON_5$,HCl requires C, 47·2; H, 4·7; N, 27·6%). The *base* obtained by the action of aqueous ammonia on the hydrochloride crystallised from methyl ethyl ketone in small yellow needles, m. p. 232° (decomp.) (Found: C, 55·3; H, 5·1; N, 32·1. $C_{10}H_{11}ON_5$ requires C, 55·3; H, 5·1; N, 32·2%).

N-*Methylisatin* anti-β-*Guanylhydrazone*.—The above hydrochloride (2·71 g.) was treated with 0·5N-sodium hydroxide solution (50 c.c.) on the boiling water-bath for 8 hours. The anti-*base* (2·36 g.) separated in tablets which crystallised from spirit (185 c.c.) with the addition of a drop of water in large elongated leaflets, m. p. 274° (efferv.) but becoming opaque at 235° (Found on 2 different preparations: C, 53·3, 53·8; H, 5·2, 5·3; N, 30·4, 31·1. $C_{10}H_{11}ON_5,0{\cdot}5H_2O$ requires C, 53·1; H, 5·3; N, 31·0%).

The *hydrochloride* crystallised in fine yellow needles, m. p. 312° (decomp.) (Found on solid dried at 100°: C, 47·2; H, 4·5; N, 28·0. $C_{10}H_{11}ON_5$,HCl requires C, 47·3; H, 4·7; N, 27·6%).

Acetyl-N-*methylisatin* anti-β-*Guanylhydrazone* (VII).—The base (0·5 g.) was boiled with acetic anhydride (5 c.c.) and pyridine (2 drops) for 5 minutes. The product [0·55 g., m. p. 238° (decomp.)] was dissolved in boiling methyl ethyl ketone (125 c.c.) and separated in long needles of the *acetyl* derivative which slowly changed to small plates, yield 0·5 g., m. p. 237° (decomp.) (Found: C, 54·0; H, 5·4. $C_{12}H_{13}O_2N_5,0{\cdot}5H_2O$ requires C, 53·7; H, 5·3%). The water of crystallisation was not lost at 140° and micro-Dumas estimates of nitrogen gave very low values. On hydrolysis on the water-bath with 0·5N-aqueous sodium hydroxide the parent base was obtained in elongated leaflets, m. p. 270° not depressed by the pure *anti*-base. If crystallised from acetic acid it retained one molecule of acetic acid after drying at 85° (Found: C, 52·6; H, 5·3; N, 22·1. $C_{12}H_{13}O_2N_5,C_2H_4O_2$ requires C, 52·7; H, 5·3; N, 22·0%).

Action of 16% *hydrochloric acid*. The acetyl compound (6·4 g.) was boiled for 30 hours with 16% hydrochloric acid (100 c.c.). The red solid was collected; yield 2·4 g. It crystallised from pyridine or from acetone in deep red needles, m. p. 268° (Found: C, 74·1; H, 4·8; N, 9·6. Calc. for $C_{18}H_{14}O_2N_2$: C, 74·5; H, 4·8; N, 9·7%). It could also be purified by sublimation in a high vacuum and was identified as *NN'*-dimethyl*iso*indigotin (VIII) by comparison with an authentic specimen prepared either by Stollé's method (*J. pr. Chem.*, 1930, **128**, 35) or by condensation of *N*-methylisatin with *N*-methyloxindole. On boiling with phenylhydrazine in alcohol it gave *N*-methylisatin β-phenylhydrazone, m. p. 136°, as did authentic *N*-methyl*iso*indigotin and a mixture showed no depression of m. p.

Preparation of 2-*Amino*-1 : 3 : 4-*indotriazine* (IV).—Isatin *syn*-β-guanylhydrazone hydrochloride (25·3 g.) was dissolved in water (5 l.) and ammonia solution (*d* 0·88) added in slight excess. The solution was boiled for 6 hours, and the solid which had separated during the boiling was collected whilst the solution was still hot. It consisted of buff-coloured prisms, yield 12·7 g., unmelted at 300°. It was converted into the *hydrochloride*, pale yellow slender needles, m. p. 324° (efferv.) (Found in solid dried at 105°: C, 49·1; H, 3·6; N, 31·5. $C_9H_7N_5$,HCl requires C, 48·8; H, 3·6; N, 31·6%). The corresponding *nitrate* separated from dilute nitric acid in pale yellow prisms, m. p. 228° (Found in solid dried at 105°: C, 43·7; H, 3·5; N, 33·4. $C_9H_7N_5,HNO_3$ requires C, 43·5; H, 3·2; N, 33·9%). The *base* crystallised from pyridine in tiny colourless needles, m. p. 350—354° (decomp.) (Found: C, 58·3; H, 3·9; N, 38·1. $C_9H_7N_5$ requires C, 58·4; H, 3·8; N, 37·8%). It sublimes readily on heating in a high vacuum. It is sparingly soluble in water and all organic solvents but readily souble in hot aqueous sodium hydroxide solution and separates unchanged on cooling.

2-Amino-1 : 3 : 4-indotriazine is also formed from isatin *anti*-β-guanylhydrazone by heating to 250° in a high vacuum (0·3 mm.) and sublimes out slowly.

2-*Acetamido*-9-*acetyl*-1 : 3 : 4-*indotriazine*.—2-Amino-1 : 3 : 4-indotriazine (1·85 g.) was refluxed with acetic anhydride (50 c.c.) and 1 drop of pyridine for 30 minutes. The crystalline product (2·6 g.) which began to separate during the boiling was collected when the solution was cool and was crystallised from glacial acetic acid from which it separated in colourless prisms, m. p. 283°. 2-*Acetamido*-9-*acetyl*-1 : 3 : 4-*indotriazine* could be sublimed without residue in a high vacuum at 250° (Found: C, 57·8; H, 4·3; N, 26·2. $C_{13}H_{11}O_2N_5$ requires C, 58·0; H, 4·1; N, 26·0%).

2-*Amino*-1 : 3 : 4-*indotriazine*-6-*sulphonic Acid*.—The above triazine (IV) (5 g.) was dissolved in sulphuric acid and the solution heated on the water-bath for 8 hours. On pouring into water, the *sulphonic acid* (7·8 g.) separated in yellow needles, unmelted at 310° (Found: C, 38·6; H, 3·4; N, 24·9. $C_9H_7O_3N_5S,H_2O$ requires C, 38·2; H, 3·2; N, 24·7%). The *sodium* salt crystallised from water in colourless prisms, unmelted at 300° (Found: Na, 7·6. $C_9H_6O_3N_5SNa$ requires Na, 8·0%). The calcium and ammonium salts were also colourless. The free sulphonic acid is precipitated on the addition of acetic acid to the aqueous solution of the sodium salt.

The corresponding *sulphonamide* was prepared by warming the sulphonic acid in chlorosulphonic acid to 80° for 1½ hours, pouring on to ice, collecting the solid and grinding with concentrated ammonia solution. It was purified by precipitation from solutions of its hydrochloride in water by the addition of ammonia solution and was obtained as small colourless prisms, unmelted at 320° (Found: C, 40·9; H, 2·9. $C_9H_8O_3N_6S$ requires C, 40·9; H, 3·0%).

Preparation of 2-*Amino*-9-*methyl*-1 : 3 : 4-*indotriazine* (IX).—This preparation was carried out in the same way as that of its unmethylated homologue (above). The *hydrochloride* crystallised from dilute hydrochloric acid in pale yellow slender needles which retained water of crystallisation when dried at 105° (Found: C, 47·7; H, 4·7; N, 27·8. $C_{10}H_9N_5$,HCl,H_2O requires C, 47·3; H, 4·7; N, 27·6%). The *base* could be crystallised from pyridine but was best purified by sublimation in a high vacuum and thus obtained in colourless prisms, m. p. 314° (Found: C, 59·9; H, 4·5; N, 35·5. $C_{10}H_9N_5$ requires C, 60·3; H, 4·5; N, 35·2%). Unlike its lower homologue it is insoluble in dilute sodium hydroxide solution. The *nitrate* separated from dilute nitric acid in long, pale yellow needles, m. p. 210° (decomp.) (Found: N, 31·8; $C_{10}H_9N_5,HNO_3$ requires N, 32·1%).

2-Amino-9-methyl-1 : 3 : 4-indotriazine was also obtained by heating *N*-methylisatin *anti*-β-guanylhydrazone in a high vacuum in a sublimation apparatus to 250°. The product had to be resublimed several times and was finally extracted with boiling acetone which removed a soluble red solid, m. p. 268°, which proved to be *NN'*-dimethyl*iso*indigotin. The insoluble solid was resublimed and was then shown

by mixed m. p. determinations on the base and salts to be identical with 2-amino-9-methyl-1 : 3 : 4-indotriazine.

Methylation of 2-Amino-1 : 3 : 4-indotriazine.—This triazine (2 g.) was dissolved in excess of a solution of sodium methoxide in methyl alcohol (100 c.c.) and freshly distilled dimethyl sulphate (5 c.c.) was gradually added. The reaction was completed by heating on the water-bath for 2 hours during which period a green solid separated. It was crystallised from pyridine and found to be 2-amino-9-methyl-1 : 3 : 4-indotriazine (0·5 g.) identical with the previously described material. Unmethylated triazine (1·2 g.) was recovered from the methyl alcoholic mother liquor by acidification with acetic acid.

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