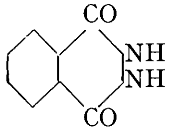
4. *Chemiluminescent Organic Compounds. Part I. Isomeric Simple and Complex Hydrazides of Phthalic Acid and Mode of Formation of Phthalazine and* iso*Indole Rings.*

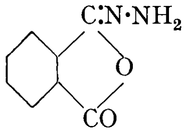
By H. D. K. Drew and H. H. Hatt.

Several classes of organic substances are chemiluminescent in presence of oxidising agents. The object of the work to be described in this series of papers is the further study of the chemistry of such substances and the ultimate application of its results to the luminescence problem. The *cyclo*phthalhydrazides (phthalaz-1 : 4-diones), a series showing notable chemiluminescent properties (Albrecht, *Z. physikal. Chem.*, 1928, **29**, 321), have first been studied.

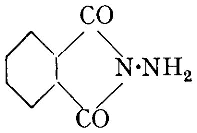
Condensation between hydrazine and phthalic anhydride was shown by Curtius and Fösterling (*J. pr. Chem.*, 1895, **51**, 371) to give phthalaz-1 : 4-dione (I), a substance also obtainable from phthalyl chloride or a phthalic ester and hydrazine hydrate (Davidis, *J. pr. Chem.*, 1896, **54**, 72). Rothenburg (*Ber.*, 1894, **27**, 691) prepared from phthalimide and hydrazine hydrate a different substance, to which he assigned structure (II); Curtius and Fösterling, however, regarded it as (III). A supposed third isomeride was obtained by Mihailescu and co-workers (*Bull. Acad. Sci. Roumaine*, 1923, **8**, 310; *Bul. Soc. Chim. România*, 1930, **12**, 95) from phthalic anhydride and hydrazine in acetic acid, and this also was given structure (III). Radulescu and collaborators (*Bull. Soc. chim.*, 1925, **37**, 886; *Bul. Soc. Chim. România*, 1926, **8**, 117, 120, 137, 140) showed that Mihailescu's substance was identical with that of Curtius (I) and that Rothenburg's substance was spurious. On these grounds the more recent view has been held (*e.g.*, by Alexa and Gheorghiu, *Bull. Soc. chim.*, 1931, **49**, 112) that only the six-ring structure of *cyclo*phthalhydrazides is stable, the five-ring structures being either very unstable or incapable of formation.



(I.)



(II.)

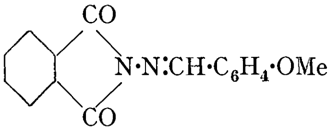


(III.)

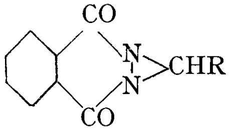
This deduction is incorrect, however, since we now find that Rothenburg's condensation of phthalimide and hydrazine in alcoholic solution, although it yields only (I) if interaction is prolonged, gives a yield of some 50% of N-*aminophthalimide* (III) if the time is curtailed. *N*-Aminophthalimide has quite other properties than those recorded by Rothenburg for his material, which was doubtless a mixture of substances. It condenses readily with acetone and with benzaldehyde, the products being entirely different from those obtained by Rothenburg. At the melting point it changes completely into the six-ring structure (I). Nitrous acid converts it into phthalimide and nitrous oxide, a result which eliminates structure (II). Hydrolysis with acid, alkali, or boiling water brings about partial conversion into (I), though phthalic acid and hydrazine also are produced.

The ready convertibility of *N*-aminophthalimide into the six-ring hydrazide may be contrasted with the known behaviour of its *N*-substituted derivatives, where the change occurs only with difficulty: for example, *N*-phenylaminophthalimide is converted into 3-phenylphthalaz-1 : 4-dione only by heating for long periods in glycerol or with alcoholic sodium hydroxide (Chattaway and Tesh, J., 1920, **117**, 711).

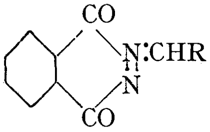
The reverse transformation, that of a six- into the corresponding five-ring compound, has not hitherto been recorded in this series, but we have now observed an example: the condensation of Mihailescu's product, now known to be (I) but supposed by him to be (III), with *p*-anisaldehyde gave an anisylidene derivative to which he correctly (though for an incorrect reason) assigned formula (IV), and we find that it is identical with the product of the much more facile condensation between *N*-aminophthalimide and *p*-anisaldehyde. The six-ring compound, which cannot form a normal condensation product with an aldehyde or a ketone, is therefore changed into the five-ring compound under the influence of these reagents. In accordance with this, also, we find that, contrary to the statements of a number of authors, the six-ring hydrazide (I) condenses slowly with benzaldehyde to give *N*-benzylideneaminophthalimide. The structures (V) and (VI) suggested by Radulescu (*loc. cit.*) for the anisylidene and cinnamylidene derivatives of (I) are in both cases erroneous, that of the anisylidene derivative for the reason already stated, and that of the cinnamylidene derivative owing to a further condensation which gives rise to the 3-*phenyl*-1 : 2-*phthalopyrazoline* (VII) or (VIII).



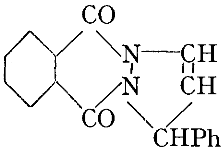
(IV.)



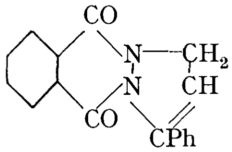
(V.)



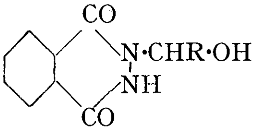
(VI.)



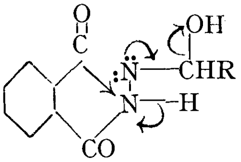
(VII.)



(VIII.)



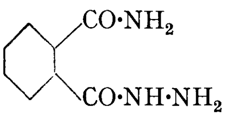
(IX.)



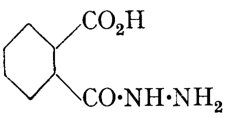
(IX*a*.)

This observation is of interest, since it affords evidence that the transformation of the six- into the five-ring occurs in all cases only after preliminary condensation with the aldehyde to give a substance of structure (IX). A probable mechanism for the molecular rearrangement involved in the change from (IX) to (IV), indicating a resemblance to the pinacol–pinacolin change, is shown in (IX*a*). In the case of cinnamaldehyde the further condensation at the double bond arrests the normal ring change. With (III), the condensation of cinnamaldehyde proceeds normally, to give the expected analogue of (IV).

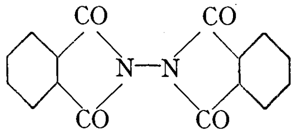
Following on the isolation of *N*-aminophthalimide, we re-examined in some detail the condensation of hydrazine with phthalimide and with phthalic anhydride. With phthalimide in alcoholic medium the first product was o-*carbamylbenzhydrazide* (X), which in boiling alcohol soon lost ammonia to give a mixture of *N*-aminophthalimide and the *cyclo*-hydrazide (I), the latter being present in part as its ammonium salt. When heated alone at 200°, (X) gave (I) together with hydrazine and phthalimide, so cyclisation evidently proceeds in three ways simultaneously.



(X.)



(XI.)

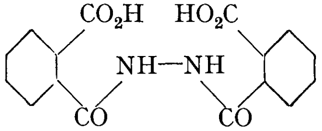


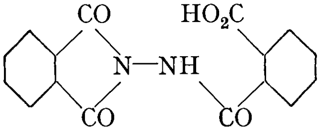
(XII.)

With phthalic anhydride and hydrazine in acetic acid, the evidence indicated that the half-hydrazide (XI) was the first product, though it was not isolated, and that it underwent cyclisation to (III) and (I) in the approximate ratio 3 : 2. Prolonged interaction of equimolecular quantities of hydrazine and phthalic anhydride in boiling acetic acid gave only (I), but if the reaction was stopped after only a few minutes, (III) was isolated in various proportions. When, however, an excess of phthalic anhydride was employed in the prolonged reaction, a mixture of (I) and N-*phthalimidophthalimide* (XII) was obtained, the yield of the latter being sometimes as high as 60%. Interaction of *N*-aminophthalimide with an excess of phthalic anhydride in acetic acid led to the quantitative production of (XII), a reaction which elucidates the structure of the latter and explains its formation in the foregoing condensation.

An obvious alternative mechanism for the production of (XII) in the above reaction is the formation and self-condensation of s-*dibenzoylhydrazine*-2 : 2′-*dicarboxylic acid* (XIII), but this appears not to be utilised. The acid was synthesised through formation of its *methyl* ester from hydrazine and *o*-carbomethoxybenzoyl chloride in pyridine and subsequent hydrolysis of the ester. It is in part cyclised to (XII) when heated in acetic acid, but the yield of (XII) is actually smaller than that obtained in the direct condensation of hydrazine with phthalic anhydride in the same medium.

(XIII.)





(XIV.)

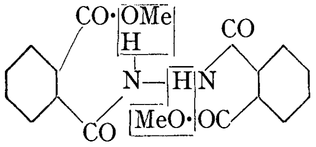
The *di*-N-*methyl* derivative of the methyl ester of (XIII) is unchanged by fusion, whereas the unsubstituted methyl ester cyclises quantitatively when heated.

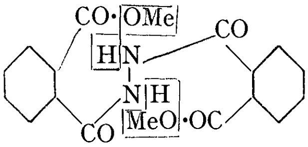
All attempts to isolate (XIII) as a product of the reaction between hydrazine and two molecular proportions of phthalic anhydride failed, the first product being N-*phthalimidophthalamic acid* (XIV); and this was the case also in the reaction between phthalic anhydride and *N*-aminophthalimide. It therefore seems proved that (XII) arises through preliminary formation of (III), and that the condensation between phthalic anhydride and hydrazine in acetic acid proceeds according to the scheme :

$$\begin{tikzcd}(XI) \arrow[r, "cyclises"] \arrow[rr, bend right, "cyclises"'] & (I) & (III) \arrow[l, "rearranges"'] \arrow[r, "phthalic", "anhydride"'] & (XIV) \arrow[r, "cyclises"] & (XII)\end{tikzcd}$$

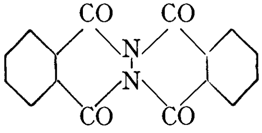
From the facts that the thermal cyclisation of (XIII), which probably proceeds through (XIV) as intermediate, leads to (XII) as the main product, and that (XII) is the sole product when the methyl ester of (XIII) is cyclised, it is obvious that cyclisation occurs in accordance with scheme (A), where the ester is formulated. The cyclisation can also be represented formally by scheme (B), which would lead to a product (XV) instead of (XII). To supply further evidence that (XII) and not (XV) represents the structure of *N*-phthalimidophthalimide, this was synthesised by condensing *N*-aminophthalimide with *o*-carbomethoxybenzoyl chloride in presence of pyridine; the *methyl* ester of (XIV) that resulted gave (XII) quantitatively on thermal cyclisation. That the preference for the formation of the di*iso*indole system [scheme (A)] is not due to lack of stability in compounds containing the double nitrogen bridge seems to be shown by the considerable stability of (VII); it is probably to be attributed to the steric disposition of the groups in such compounds as (XIII). The case recalls the preference for the formation of the di-indole rather than the alternative epindoline system noted by Robinson and Ainley (J., 1934, 1509) and other authors.

(A.)

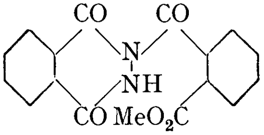




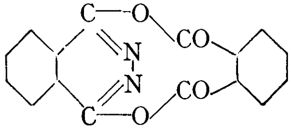
(B.)



(XV.)



(XVI.)

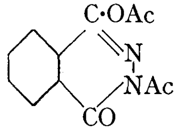


(XVII)

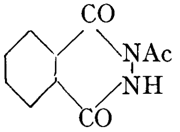
For the preparation of (XV), the obvious method of condensing (I) with phthalic acid was abortive, no reaction occurring, and although 2-o-*carbomethoxybenzoylphthalaz*-1 : 4-*dione* (XVI) was obtained by condensing (I) with *o*-carbomethoxybenzoyl chloride in pyridine, its thermal cyclisation was a complex process leading to (I) and (XII). Condensation of *s*-phthalyl chloride with (I), however, led to the desired 2 : 3-*phthalophthalaz*-1 : 4-*dione* (XV). It is a crystalline, faintly yellow substance, sublimable under reduced pressure, and readily hydrolysed by dilute acid or alkali to phthalic acid and (I). Alternative structures, such as (XVII), derived from the enolised forms of (I), appear impossible or very improbable owing to strain, as may be seen from models; we attempted, however, to synthesise (XVII) by acting upon 1 : 4-dichlorophthalazine with phthalic acid and obtained only 4-chlorophthalaz-1-one, phthalic anhydride, and hydrogen chloride, indicating that the probable initial product, 4-chloro-1-phthalazyl hydrogen phthalate, fails to cyclise to (XVII). Again, only if structure (XV) were correct should the same compound result from the condensation of 5-nitrophthalaz-1 : 4-dione with phthalyl chloride on the one hand and of phthalaz-1 : 4-dione with 3-nitrophthalyl chloride on the other; actually, both condensations gave very similar mixtures, from which only (XV) was isolated, a result which is probably to be attributed to disproportionation of the initial unsymmetrical tetracyclic products. Similar results were obtained with the 6-nitro-compound; and the condensation of *s*-phthalyl chloride with diacetylhydrazine likewise gave rise to (XV).

The isomeric compounds (XII) and (XV) are of particular interest with regard to the stereochemistry of tervalent nitrogen.

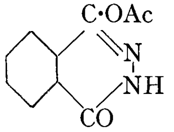
Whether *cyclo*phthalhydrazide should be represented by (I) or by the di- or the mono-enolic (lactim) form is still an open question. Radulescu (*loc. cit.*) adopted structure (I) for most purposes; but Rowe and Peters (J., 1933, 1331) represented the hydrazide as a dienol in acid or neutral solution and as a monoenol in alkaline solution, finding no support for structure (I). We consider that our experiments tend to support formula (I), especially the reaction with cinnamaldehyde, though obviously there is tautomerism. We have been unable to confirm the statement of Rowe and Peters that diacetylation leads to 1 : 4-diacetoxyphthalazine. They obtained the same monoacetyl derivative (m. p. 173°) both by direct acetylation with acetic anhydride–acetic acid and by partial hydrolysis of the diacetyl compound with alcohol. Repeating these experiments, we obtained two substances, which, although they have nearly the same melting point, melt at a lower temperature when mixed and are not identical. Since with acetic anhydride each gives the same known diacetyl derivative, this cannot be 1 : 4-diacetoxyphthalazine as supposed by Rowe and Peters, but must be 4-*acetoxy*-2-*acetylphthalaz*-1-*one* (XVIII). The two monoacetyl derivatives are then (XIX) and (XX). The product of direct acetylation is identical with the monoacetyl derivative resulting from acetylation with acetyl chloride and pyridine. The reaction of diacetylhydrazine with phthalic anhydride takes an unexpected course, yielding N-*acetamidophthalimide* and acetic acid; and the same acetyl derivative is obtained when acethydrazide is used.



(XVIII.)



(XIX.)



(XX.)

EXPERIMENTAL.

Phthalaz-1 : 4-*dione* (I).—Phthalic anhydride (14·8 g.) was refluxed for 4 hours with the requisite amount (Mihailescu and Florescu, *Bull. Acad. Sci. Roumaine*, 1923, **8**, 310) of a solution of hydrazine sulphate and sodium acetate in dilute acetic acid. After cooling, the crystals were removed and washed with dilute acetic acid and water (yield, 9·7 g.); they melted at 333—336° and were completely soluble in aqueous ammonia. Concentration of the mother-liquor gave a second fraction (4·0 g.), of which 0·8 g. was insoluble in aqueous ammonia and consisted of nearly pure *N*-phthalimidophthalimide, m. p. 311—313° after crystallisation from acetic acid. The phthalaz-1 : 4-dione present in the ammoniacal liquors was precipitated by carbon dioxide or hydrochloric acid and recrystallised from alcohol, nitrobenzene, or acetic acid. The same material was also prepared from hydrazine hydrate and phthalic anhydride in alcohol (method of Fösterling, *loc. cit.*) and from hydrazine hydrate and phthalimide by refluxing in alcohol for 6 hours (method of von Rothenburg, *loc. cit.*). All these products melted at 341—344° (corr.) with shrinkage from 320—324°. This manner of melting suggests that phthalaz-1 : 4-dione undergoes tautomeric change to the lactim shortly before melting.

N-*Phthalimidophthalimide* (XII).—Hydrazine hydrate (2 g.) in glacial acetic acid (20 c.c.) was added during ½ hour, with shaking, to a refluxing solution of phthalic anhydride (12 g.) in glacial acetic acid (40 c.c.). After 1 hour, the mixture was cooled, and the precipitate removed, washed, crushed, and digested for 2 hours with 400 c.c. of *N*/4-aqueous ammonia. The insoluble N-*phthalimidophthalimide* (5·25 g.), recrystallised from acetic acid, formed large colourless prisms, m. p. 311—313° (corr.), subliming at a slightly higher temperature (Found : C, 65·6; H, 2·8; N, 9·6; *M*, in camphor, 280, 285. $C_{16}H_8O_4N_2$ requires C, 65·75; H, 2·8; N, 9·6%; *M*, 292). On acidification the ammoniacal liquor gave 3·24 g. (50%) of phthalaz-1 : 4-dione. The yield of (XII) falls to 4·8 g. (41%) if the hydrazine solution is added in one lot and is raised to 6·6 g. (56%) if excess of phthalic anhydride (24—30 g.) is used. With alcohol, ether, and water as solvents, the yields were respectively 16, 13, and 1%. *N*-Phthalimidophthalimide is insoluble in water, sparingly soluble in alcohol and benzene, and readily in aniline. Its solubility in boiling acetic acid is 2·5 parts in 100. Hydrolysis with dilute sulphuric acid yields a mixture of (I) and phthalic acid.

Hydrolysis with hydrazine. *N*-Phthalimidophthalimide (0·50 g.) was added to a solution of hydrazine hydrate (0·2 g.) in glacial acetic acid (25 c.c.), and the mixture boiled for 1 hour. Excess of water was added, and the whole evaporated to dryness under reduced pressure : this process was repeated twice. The residues were treated with water (25 c.c.) containing a drop of hydrochloric acid; the insoluble material was pure phthalaz-1 : 4-dione (0·52 g.; calc., 0·55 g.). The formation of (XII) in the preparation of (I) in acetic acid may therefore be prevented by using a slight excess of hydrazine.

Hydrolysis with alkali. *N*-Phthalimidophthalimide (8·8 g.) and *N*-sodium hydroxide (100 c.c.) were refluxed together for 2 hours and ether was added to the ice-cold liquor, followed by 2*N*-sulphuric acid (53 c.c.). The colourless needles of *s*-dibenzoylhydrazine-2 : 2′-dicarboxylic acid (XIII) were collected after 10 minutes [prolonged standing leads to admixture with (I)], washed with water and ether, and dried over phosphoric oxide (yield, 8·4 g.). The acid lost water at 170—190° and melted at 260—305°. It was identical with the *s*-dibenzoylhydrazine-2 : 2′-dicarboxylic acid obtained by hydrolysis of its ester.

N-*Aminophthalimide* (III).—(1) Small and variable amounts of this substance result from short-period reaction between phthalic anhydride and hydrazine. To 96% hydrazine hydrate (4·3 c.c.) in acetic acid (50 c.c.) was added powdered phthalic anhydride (12 g.), and the mixture heated at once, with shaking, for 1—1½ minutes. A strong yellow colour developed, but a clear solution was never obtained. After rapid cooling, pouring into water (800 c.c.), and 1 hour's keeping, the precipitate was removed (A), and the filtrate left for 12 hours. Crude *N*-aminophthalimide (0·5—1·0 g.) separated; it crystallised from alcohol in faintly yellow needles, which melted at 200—205°, resolidified, and melted again at 338—341°. The material (A) was largely (I) with a little of (III) and (XII).

(2) 96% Hydrazine hydrate (4·4 g.) in 96% ethyl alcohol (80 c.c.) was treated with powdered phthalimide (12 g.), the mixture shaken for 2 minutes at room temperature, the resulting spongy mass quickly heated, and refluxed for 3 minutes (ammonia was evolved), water (50 c.c.) added at once, and the nearly clear solution added to water (200 c.c.). Pure N-*aminophthalimide* crystallised during an hour. It was recrystallised from 96% alcohol, in which it dissolved (1 part in 44 at b. p.) to form a yellow solution. Yield, 5·5—6·0 g. (Found : C, 59·3; H, 3·9; N, 17·4. $C_8H_6O_2N_2$ requires C, 59·3; H, 3·7; N, 17·3%). The aqueous filtrate on acidification gave about 6 g. of (I).

N-Aminophthalimide rapidly reduces Nessler's solution and warm Fehling's solution. It crystallises well from hot water, but at the same time undergoes a slow change; *e.g.*, 0·575 g., refluxed with water for 15 hours, left 0·48 g. of insoluble (I) and the solution contained hydrazine phthalate. The rearrangement to (I) is hastened and rendered quantitative by the presence of alkali; acids accelerate both rearrangement and decomposition. At its m. p. *N*-aminophthalimide is converted almost quantitatively into (I), but the latter contains about 1% of an unidentified yellow solid, removable through its insolubility in ammonia. *N*-Aminophthalimide is stable below its m. p. and can be sublimed under reduced pressure at 150°. It is stable in neutral alcoholic solution.

Action of potassium nitrite. *N*-Aminophthalimide (0·28 g.), suspended in glacial acetic acid (10 c.c.), was treated at room temperature with a concentrated aqueous solution of potassium nitrite (0·2 g.). After an hour water was added in excess; the insoluble material (0·22 g.) melted at 230—231° and was identified as phthalimide.

N-*Acetamidophthalimide*, obtained by refluxing (III) with a little acetic anyhdride for a few minutes, formed colourless prismatic needles, m. p. 228—230°, from hot water (Found : C, 58·7; H, 3·7; N, 13·9. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 3·9; N, 13·7%). *N*-Aminophthalimide on prolonged refluxing in acetic acid solution was converted into a mixture of its acetyl derivative with (I), (XII), and hydrazine. *N*-Acetamidophthalimide is only slightly changed by long boiling with water, but is hydrolysed by hot dilute mineral acid or alkali into acetic acid, phthalic acid, hydrazine, and (I).

N-iso*Propylideneaminophthalimide*.—*N*-Aminophthalimide (1 g.) and acetone (20 c.c.) were refluxed together for 2 hours, and the acetone removed in a vacuum. The dried residue was analytically pure (yield, 1·2 g.). After recrystallisation from aqueous acetone, it formed large colourless prisms, m. p. 97—100° (Found : C, 65·2; H, 5·2. $C_{11}H_{10}O_2N_2$ requires C, 65·3; H, 5·0%). Rothenburg gives m. p. above 260°. It was readily hydrolysed by water or aqueous alcohol to acetone (identified as dibenzylideneacetone), *N*-aminophthalimide, and hydrazine phthalate.

N-*Benzylideneaminophthalimide*, prepared by refluxing benzaldehyde (1 g.), *N*-aminophthalimide (1 g.), and 96% alcohol (25 c.c.) for 1 hour, separated overnight in colourless needles, m. p. 166—167°, unchanged by recrystallisation (Found : C, 72·15; H, 4·5; N, 11·3. $C_{15}H_{10}O_2N_2$ requires C, 72·0; H, 4·0; N, 11·2%). Rothenburg gives m. p. above 250°. The substance was slowly hydrolysed by boiling water, benzaldehyde (identified as benzylideneazine) distilling in the steam and the solution containing a mixture of (III), (I), hydrazine, and phthalic acid. Hydrolysis with hot *N*/10-sulphuric acid was rapid and led to a greater proportion of (I).

N-*p*-Anisylideneaminophthalimide (IV), similarly prepared from *N*-aminophthalimide (1 g.) and *p*-anisaldehyde (1 g.), was extracted from the separated crystals by means of benzene and recrystallised from alcohol, forming stout sulphur-yellow crystals, m. p. 189—191° (Found : C, 68·1; H, 4·8; N, 10·1. Calc. for $C_{16}H_{12}O_3N_2$: C, 68·5; H, 4·3; N, 10·0%). Water hydrolyses it slowly; dilute acids, rapidly.

N-*Cinnamylideneaminophthalimide* was similarly prepared from cinnamaldehyde (0·55 g.), *N*-aminophthalimide (0·5 g.), and 96% alcohol (20 c.c.). It separated on cooling and after recrystallisation from alcohol formed flocks of nearly colourless, hairy crystals, which invariably changed after a time into compact sulphur-yellow crystals : both varieties melted at 199—200° (Found for the yellow form : C, 73·9; H, 4·7; N, 10·1. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·35; N, 10·1%). When the compound was heated with *N*/10-sulphuric acid in a current of steam, cinnamaldehyde (identified as cinnamylideneazine) distilled slowly, and (I), hydrazine and phthalic acid were left behind.

N-*Piperonylideneaminophthalimide* was obtained similarly from piperonal (1·1 g.), *N*-aminophthalimide (1 g.), and 96% alcohol (10 c.c.). It was precipitated from the cool filtered solution by the gradual addition of water. Crystallisation from benzene–alcohol gave sulphur-yellow needles (0·65 g.), m. p. 186·5—187° (Found : N, 9·8. $C_{16}H_{10}O_4N_2$ requires N, 9·5%).

o-*Carbamylbenzhydrazide* (X).—Powdered phthalimide (1·47 g.) in 99% alcohol (25 c.c.) was treated at 0° with a solution of hydrazine hydrate (0·5 g.) in 99% alcohol (10 c.c.). The mixture was shaken and watched under a microscope until phthalimide was no longer seen. After shaking at 0° for ½ hour, the colourless micro-crystals were removed, washed with alcohol and absolute ether, and dried in a vacuum over phosphoric oxide (Found : C, 53·95; H, 5·4; N, 23·4. $C_8H_9O_2N_3$ requires C, 53·65; H, 5·05; N, 23·45%). This *substance* reduced cold Nessler's and warm Fehling's solution. When heated, it lost ammonia, began to shrink at 220° and melted at 300—320° to a yellow liquid. When 0·5 g. of a specimen that had been kept 4 days was heated for 3 minutes in 4 c.c. of alcohol, ammonia was evolved and the product, when worked up as in the preparation of *N*-aminophthalimide (method 2), gave a 51% yield of this, the other product being (I). When heated in acetic acid with phthalic anhydride, (X) was converted to the extent of 35% into (XII).

When (X) (0·3764 g.) was heated at the boiling point of nitrobenzene in a current of nitrogen for 2 hours, ammonia and hydrazine were evolved : they were absorbed in dilute acid, and the hydrazine estimated by means of Fehling's solution (yield, 0·001 g.; 5%). The loss in weight was 0·0335 g. (calc. for maximum possible loss of ammonia, 0·0355 g.). The residue consisted of (I) and a small sublimate of phthalimide (m. p. 230—233°).

Condensation of Phthalaz-1 : 4-*dione with Aldehydes*.—(A) *With benzaldehyde*. Phthalaz-1 : 4-dione (2 g.) and benzaldehyde (10 g.) were refluxed together for 15 hours, the water evolved being allowed to escape. The brownish crystals which separated on cooling were removed, washed with ether (yield, 2·2 g.; m. p. 159—162°), and recrystallised from alcohol (charcoal), *N*-benzylideneaminophthalimide being obtained in colourless needles identical with the material prepared from (III).

(B) *With anisaldehyde.* Phthalaz-1 : 4-dione (2 g.) and anisaldehyde (10 c.c.) were refluxed together for 2 hours and the reddish paste was rubbed with ether, filtered, and washed with ether. Crystallised from alcohol, the product (2 g.) melted at 189—190° (Mihailescu and Florescu reported 188—190°) and was identical with the material prepared from (III).

3-*Phenyl*-1 : 2-*phthalopyrazoline* (VII or VIII).—Phthalaz-1 : 4-dione (12 g.) and freshly distilled cinnamaldehyde (20 c.c.) were mixed and heated rapidly to boiling over a naked flame for not more than 4 minutes. After cooling, the glue-like mass was crushed with ether, and the insoluble yellow powder washed with ether until free of resin. The resulting solid (12—14 g.) was extracted several times with hot chloroform (100 c.c. in all), leaving a white residue containing (I) and unidentified substances. The chloroform liquors gave the required *substance*, which formed sulphur-yellow crystals, m. p. 224—228°, from alcohol or chloroform–ether; it slowly turned green in bright light, was almost insoluble in ether, dissolved in about 90 parts of hot 96% alcohol, and was very soluble in chloroform (Found: C, 73·8; H, 4·3; N, 10·2. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·35; N, 10·1%). When heated for several hours with dilute sulphuric acid in a current of steam, the substance evolved no cinnamaldehyde.

Action of alcoholic sodium ethoxide. 3-Phenyl-1 : 2-phthalopyrazoline (4 g.) was added to a solution of sodium ethoxide (9 g.) in 99% alcohol (70 c.c.), and the mixture refluxed for an hour in an atmosphere of nitrogen. A fuchsine colour developed and then faded to yellow, sodium phthalate separating (2·66 g.; calc., 3·04 g.). The alcoholic filtrate was evaporated several times with water under reduced pressure in an atmosphere of nitrogen; the oil that separated was extracted in chloroform (yield, 1·5 g.) and identified as 5-phenylpyrazoline, or an isomer, by conversion into 1-nitroso-5-phenylpyrazoline (von Auwers and Heimke, *Annalen*, 1927, **458**, 210), which formed buff micaceous plates, m. p. 157°, from methyl alcohol (Found: C, 61·1; H, 5·6; N, 23·4. Calc. for $C_9H_9ON_3$: C, 61·7; H, 5·1; N, 24·0%). It was identical with the nitroso-compound prepared from synthetic 5-phenylpyrazoline (Rothenburg, *Ber.*, 1894, **27**, 788; see also Knorr, *Ber.*, 1895, **28**, 688; *J. pr. Chem.*, 1896, **53**, 127). The isolation of 1-nitroso-5-phenylpyrazoline by nitrous acid treatment does not fix the position of the double bond in the phenylpyrazoline, since, owing to isomerisation, 3- and 5-phenylpyrazoline give the same nitroso-derivative.

The Action of Phthalic Anhydride on N-*Aminophthalimide.*—*N*-Aminophthalimide (0·48 g.) and phthalic anhydride (1·0 g.) were refluxed in acetic acid (5 c.c.) for 10 minutes. After cooling, and addition of water, the precipitate of *N*-phthalimidophthalimide (XII) obtained was washed with alcohol to remove phthalic acid; m. p. 311—313° after one crystallisation (yield, nearly quantitative). When *N*-aminophthalimide (0·8 g.) and phthalic anhydride (2 g.) were heated together at 160°, 1·32 g. of (XII) were obtained.

N-3′-*Nitrophthalimidophthalimide*, prepared by refluxing *N*-aminophthalimide (0·5 g.) and 3-nitrophthalic anhydride (1·2 g.) in acetic acid (5 c.c.) for 15 minutes, separated on cooling (yield, 1 g.); it was crushed with aqueous ammonia and crystallised from acetic acid, forming colourless hexagonal plates, m. p. 249—250° (Found: N, 12·9. $C_{16}H_7O_6N_3$ requires N, 12·5%). The condensation proceeds without solvent at 180—190°.

N-4′-*Nitrophthalimidophthalimide* (1·4 g.), similarly prepared from *N*-aminophthalimide (0·7 g.) and 4-nitrophthalic anhydride (1·5 g.), formed faintly yellow needles, m. p. 250°, from acetic acid (Found: N, 12·6%).

Methyl s-*Dibenzoylhydrazine*-2 : 2′-*dicarboxylate.*—8·3 G. of *o*-carbomethoxybenzoyl chloride (Meyer, *Monatsh.*, 1901, **22**, 277) were added to ice-cold pyridine (20 c.c.) with cooling. A spongy yellow mass was produced and the pyridine became red. Hydrazine hydrate (1 g.) in pyridine (10 c.c.) was then added, with cooling in ice and shaking. After warming at 40° for a few minutes, the solid dissolved. The mixture was left overnight, poured into water (400 c.c.) containing sufficient sulphuric acid to neutralise the pyridine, and left for 2—3 hours [longer standing leads to contamination with (I)]; the precipitate obtained crystallised from alcohol in colourless hair-like needles (Found: C, 60·8; H, 4·5; N, 8·1. $C_{18}H_{16}O_6N_2$ requires C, 60·7; H, 4·5; N, 7·9%). It melted between 180° and 200° according to the rate of heating, with evolution of gas and resolidification, melting again at 303—306°. *Methyl* s-*dibenzoylhydrazine*-2 : 2′-*dicarboxylate* is fairly readily soluble in acetone, readily soluble in acetic acid, but only slightly in water or ether.

Cyclisation.—(A) *By heat.* The ester (0·324 g.) was heated at 190—200° in a stream of carbon dioxide. On melting, the substance gave off a vapour, which was condensed in a freezing mixture. The residue was finally heated for a few minutes at 280°; pure *N*-phthalimidophthalimide, m. p. 311—313°, was obtained in theoretical amount. The condensate (0·054 g.; calc., 0·056 g.) was methyl alcohol, identified as methyl 3 : 5-dinitrobenzoate.

(B) *By acetic acid.* When the ester (0·324 g.) was heated in acetic acid for 4 hours, 0·257 g. of (XII) was obtained.

The ester reacts in a more complicated manner with mineral acids: heating with 0·1 *N*-sulphuric acid hydrolysed the ester into (XII) (yield, 30%), phthalic acid, and (I) (yield, 65%), together with some free hydrazine.

s-*Dibenzoylhydrazine*-2 : 2′-*dicarboxylic Acid* (XIII).—Treatment of the methyl ester with cold dilute aqueous alkali produces a light yellow solution (probably of the lactim sodium salt of the ester), from which immediate acidification precipitates much of the ester unchanged; but on standing the yellow colour quickly disappears and acidification then liberates the *dicarboxylic acid.* The methyl ester (0·47 g.) was shaken as a powder with 0·25*N*-sodium hydroxide (16 c.c.), and the solution kept till colourless. Ether was added, and dilute sulphuric acid until the mixture was acid to methyl-orange. The dicarboxylic acid separated mixed with a little of (I), which was removed by solution in 80% aqueous acetone and filtration; the filtrate, concentrated and precipitated by ether, gave the acid as colourless needles (0·3 g.). It lost water between 170° and 190° and melted from 260—320°; it decomposed aqueous sodium carbonate and was reprecipitated by acetic acid (Found: C, 58·5; H, 4·0; N, 8·7; equiv., by titration with barium hydroxide, 166. $C_{16}H_{12}O_6N_2$ requires C, 58·5; H, 3·7; N, 8·5%; equiv., 164). Heated on a bath of nitrobenzene, the acid lost water and gave a sublimate of phthalic anhydride, the residue consisting of a mixture of (XII), (I), and phthalic anhydride. In boiling acetic acid the acid decomposed, giving the same three products, the yield of (XII) being 30%. The *hydrazine* salt separated as a powder when the acid was warmed in alcohol with hydrazine hydrate (Found: C, 53·0; H, 4·8. $C_{16}H_{16}O_6N_4$ requires C, 53·3; H, 4·5%). The *silver* salt was obtained as light yellow crystals from the ammonium salt and silver nitrate in aqueous alcoholic solution; it was washed with alcohol and dried (Found: Ag, 40·6. $C_{16}H_{10}O_6N_2Ag_2$ requires Ag, 39·8%). The silver salt was shaken in a sealed tube with methyl iodide in dry benzene and after several days the insoluble material was removed and extracted with hot alcohol, which, on cooling, deposited hair-like crystals identified as methyl *s*-dibenzoylhydrazine-2 : 2′-dicarboxylate.

Methyl s-*Dibenzoyldimethylhydrazine*-2 : 2′-*dicarboxylate.*—To *o*-carbomethoxybenzoyl chloride (9·5 g.) in ice-cold pyridine (20 c.c.) was added, with shaking, a solution of *s*-dimethylhydrazine (1·4 g.) (Hatt, "Organic Syntheses," **16**, p. 18) in pyridine (12 c.c.). After a day the crystals of pyridine hydrochloride were removed, and the filtrate added to an excess of water; the solution gradually deposited very long, colourless, refractive prisms, which were recrystallised from 50% alcohol; m. p. 171—172° (Found: C, 62·7; H, 5·8; N, 7·6. $C_{20}H_{20}O_6N_2$ requires C, 62·5; H, 5·2; N, 7·3%).

N-*Phthalimidophthalamic Acid* (XIV).—A hot solution of phthalic anhydride (12 g.) in acetic acid (40 c.c.) was treated rapidly with hydrazine hydrate (2 g.) in acetic acid (20 c.c.). The mixture, refluxed for ½ minute, became yellow and a solid began to separate; the whole was quickly cooled and poured into 600 c.c. of water, and the precipitate collected after 1—2 hours, washed, and left overnight in 100 c.c. of 80% acetone. The undissolved material [chiefly (XII) and (I)] was removed, and the acetone filtrate concentrated at room temperature under reduced pressure, giving 2·5—3 g. of the crude *acid* as colourless plates; it was dried, dissolved in the calculated quantity of aqueous sodium carbonate, and the filtered solution precipitated with acetic acid; the acid was then dissolved in 80% aqueous acetone, and the filtered solution caused to crystallise by gradual addition of water. The acid was finally obtained in colourless hexagonal plates, which decomposed with loss of water at 160—190° and gave a residue of m. p. 307—310° (Found: C, 61·8; H, 3·9; N, 9·3. $C_{16}H_{10}O_5N_2$ requires C, 61·9; H, 3·3; N, 9·0%). It does not reduce Fehling's solution; it decomposes aqueous sodium carbonate, but more slowly than *s*-dibenzoylhydrazine-2 : 2′-dicarboxylic acid; it is also more soluble than the latter in 80% aqueous acetone. Cyclisation to (XII) was not quantitative at 200° and the amount of water produced was less than that calculated; the yield of (XII) was about 70%, the other products being (I) and phthalic anhydride. In hot acetic acid the cyclisation was quantitative only if an excess of phthalic anhydride was present; in its absence the products were those of the thermal decomposition, although the yield of (XII) was higher (80%); no free hydrazine was produced. Aqueous sodium hydroxide brought about conversion into the sodium salt of (XIII).

Preparation from N-*aminophthalimide.* *N*-Aminophthalimide (1 g.) and phthalic anhydride (1 g.) were refluxed in acetic acid (10 c.c.) for ¾ minute; the mixture was then cooled and poured into excess of water. From the precipitate, *N*-phthalimidophthalamic acid (0·9 g.) was isolated as described above. The *silver* salt (white) was obtained from the ammonium salt and silver nitrate in aqueous alcohol (Found: Ag, 25·55. $C_{16}H_9O_5N_2Ag$ requires Ag, 25·9%).

Methyl N-*Phthalimidophthalamate.*—*o*-Carbomethoxybenzoyl chloride (5 g.) was added to ice-cold pyridine (15 c.c.) and treated at 0° with a mixture of *N*-aminophthalimide (3·5 g.) and pyridine (12 c.c.). The mixture was rubbed or shaken at 0° until the acyl chloride–pyridine addition compound had disappeared. Next day the precipitate of pyridine hydrochloride and (XII) was removed, and the filtrate poured into an excess of water and made just acid. A mixture (5 g.), at first oily, of the desired *ester* and (XII) separated; this was dissolved in a little cold chloroform, the precipitate formed on addition of ether removed, and the filtrate further precipitated with more ether. The first precipitate was initially (XII), but after several repetitions of the process only the required ester separated (Found: C, 63·2; H, 3·9. $C_{17}H_{12}O_5N_2$ requires C, 63·0; H, 3·7%). The ester formed white microneedles, which melted with effervescence at 166—168°, re-solidified, and melted again at 310—313°, conversion into (XII) having taken place. When heated in a bath of boiling nitrobenzene, it lost methyl alcohol, identified as methyl 3 : 5-dinitrobenzoate (Found: loss in weight, 9·6. Calc., 9·9%). It was very soluble in hot organic solvents, but in all cases underwent some cyclisation to (XII); in acetic acid the process was complete in a few minutes. The yellow solution of the ester in aqueous sodium hydroxide probably contains a salt of the lactim modification; it becomes colourless if kept, and addition of acetic acid then precipitates only (XIII), whereas with the fresh solution it gives the initial ester.

The same methyl ester was obtained, together with much of (XII), when the corresponding silver salt was shaken in dry benzene with methyl iodide.

2-o-*Carbomethoxybenzoylphthalaz*-1 : 4-*dione* (XVI).—A mixture of *o*-carbomethoxybenzoyl chloride (5 g.) and phthalaz-1 : 4-dione (4 g.) in pyridine (30 c.c.) was left for 2 days, the pyridine hydrochloride and unchanged hydrazide removed, and the filtrate treated slowly with an excess of water. The crude *ester* was collected after 2 hours and purified from methyl alcohol or by solution in chloroform and addition of ether. It melted at 165—170° with decomposition and resolidification, melting again from 270—290°; a mixed m. p. with the methyl ester of (XIV) was depressed to 134—149° (Found: C, 63·1; H, 3·8. $C_{17}H_{12}O_5N_2$ requires C, 63·0; H, 3·7%). Thermal decomposition of the ester was complex, varying with the temperature. At 200—210° decomposition was rapid, but no methyl alcohol was produced; phthalic anhydride, (I), and a little of (XII) were isolated. But at 280°, methyl alcohol was evolved and a greater proportion of (XII) (0·14 g. from 0·45 g. of ester) was produced. The carbomethoxybenzoyl group can be removed from the phthalazine ring without complete hydrolysis of the carbomethoxy-group, for when the ester was refluxed with acetic acid for 2 hours, (I) was produced in the calculated quantity together with phthalic acid and methyl hydrogen phthalate. Aqueous alkali gave (I), phthalic acid, and methyl alcohol.

2 : 3-*Phthalophthalaz*-1 : 4-*dione* (XV).—Phthalaz-1 : 4-dione (5·7 g.) and *s*-phthalyl chloride (7·4 g.) were mixed with nitrobenzene (50 c.c.) and heated in an oil-bath at 160° with shaking. When the evolution of hydrogen chloride ceased (¾ hour), the temperature was raised to 210° for ¼ hour. The crystals which separated on cooling were usually free from (I); this, if present, was removed by solution in dilute aqueous ammonia. Crystallised from nitrobenzene, 2 : 3-*phthalophthalaz*-1 : 4-*dione* formed faintly yellow needles, m. p. 350—360° (slight decomp.) to a red liquid. It sublimed readily with little decomposition at 345—350°/15 mm. (Found: C, 65·7; H, 3·0; N, 9·9. $C_{16}H_8O_4N_2$ requires C, 65·7; H, 2·8; N, 9·6%). The yield was 9·4 g. (calc., 10·2 g.). The same condensation took place in pyridine at 100—110°, but the yield was smaller. (XV) was almost insoluble in the majority of organic solvents, but dissolved slightly in hot acetic acid, anisole, and amyl alcohol. Its solubility in nitrobenzene was 1 part in 35 (boiling) and 1 part in 500 (room temperature). Hydrazine, in aqueous or acetic acid solution, caused nearly quantitative conversion into (I). Boiling with 0·1*N*-sulphuric acid in acetic acid or with aqueous caustic soda brought about complete conversion into (I) and phthalic acid, and ammonium acetate in acetic acid gave (I) and phthalimide.

Condensation of Phthalyl Chlorides with Nitrophthalaz-1 : 4-*diones.*—6-Nitrophthalaz-

1 : 4-dione (2 g.) and *s*-phthalyl chloride (2·1 g.) in nitrobenzene (15 c.c.) were heated on an oil-bath at 190° for ¼ hour (longer heating had no effect) in a stream of carbon dioxide. The solid dissolved, hydrogen chloride was evolved, and, on cooling, yellow crystals (3·3 g.) were obtained, m. p. 250—350°; extraction of these with hot anisole (25 c.c.) left pale yellow needles (0·75 g.), identified as (XV), m. p. 350—360°. The anisole extract gave an inseparable mixture of substances readily hydrolysed by cold aqueous ammonia.

A parallel result was obtained with 5-nitrophthalaz-1 : 4-dione. Substitution of pyridine for nitrobenzene caused no change in the nature of the products.

When 3-nitrophthalyl chloride (2·5 g.) and phthalaz-1 : 4-dione (2 g.) were condensed in nitrobenzene, a yield of 0·75 g. of (XV) was obtained.

1 : 4-*Dichlorophthalazine*.—Wolfram's method (D.R.-P. 481,650) was modified as follows : Phthalaz-1 : 4-dione (8 g.) and phosphorus pentachloride (25 g.) were heated on an oil-bath at 150° for 4 hours and the product was cooled, crushed, washed with petroleum, extracted (Soxhlet) with benzene, recovered from the extract, and crystallised from dry benzene; it formed long colourless needles (7 g.), m. p. 162—164°.

Condensation between phthalic acid and 1 : 4-dichlorophthalazine at 180° (alone or in nitrobenzene) gave chiefly 4-chlorophthalaz-1-one, m. p. 274°, insoluble in benzene, and phthalic anhydride. Pure 4-chlorophthalaz-1-one is colourless, and not yellow as stated by Radulescu.

*Acetyl Derivatives of Phthalaz-*1 : 4-*dione*.—*Diacetyl derivative*. Phthalaz-1 : 4-dione (3·2 g.) and acetic anhydride (20 c.c.) were refluxed together (½ hour to 24 hours); the crystals deposited on cooling were washed with dry ether; a further crop was obtained from the mother-liquor. 4-*Acetoxy-2-acetylphthalaz-*1-*one* formed colourless gable-ended needles from dry benzene; the m. p. was m. p. 139—140°, but invariably there was shrinkage from about 133° (Found : C, 58·6; H, 4·4; N, 11·6. $C_{12}H_{10}O_4N_2$ requires C, 58·55; H, 4·1; N, 11·4%). The substance was rapidly hydrolysed by aqueous alcohol, as found by Rowe and Peters.

Radulescu and Georgescu (*loc. cit.*) described a diacetyl derivative, m. p. 126°, obtained by using acetic anhydride and sodium acetate. Repetition of their experiment gave a crude product, m. p. 114—126°, but on purification this substance was found to be identical with the above diacetyl derivative, melting then at 137—140°.

Monoacetyl derivatives. (A) Phthalaz-1 : 4-dione (4·0 g.), acetyl chloride (2·4 g.), and pyridine (25 c.c.) were mixed at 0°, shaken in a freezing mixture, and then refluxed for 2 hours. After several days, crystals separated; they were washed with alcohol and ether and recrystallised from dry benzene, forming colourless needles (1·5 g.), which usually melted at 175—176°, but when placed in a bath at 165° and heated rapidly, melted at 180—183° (Found : C, 58·3; H, 4·2; N, 13·9. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 4·0; N, 13·7%). Melting was accompanied by decomposition; a cloud of crystals always remained until near 200°. The *monoacetyl* derivative was completely converted into the preceding diacetyl derivative by refluxing with acetic anhydride. It was completely hydrolysed to (I) by boiling with 60% alcohol for 2 hours or by heating with dilute sodium hydroxide solution.

(B) 4-Acetoxy-2-acetylphthalazone (1 g.), absolute alcohol (0·3 c.c.), and benzene (5 c.c.) were refluxed on a water-bath for 3 hours and cooled; the crystals which had separated were extracted twice with boiling dry benzene. The residue, m. p. 165—170°, formed, after several recrystallisations from large volumes of dry benzene, flocks of white fibrous needles, electrified on rubbing, m. p. 172—173° (decomp.), a cloud of crystals remaining until 200°. The same product was obtained when the diacetyl derivative was boiled for a short time with 99% alcohol (Found : C, 58·6; H, 4·15; N, 14·2%). A mixture with the product obtained in (A) melted mostly at 160—165°, crystals remaining until 190°. Specimens of each of the pure materials, heated at the same time, were not molten at 172°.

(C) Phthalaz-1 : 4-dione was acetylated with acetic anhydride–acetic acid by the method of Rowe and Peters (*loc. cit.*). Repeated fractionation of the product from benzene gave a substance, m. p. 162—170°, but further fractionation from acetic acid yielded a product, m. p. 172—175° (a cloud of crystals remaining until 200°), and this was apparently a single substance. When it was mixed with the monoacetyl derivative obtained in (B), its m. p. was depressed to 160—170°. This substance was identical with the acetyl derivative obtained in (A).

Acethydrazide and Phthalic Anhydride.—Acethydrazide (1 g.) and phthalic anhydride (2 g.) were refluxed in acetic acid (10 c.c.) for ¼ hour, cooled, and the crystalline product collected. After removal of small quantities of (XII) by boiling with benzene, *N*-acetamidophthalimide (2 g.) remained, m. p. 227—229° (Found : C, 58·45; H, 4·1%). The same condensation also took place at 140° in absence of a solvent.

Diacetylhydrazine and Phthalic Anhydride.—When diacetylhydrazine (3·5 g.) and phthalic anhydride (5 g.) were heated together at 140° for 15 hours, acetic acid distilled. The residue was extracted with boiling water and left 0·48 g. of (XII); the filtrate deposited *N*-acetamidophthalimide (2 g.), m. p. 228—230°.

Diacetylhydrazine (2·2 g.), phthalyl chloride (4 g.), and nitrobenzene (5 c.c.), when heated at 160° for 20 minutes, gave at first a clear solution, hydrogen chloride being evolved, and later deposited light yellow crystals (1·1 g.), identified as (XV).

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