387. *The Constitution of Ciba Yellow 3G.*

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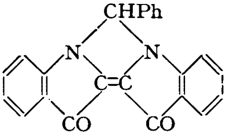
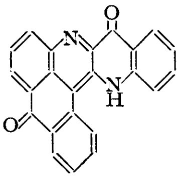
It is shown that, of the five structural formulæ proposed for Ciba Yellow 3G, only one, *viz.*, formula (V), is consistent with the formation of the new degradation products (XII) and (XV). The structure of (XII) has been proved by its further degradation reactions, and the structure of (XV) by synthesis.

CIBA YELLOW 3G is a vat dye first prepared by Engi (G.P. 249,145; *Z. angew. Chem.*, 1914, **27**, 144) by the action of benzoyl chloride, copper powder, and nitrobenzene on indigo. Its constitution has been investigated by numerous workers, and the following formulæ have been proposed: (I) (Engi, *loc. cit.*), (II) (Posner and Hofmeister, *Ber.*, 1926, **59**, 1827), (III) (Hope and Richter, *J.*, 1932, 2783), (IV) (de Diesbach, Bie, and Rubli, *Helv. Chim. Acta*, 1934, **17**, 113), and (V) (de Diesbach, Capponi, and Farquet, *ibid.*, 1949, **32**, 1214).



(I)



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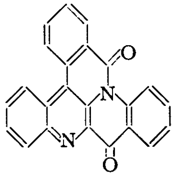
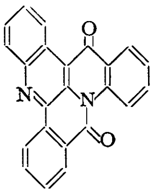


(III)

These formulæ were mostly based on a study of the degradative reactions, the most important of which may be summarised as follows. Ciba Yellow on vigorous oxidation with nitric acid yields phthalic acid. On fusion with sodium hydroxide it yields, *inter alia*, phthalic acid and indolo(3′ : 2′-3 : 4)quinoline. It dissolves in boiling sodium hydroxide solution with fission of a lactam group, to give the sodium salt of a monocarboxylic acid from which Ciba Yellow is regenerated by treatment with acid. This sodium salt is readily methylated to give a *N*-methyl-acid which cannot be cyclised but can be decarboxylated. The formula (VI) would also give a ready explanation of these reactions. Formulæ (I) and (II) are not those of lactams and so may be discounted. Substances (II) and (IV) were synthesised by de Diesbach and Miserez (*Helv. Chim. Acta*, 1948, **31**, 673) and by de Diesbach and Klement (*ibid.*, 1941, **24**, 158) respectively, and were different from Ciba Yellow. Formula (VI) is the only one which gives a ready explanation of the formation of indolo(3′ : 2′-3 : 4)quinoline on fusion with sodium hydroxide. This compound was first isolated from Ciba Yellow by de Diesbach, Bie, and Rubli (*loc. cit.*), who proved its constitution by a study of its further degradation reactions. It had however been synthesised already by Clemo and Perkin (*J.*, 1924, **125**, 1608). We repeated the work of these authors and proved the identity of the indoloquinoline from both sources (mixed melting point determination and *X*-ray powder photographs).



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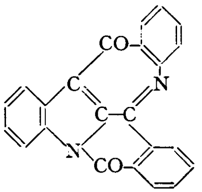
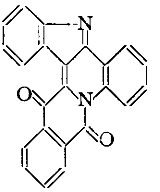
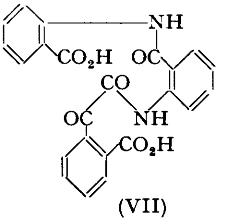


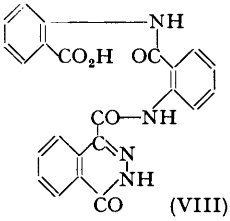
(V)



(VI)

Ciba Yellow in sodium hydroxide solution was readily oxidised by permanganate at 20°, yielding a compound, $C_{23}H_{16}O_7N_2$, which titrated as a dicarboxylic acid and on hydrolysis yielded phthalonic acid and two mols. of anthranilic acid. This result disproved formula (III) and appeared to be most consistent with formula (VI), leading to the formula (VII) for the permanganate degradation product. This degradation product was next treated under mild conditions with hydrazine: this should yield (VIII) if structure (VII) were correct. The product was, however, the compound (IX), condensation with hydrazine having been accompanied by loss of one mol. of anthranilic acid. The structure of (IX) was proved by synthesis: phthalonic anhydride and anthranilic acid yielded the anilide-dicarboxylic acid (X), which with hydrazine gave (IX). The formation of compound (IX) from the permanganate degradation product with loss of one mol. of anthranilic acid suggests that in the permanganate degradation product one mol. of anthranilic acid is attached to the keto-group of the phthalonic acid fragment. This cannot be explained on the basis of the Ciba Yellow formula (VI), but can readily be explained on the basis of formula (V). The permanganate degradation product would then be (XI), which is in accord with all its properties except that it is only a dicarboxylic acid. Thus one of the carboxyl groups is probably involved in a cyclic "*pseudo*anilide" structure, *e.g.*, (XII): compounds of this type are well known (see, *e.g.*, Cornillot, *Ann. Chim.*, 1927, **8**, 120).


(VII)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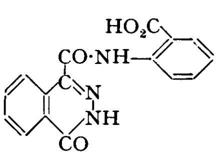
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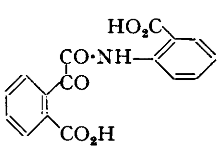
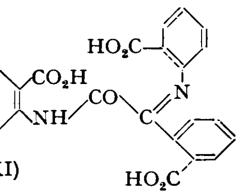

(X)

When the N-methyl-carboxylic acid from Ciba Yellow is decarboxylated (Hope and Richter, *loc. cit.*) and the product is heated with hydrazine a primary aromatic amine $C_{23}H_{18}N_4$ is obtained which on diazotisation and treatment with hypophosphorous acid yields a new base $C_{23}H_{17}N_3$. These results can be explained on the basis of the formula (V) for Ciba Yellow, leading to the formulæ (XIII), (XIV), and (XV) for the product of decarboxylation, the primary aromatic amine, and the base $C_{23}H_{17}N_3$ respectively. The structure (XV) was proved by synthesis. First it was shown that 1 : 2-dihydro-1-keto-2 : 4-diphenylphthalazine (XVI) on treatment with phenylmagnesium bromide gave 1 : 2 : 4-triphenylphthalazinium bromide (XVII) (compounds of this type are already known; see, *e.g.*, Thiele and Falk, *Annalen*, 1906, **347**, 114) which when heated with hydrazine yielded 1 : 4-diphenylphthalazine (XVIII). 3-Benzoyl-1-methylindole-2-carboxylic acid (XIX) was prepared both by the action of diphenylcadmium on 1-methylindole-2 : 3-dicarboxylic anhydride and by a Fischer indole synthesis from *N*-methyl-*N*-phenylhydrazine and ethyl benzoylpyruvate. Condensation of the keto-acid (XIX) with phenylhydrazine yielded 2 : 3-dihydro-3-keto-1′-methyl-2 : 6-diphenylindolo-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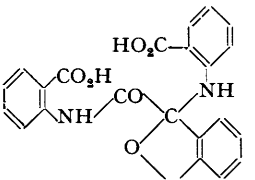
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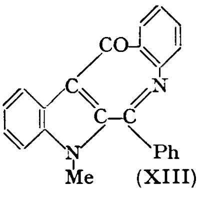
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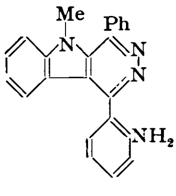
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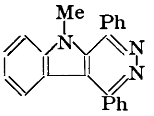
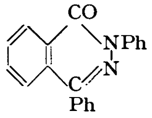
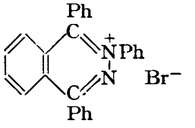

(XV)

(2′ : 3′-4 : 5)pyridazine (XX). This on treatment with phenylmagnesium bromide gave 1′-methyl-2 : 3 : 6-triphenylindolo(2′ : 3′-4 : 5)pyridazinium bromide (XXI) which when heated with hydrazine gave the required 1′-methyl-3 : 6-diphenylindolo(2′ : 3′-4 : 5)-pyridazine (XV), identical with that obtained from Ciba Yellow.


(XVI)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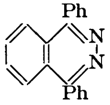
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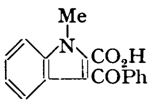
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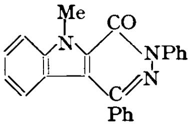
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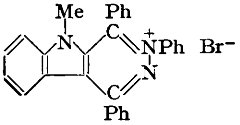
(XXI)

It is now clear that Ciba Yellow 3G is correctly represented by (V).

EXPERIMENTAL

Preparation of Ciba Yellow from Indigo.—Ciba Yellow used in this work was prepared as follows: Indigo powder (225 g.), copper bronze (22·5 g.), cuprous chloride (35·1 g.), benzoyl chloride (738 c.c.), and nitrobenzene (540 c.c.) were stirred at 160° ± 5° during 30 min. After cooling, the mixture was added to ethanol (540 c.c.) and kept overnight. The solid was filtered off, well washed with ethanol, and dried. The combined yield from three such experiments was boiled during 6 hr. with 4N-sodium hydroxide (4800 c.c.), more water being added as required to maintain the volume. The mixture was filtered hot through glass cloth, and the solid washed with hot dilute aqueous sodium hydroxide. The combined filtrate was acidified hot with 5N-hydrochloric acid (3780 c.c.). The solid was collected, washed with water, dried, and recrystallised from pyridine (3 l.) (yield, 88 g.; m. p. 277—279°). By re-boiling the solid which had not dissolved in the pyridine with the pyridine filtrate from the first crop, a second crop was obtained of 45 g. (m. p. 278—281°). A sample, recrystallised from xylene (35 parts), had m. p. 280—283° (Found: C, 79·7; H, 3·45; N, 8·25. Calc. for $C_{23}H_{12}O_2N_2$: C, 79·3; H, 3·5; N, 8·0%).

Clemo and Perkin's Indolo(3′ : 2′-3 : 4)*quinoline Synthesis.*—Clemo and Perkin obtained two products from the reaction of toluene-*p*-sulphonanilide with β-chloropropionic acid, one the desired *N*-phenyl-*N*-toluene-*p*-sulphonyl-β-alanine and the other an unidentified product. Formation of the by-product was prevented by mixing the solutions at 20° and stirring at this temperature during 1 hr. before refluxing during 5 hr. Otherwise the details given by Clemo and Perkin are adequate.

Hope and Richter's Degradation of Ciba Yellow.—The degradation to the *N*-methyl-carboxylic acid is adequately described by the original authors but the decarboxylation proceeds much better as follows. The *N*-methyl-acid (4·7 g.) was refluxed in quinoline (15 c.c.) with copper bronze (1 g.) for 5 min. After cooling, the mixture was diluted with ether, filtered, and shaken with 2N-hydrochloric acid (60 c.c.). The solid was filtered off, washed with ether and water, and dried (yield, 3·1 g.; m. p. 168—170°). A further 0·5 g. was obtained from the ethereal layer of the filtrate. 4 G., recrystallised from ethyl acetate (100 c.c.; charcoal), gave 2 g. of m. p. 174—175° (Hope and Richter give m. p. 168°) (Found: C, 81·8; H, 5·0; N, 8·5; NMe, 8·7. Calc. for $C_{23}H_{16}ON_2$: C, 82·1; H, 4·8; N, 8·3; 1NMe, 8·6%).

Degradation of Ciba Yellow with Permanganate.—Ciba Yellow (30 g.) and 4N-sodium hydroxide (260 c.c.) were stirred and refluxed during 16 hr., then cooled and filtered from undissolved dye (0·4 g.). Potassium permanganate (197 g.) in cold water (3940 c.c.) was added. The mixture was stirred during 1 hr. and kept overnight. Ethanol (394 c.c.) was added to decompose the excess of permanganate, and solid carbon dioxide was added to slight alkalinity. The manganese dioxide was filtered off and well washed with water. The combined filtrate was acidified with hydrochloric acid. The solid was filtered off, washed with water, dried in a vacuum-desiccator (yield, 9 g.), and repeatedly digested with small portions of cold ethanol (70 c.c. in all; to remove a dark impurity), giving 3-o-*carboxyanilinophthalide*-3-*carboxy*-(o-

carboxyanilide) (XII) (5 g.), m. p. 224—225° (decomp.). The further purification of this compound by recrystallisation is attended by serious loss. It was considered sufficiently pure for the further degradative work, but for analysis 0·5 g. was refluxed during 30 min. with absolute ethanol (15 c.c.). After filtration colourless prisms slowly separated. These were collected and on drying broke down to a fine powder (0·06 g.), m. p. 226° (decomp.) (Found: C, 63·45; H, 3·75; N, 6·65. $C_{23}H_{16}O_7N_2$ requires C, 63·9; H, 3·7; N, 6·5%).

Further degradation, etc. (*a*) The product (XII) (0·33 g.) was refluxed during 5 hr. with 2N-hydrochloric acid (10 c.c.), filtered, and evaporated to dryness. The residue was washed with ether, dissolved in water (5 c.c.), and treated with sodium acetate (hydrated; 0·3 g.) in water (1 c.c.). After cooling in ice, anthranilic acid (0·05 g.), m. p. and mixed m. p. 140—142°, was collected.

(*b*) The product (XII) (0·743 g.) was dissolved in hot ethanol (100 c.c.). The solution was cooled, water (50 c.c.) was added, and the solution was titrated with 0·2006N-sodium hydroxide (pH meter) [Found: equiv., 227. $C_{21}H_{14}O_3N_2(CO_2H)_2$ requires equiv., 216].

(*c*) The anilide (XII) (0·700 g.) was refluxed during 3 hr. with N-sodium hydroxide (25 c.c.), then cooled. 1·023N-Hydrochloric acid (25 c.c.) was added. The solution and a control were titrated with sodium hydroxide (pH meter) (Found: equiv., 116. Four CO_2H, from hydrolysis of $C_{23}H_{16}O_7N_2$, require equiv., 108).

The solution remaining after titration was made up to a volume of 250 c.c. A portion (50 c.c.) was treated with 10N-hydrochloric acid (1 c.c.) and titrated with 0·0996N-sodium nitrite (Found: equiv., 228·5. Two NH_2 from hydrolysis of $C_{23}H_{16}O_7N_2$ require equiv., 216). As confirmation that the amine titrated was anthranilic acid, the diazotised amine was coupled with β-naphthol, yielding 0·16 g. of the azo-compound, m. p. 269° (decomp.) [lit., 272° (decomp.)].

The remaining 200 c.c. were acidified with 10N-hydrochloric acid (20 c.c.) and continuously extracted with ether overnight. The ethereal solution was filtered and evaporated. The residue was dissolved in hot water (20 c.c.). A solution of phenylhydrazine (1·1 c.c.) in hydrochloric acid (19 c.c.; 0·63N) was added. The solution was heated for 20 min. on the steam-bath and cooled in ice. The precipitated 1 : 2-dihydro-1-keto-2-phenylphthalazine-4-carboxylic acid (0·13 g.), washed with water and ethanol, had m. p. and mixed m. p. 208° (decomp.) (Found: C, 67·8; H, 4·1; N, 10·45. Calc. for $C_{15}H_{10}O_3N_2$: C, 67·7; H, 3·8; N, 10·5%).

(*d*) The product (XII) (0·5 g.), 60% aqueous hydrazine hydrate (1 c.c.), and water (2 c.c.) were heated on the steam-bath during 15 min., then cooled, diluted with water (3 c.c.), and acidified with hydrochloric acid. The 4-*phthalazone*-1-*carboxy*-(o-*carboxyanilide*) (IX) (0·3 g.) was filtered off, washed with water and dried. Recrystallised from acetic acid it had m. p. 333° (decomp.), undepressed in admixture with the synthetic product. The equivalent was determined by dissolution in pyridine and titration with sodium hydroxide (Found: C, 61·8; H, 3·9; N, 13·3%; equiv., 301. $C_{15}H_{10}O_2N_3{\cdot}CO_2H$ requires C, 62·1; H, 3·6; N, 13·6%; equiv., 309).

Condensation of Phthalonic Anhydride with Anthranilic Acid.—A mixture of phthalonic anhydride (2 g.), anthranilic acid (4 g.), and pyridine (5 c.c.) was kept at 95° during 30 min., with stirring at first to yield a clear solution. After cooling, the solution was added to 2N-hydrochloric acid (50 c.c.). The precipitated *phenylglyoxylanilide*-2 : 2′-*dicarboxylic acid* (X) (2·8 g.) soon crystallised. Recrystallised from anisole (14 c.c. per g.), washed with benzene, and dried at 100° *in vacuo*, it had m. p. 193—195° (decomp.) (Found: C, 61·8; H, 3·6; N, 4·4. $C_{16}H_{11}O_6N$ requires C, 61·35; H, 3·5; N, 4·5%).

Synthesis of 4-*Phthalazone*-1-*carboxy*-(o-*carboxyanilide*) (IX).—Phenylglyoxylanilide-2 : 2′-dicarboxylic acid (0·5 g.), water (2 c.c.), and 60% hydrazine hydrate (1 c.c.) were stirred for a few min., then heated on the steam-bath during 15 min. After cooling, the mixture was diluted with water and acidified with hydrochloric acid. The solid, when washed with water, dried, and recrystallised from acetic acid (200 c.c.) (yield 0·27 g.), had m. p. 333° (decomp.) (Found: C, 61·5; H, 3·5; N, 13·7%).

Reaction of Hope and Richter's Degradation Product with Hydrazine.—Hope and Richter's degradation product (XIII) (2·6 g.) in 2-ethoxyethanol (41·5 c.c.) was refluxed with 60% hydrazine hydrate (5·2 c.c.) during 6 hr. After cooling, the 6-o-*aminophenyl*-1′-*methyl*-3-*phenylindolo*(2′ : 3′-4 : 5)*pyridazine* (1·7 g.) was filtered off and washed with ethanol. Recrystallised from ethanol (150 c.c. per g.) it had m. p. 256—257° (Found: C, 78·6; H, 5·2; N, 16·2. $C_{23}H_{18}N_4$ requires C, 78·8; H, 5·2; N, 16·0%).

1′-*Methyl*-3 : 6-*diphenylindolo*(2′ : 3′-4 : 5)*pyridazine.*—(a) *Preparation by degradation.* 6-*o*-Aminophenyl-1′-methyl-3-phenylindolo(2′ : 3′-4 : 5)pyridazine (1 g.) was dissolved in 2N-hydrochloric acid (60 c.c.). The solution was cooled, filtered from a trace of insoluble matter, and stirred with ice-cooling whilst 0·5N-sodium nitrite (5·5 c.c.) was added dropwise. Hypophosphorous acid (10 c.c. of 30%) was then added. The mixture was kept in ice during several hours and then at 20° overnight. The mixture then no longer exhibited a coupling reaction. The solid was filtered off, washed with water, dried, dissolved in pyridine (5 c.c.), and precipitated with water (50 c.c.). The *1′-methyl-3 : 6-diphenylindolo(2′ : 3′-4 : 5)pyridazine* (0·25 g.) was filtered off, washed with water, and recrystallised from toluene, then having m. p. 229°, undepressed in admixture with the synthetic material and giving an identical *X*-ray powder photograph (Found : C, 82·2; H, 4·9; N, 12·5. $C_{23}H_{17}N_3$ requires C, 82·35; H, 5·1; N, 12·5%). A further 0·25 g. was obtained from the hydrochloric acid filtrate by basification and recrystallisation from ethanol.

(b) *Synthesis.* 1′-Methyl-2 : 3 : 6-triphenylindolo(2′ : 3′-4 : 5)pyridazinium bromide (0·1 g. of the impure material A, below) was refluxed with hydrazine hydrate (1 c.c.; 60%) in 2-ethoxyethanol (10 c.c.) during 2 hr., kept at 20° overnight, and then evaporated on the steam-bath. The residue was dissolved in ethanol (2 c.c.), and the solution filtered from a trace of insoluble matter and cooled. 1′-Methyl-3 : 6-diphenylindolo(2′ : 3′-4 : 5)pyridazine crystallised and had m. p. 229—230° (Found : C, 82·2; H, 5·1; N, 12·5%).

3-Benzoyl-1-methylindole-2-carboxylic Acid.—(*a*) Dry cadmium chloride (3·5 g.) was added to the Grignard reagent prepared from magnesium (0·55 g.), bromobenzene (2·75 c.c.), and ether (10 c.c.). The mixture was stirred and refluxed during 1 hr. by which time no phenylmagnesium bromide remained. A solution of 1-methylindole-2 : 3-dicarboxylic anhydride (2·8 g.) in hot benzene (100 c.c.) was added. The mixture was stirred and refluxed during 2 hr. Dilute hydrochloric acid was added, and the mixture was again stirred, refluxed for several min., and filtered. The organic layer was separated, washed with water, and extracted with sodium hydrogen carbonate solution. The extract was acidified with hydrochloric acid, and the gum was washed with water and crystallised from ethanol (15 c.c.), giving *3-benzoyl-1-methylindole-2-carboxylic acid* (0·8 g.), m. p. 163—164°. A further 1·9 g. of this compound were obtained by dilution of the filtrate with water. For analysis the first crop was recrystallised from ethanol (5 c.c.), forming very pale yellow plates, m. p. 165—166° (Found : C, 73·5; H, 4·8; N, 5·2. $C_{17}H_{13}O_3N$ requires C, 73·1; H, 4·7; N, 5·0%).

(*b*) A mixture of *N*-methyl-*N*-phenylhydrazine (8 c.c.) and ethyl benzoylpyruvate (15 g.) was heated on the steam-bath during 30 min., then at 100° under reduced pressure to remove water. Powdered zinc chloride (90 g.) was added and the whole kept in a bath at 85° whilst the mixture was stirred as well as possible. An exothermic reaction set in accompanied by frothing, the flask was removed from the bath, and the temperature of the mixture rose to 160°. After the temperature had fallen to 100°, water (250 c.c.) was added, and the mixture was acidified with hydrochloric acid and stirred at 100° to effect dissolution of the zinc chloride. After cooling in ice, the liquid was decanted, the sticky residue was dissolved in ethanol (80 c.c.), and 10N-sodium hydroxide was added (20 c.c.). The mixture was refluxed on the steam-bath during 30 min. The ethanol was removed and water (100 c.c.) added. The mixture was heated on the steam-bath, filtered hot, and cooled. Sodium chloride (10 g.) was added and the mixture stirred to effect dissolution of the sodium chloride. The solid was filtered off, washed with brine, and dissolved in water (100 c.c.). This solution was added to 10N-hydrochloric acid (10 c.c.) containing some ice and a small seed-crystal. The precipitated solid (8·7 g.), recrystallised from 60% ethanol (60 c.c.; charcoal), had m. p. 165—166° (6·5 g.), undepressed in admixture with the product prepared as in (*a*).

2 : 3-Dihydro-3-keto-1′-methyl-2 : 6-diphenylindolo(2′ : 3′-4 : 5)pyridazine (XX).—Phenylhydrazine (5 c.c.) and 3-benzoyl-1-methylindole-2-carboxylic acid (10 g.) were heated in ethanol (30 c.c.) during 80 min. After cooling, the *indolopyridazine* was filtered off, washed with ethanol, and dried (11·3 g.). Recrystallised from benzene it had m. p. 157° (Found : C, 78·4; H, 4·7; N, 12·1. $C_{23}H_{17}ON_3$ requires C, 78·6; H, 4·9; N, 12·0%).

1′-Methyl-2 : 3 : 6-triphenylindolo(2′ : 3′-4 : 5)pyridazinium Bromide (XXI).—The Grignard reagent prepared from magnesium (0·41 g.), bromobenzene (2·1 c.c.), and ether (10 c.c.) was added with shaking to a hot solution of the indolopyridazone (XX) (5·7 g.) in benzene (100 c.c.). After 1 min. water and dilute hydrochloric acid were added. The solid collected after cooling was mainly starting material (5 g.), m. p. and mixed m. p. 155—157°. A portion (4 g.) of this material was boiled with dry benzene (100 c.c.), and the solid was filtered off hot, washed with warm benzene and dried (yield, 0·21 g.; m. p. 295—297°). 0·1 G. of this product, when recrystallised from pyridine–benzene, had m. p. *ca.* 310° (A; see above). This gave analyses for the expected quaternary bromide containing about 15% of the quaternary chloride (Found : C, 72·1; H, 5·0; N, 8·7; Br, 14·4. Calc. for $C_{29}H_{22}N_3Br_{0·85}Cl_{0·15}$: C, 71·7; H, 4·6; N, 8·7;

Br, 14·0%). The hot benzene filtrate was further treated with the Grignard reagent prepared from magnesium (0·29 g.), bromobenzene (1·5 c.c.), and ether (7 c.c.). The ether was distilled off and the benzene solution was refluxed during 45 min., and kept at 20° overnight. Water and dilute hydrochloric acid were added. The solid was filtered off, washed with benzene and water, and dried, giving material (3·1 g.) of m. p. 149—151° undepressed in admixture with the starting material. This product was boiled with benzene (100 c.c.); the solid, filtered off hot, washed with hot benzene, and dried, had m. p. 294—297° (1·2 g.).

1 : 4-*Diphenylphthalazine*.—Reaction of 1 : 2-dihydro-1-keto-2 : 4-diphenylphthalazine with phenylmagnesium bromide and conversion of the resulting quaternary bromide into 1 : 4-diphenylphthalazine by hydrazine were carried out substantially as described for the indolopyridazine analogue. The resulting 1 : 4-diphenylphthalazine melted at 193—194° undepressed in admixture with an authentic sample.

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