Benzonitrile *N*-(Phthalimido)imide, a Functionalised 1,3-Dipole. Preparation of 4,5,8-Triphenylpyridazino[4,5-*d*]triazine and Generation of 3,6-Diphenyl-4,5-didehydropyridazine[1]

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5-Phenyl-2-phthalimidotetrazole (1) has been prepared and shown to react readily with cyclohexene, dimethyl acetylenedicarboxylate, and dibenzoylacetylene, to give the cycloadducts of the functionalised 1,3-dipole, benzonitrile *N*-(phthalimido)imide (2). The adduct formed with dibenzoylacetylene, 4,5-dibenzoyl-3-phenyl-1-phthalimidopyrazole (5), has been converted into 4,5,8-triphenylpyridazino[4,5-*d*]triazine (8). This triazine undergoes thermal fragmentation to give diphenylbutadiyne, 3,6-diphenyl-4,5-didehydropyridazine being proposed as an intermediate. An alternative route to 3,6-diphenyl-4,5-didehydropyridazine is described which involves the preparation and oxidation of 1-amino-4,7-diphenyltriazolo[4,5-*d*]pyridazine (11).

CYCLOADDITION reactions involving 1,3-dipolar intermediates represent an important method of synthesising a wide range of heterocyclic systems. Despite the enormous number of such reactions which have been reported, very few involve the use of 1,3-dipoles which bear functional groups other than simple alkyl and aryl derivatives.[2] In this paper we describe the generation of a 1,3-dipole which bears a masked amino-group in the form of a phthalimido-substituent, and we give an example of its use in the synthesis of a fused 1,2,3-triazine.

2,5-Disubstituted tetrazoles have been widely used as a thermal or photochemical source of nitrilimines. In earlier work it was found that 1,2,3-triazoles substituted at the 1-position with a phthalimido-group are thermally much more labile than the corresponding 1-alkyltriazoles, and they decompose cleanly by extrusion of nitrogen.[3] 5-Phenyl-2-phthalimidotetrazole (1) was synthesised in order to determine whether a phthalimido-group would have a similar effect on the thermolysis of tetrazoles. 5-Phenyltetrazole has been reported to give 1- and 2-amino-5-phenyltetrazole in very low yields with hydroxylamine-*O*-sulphonic acid.[4] By a modified amination procedure we obtained a mixture of 1- and 2-amino-5-phenyltetrazole in 45% yield, with the 2-amino-isomer as the major component. This was condensed with phthaloyl chloride to give 5-phenyl-2-phthalimidotetrazole.

The tetrazole (1) was indeed much more labile than 2,5-diaryltetrazoles, and it decomposed with evolution of nitrogen when heated in benzene at 80 °C. In cyclohexene, the adduct (3) resulting from cycloaddition of the 1,3-dipole benzonitrile *N*-(phthalimido)imide (2) to the double bond was the major product. Analogous adducts (4) and (5) were isolated in good yield with dimethyl acetylenedicarboxylate and with dibenzoylacetylene in boiling benzene. A minor product of the decomposition in cyclohexene was 7-phthalimido-7-azabicyclo[4.1.0]heptane (6), which is the adduct of phthalimidonitrene and cyclohexene.[5] This indicates that the nitrilimine may undergo slow decomposition to benzonitrile and phthalimidonitrene in competition with the cycloaddition. The reactions are outlined in Scheme 1.

[1] Preliminary communication, T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *J.C.S. Chem. Comm.*, 1973, 819.

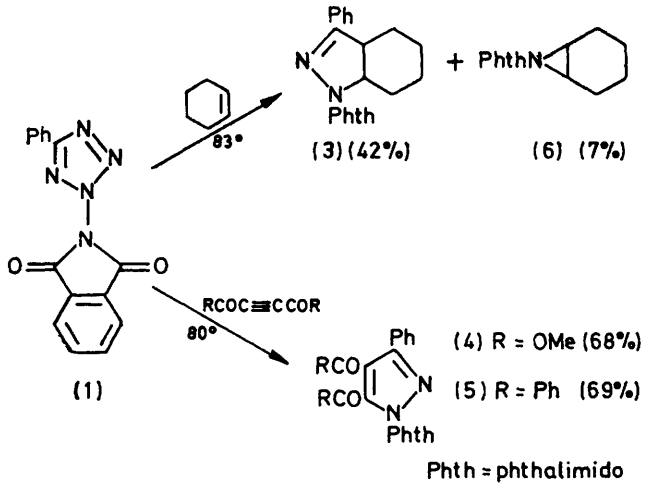
[2] J. W. Lown and B. E. Landberg, *Canad. J. Chem.*, 1974, **52**, 798.

[3] T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *J.C.S. Perkin I*, 1973, 555.

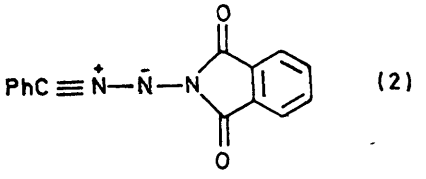
[4] R. Raap, *Canad. J. Chem.*, 1969, **47**, 3677.

[5] D. J. Anderson, T. L. Gilchrist, D. C. Horwell, and C. W. Rees, *J. Chem. Soc.* (*C*), 1970, 576.

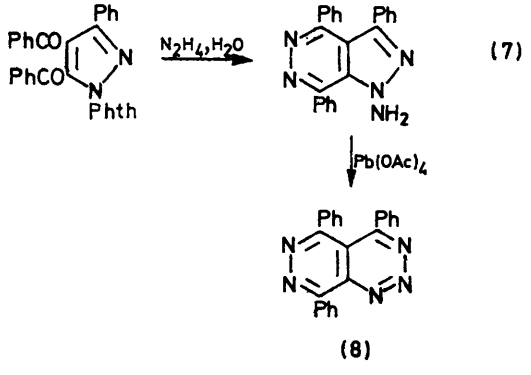
The pyrazole (5) was converted into the corresponding 1-aminopyrazolopyridazine (7) with hydrazine hydrate, which reacted both with the phthalimido-group and with



SCHEME 1



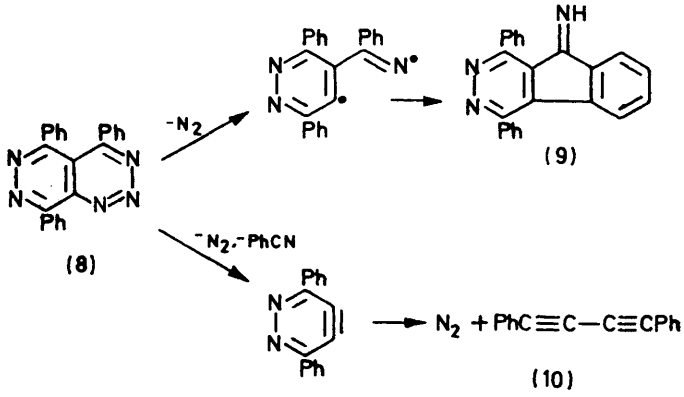
the benzoyl groups. Oxidation of the aminopyrazole (7) with lead tetra-acetate resulted in ring expansion to give the fused triazine (8) in good yield (Scheme 2). This



SCHEME 2

ring expansion is directly analogous to the preparation of 1,2,3-benzotriazines from 1-aminoindazoles.[6]

As with other fused 1,2,3-triazines,[6] compound (8) is a potential precursor of an aryne, produced by loss of nitrogen and benzonitrile from the triazine ring. Alternatively, elimination of nitrogen and retention of the nitrile residue could lead to the formation of an azete [7] or of an indenimine.[8] Vapour-phase pyrolysis of the triazine at 420 °C and 0.05 mmHg gave two products, one of which was identified as the imine (9) and the other as diphenylbutadiyne (10). The formation of diphenylbutadiyne requires the loss of two molecules of nitrogen and one of benzonitrile from the triazine; a possible mechanism for the thermolysis is fragmentation of the triazine ring to give 3,6-diphenyl-4,5-didehydropyridazine, which then undergoes further fragmentation (Scheme 3). Although benzyne and substituted benzynes normally dimerise under conditions comparable to these, 3,4-didehydropyridine does undergo fragmentation as well as dimerisation.[9] Fragmentation of 4,5-didehydropyridazine derivatives should be especially favourable because minor bond reorganisation can lead to the extrusion of molecular nitrogen.[1]



SCHEME 3

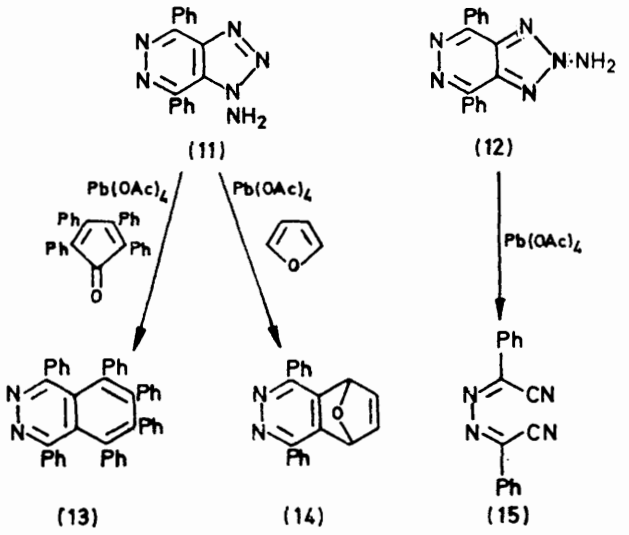
In order to test the proposal that 3,6-diphenyl-4,5-didehydropyridazine is an intermediate in the reaction, an alternative route to the aryne was devised, based on the well established oxidative fragmentation of 1-aminotriazoles. 4,5-Dibenzoyltriazole was prepared in high yield by the reaction of dibenzoylacetylene with sodium azide. The triazole was aminated with *O*-mesitylsulphonylhydroxylamine and gave a mixture of 1- and 2-amino-derivatives, which were separated only with difficulty. With hydrazine these gave the corresponding aminotriazolopyridazines (11) and (12).

The oxidation of these compounds with lead tetra-acetate in dichloromethane at room temperature gave products which are analogous to those formed from the corresponding benzotriazoles under the same conditions.[10] Thus, oxidation of the 1-amino-derivative (11) gave an aryne which was intercepted with tetracyclone and with furan as the adducts (13) and (14), respectively (Scheme 4). In the absence of a diene, no dimer was detected, however; nor was any diphenylbutadiyne formed at this low temperature. The 2-amino-derivative (12) gave benzoyl cyanide azine (15) on oxidation.

Vapour-phase pyrolysis of the furan adduct (14) gave some diphenylbutadiyne. Again this could be formed

[6] B. M. Adger, S. Bradbury, M. Keating, C. W. Rees, R. C. Storr, and M. T. Williams, *J.C.S. Perkin I*, 1975, 31.
[7] B. M. Adger, C. W. Rees, and R. C. Storr, *J.C.S. Perkin I*, 1975, 45.
[8] H. von Neunhoeffer, H. D. Vötter, and M. Gais-Mutterer, *Tetrahedron Letters*, 1973, 219.
[9] J. M. Kramer and R. S. Berry, *J. Amer. Chem. Soc.*, 1971, **93**, 1304.
[10] C. D. Campbell and C. W. Rees, *J. Chem. Soc.* (*C*), 1969, 742.

from 3,6-diphenyl-4,5-didehydropyridazine, the intermediate being generated from its adduct (14) in the vapour phase by a retro-Diels–Alder reaction.



SCHEME 4

EXPERIMENTAL

1- *and* 2-*Amino-5-phenyltetrazole* (*cf.* ref. 4).—5-Phenyltetrazole (15.0 g, 0.103 mol) was dissolved in aqueous sodium carbonate (7.5%; 400 ml) at 70—80 °C and the solution vigorously stirred while hydroxylamine-*O*-sulphonic acid (35 g, 0.36 mol) was added in portions. Crystals (7.0 g) separated when the mixture had cooled, and they were filtered off. A second crop (1.6 g) was obtained by extracting the filtrate with ethyl acetate. The solids were combined and the components separated by column chromatography (basic alumina, 400 g). Elution with benzene–ether (2 : 1) gave 2-amino-5-phenyltetrazole (5.3 g, 32%), m.p. 109—111° (from benzene–hexane) (lit.,[4] 109—111°); $\nu_{max.}$ (Nujol) 3 300, 3 190, and 1 635 cm^{-1}. Further elution with ethyl acetate gave 1-amino-5-phenyltetrazole (2.1 g, 13%), m.p. 155—157° (lit.,[11] 155°).

5-Phenyl-2-phthalimidotetrazole (1).—2-Amino-5-phenyltetrazole (1.0 g, 0.062 mol) and phthaloyl chloride (1.37 g, 0.067 mol) were stirred in dry dichloromethane (250 ml) at room temperature. Triethylamine (1.4 g) was added dropwise. After 20 h the solution was washed with water and aqueous sodium carbonate, dried, and evaporated to leave a solid which was triturated with petroleum and dried (1.6 g, 88%). This material was a single substance (t.l.c. on silica; ether–petroleum, 1 : 1) and because of its thermal instability it was used in subsequent reactions without further purification. A portion was crystallised, with considerable loss of material, from ethanol; this gave fine cream-coloured needles of *5-phenyl-2-phthalimidotetrazole* m.p. 147—148° (decomp.) (Found: C, 61.7; H, 3.2; N, 24.1. $C_{15}H_9N_5O_2$ requires C, 61.9; H, 3.1; N, 24.1%); $\nu_{max.}$ 1 765 cm^{-1} (C=O).

Reaction of 5-Phenyl-2-phthalimidotetrazole with Dipolarophiles.— (a) *With cyclohexene.* The tetrazole (100 mg) was heated in cyclohexene (3 ml) at 83 °C for 12 h. Preparative layer chromatography (silica; ether–petroleum, 1 : 1) gave (at R_F 0.7) 7-phthalimido-7-azabicyclo[4.1.0]heptane (6) (5 mg, 7%), identical (i.r., t.l.c., mass spectrum) with an authentic specimen,[5] and (at R_F 0.6) *9-phenyl-7-phthalimido-7,8-diazabicyclo*[4.3.0]*non-8-ene* (3) (50 mg, 42%) as an oil which partially crystallised (Found: M^+, 345.149. $C_{21}H_{19}N_3O_2$ requires M^+, 345.148); $\nu_{max.}$ ($CHCl_3$) 1 785w, 1 770w, and 1 730 cm^{-1} (C=O); τ (100 MHz; $CDCl_3$) 7.8—8.8 (8 H, m), 6.5—6.9 (1 H, m), 5.5—5.7 (1 H, m), 2.78 (3 H), 2.25—2.6 (2 H, m), and 2.0—2.4 (4 H, m); *m/e* 347 (M^+), 302, 199, and 147 (base).

(b) *With dimethyl acetylenedicarboxylate.* The tetrazole (100 mg) and dimethyl acetylenedicarboxylate (250 mg) were heated in benzene (5 ml) at 80 °C for 12 h. The solvent was evaporated off and the residue triturated with ether, leaving a colourless solid (95 mg, 68%). This was crystallised to give *dimethyl 3-phenyl-1-phthalimidopyrazole-4,5-dicarboxylate* (4), m.p. 202—203.5° (from ethanol) (Found: C, 61.2; H, 3.8; N, 10.8. $C_{20}H_{15}N_3O_6$ requires C, 61.1; H, 3.8; N, 10.7%); $\nu_{max.}$ 1 773, 1 754, and 1 732 cm^{-1} (C=O); τ ($CDCl_3$) 6.2 (3 H, s), 6.1 (3 H, s), and 1.9—2.8 (9 H, m); *m/e* 405 (M^+, base).

(c) *With dibenzoylacetylene.* The tetrazole (110 mg) and dibenzoylacetylene (250 mg) were heated in benzene (5 ml) at 80 °C for 5 h. The solvent was removed and the residue was digested with ether (3 ml) to remove dibenzoylacetylene. The insoluble fraction, a colourless solid (140 mg), was crystallised to give *4,5-dibenzoyl-3-phenyl-1-phthalimidopyrazole* (5) (130 mg, 69%), m.p. 180—181° (from ethanol) (Found: C, 74.9; H, 4.1; N, 8.2. $C_{31}H_{19}N_3O_4$ requires C, 74.9; H, 3.8; N, 8.5%); $\nu_{max.}$ 1 760, 1 665, and 1 655 cm^{-1} (C=O); *m/e* 497 (M^+), 420, 351, 147, and 105 (base).

1-Amino-3,4,7-triphenylpyrazolo[3,4-d]*pyridazine* (7).—4,5-Dibenzoyl-3-phenyl-1-phthalimidopyrazole (280 mg) was heated in ethanol (10 ml) under reflux with hydrazine hydrate (250 mg) for 0.5 h. The mixture was cooled and the colourless precipitate of 2,3-dihydrophthalazine-1,4-dione was filtered off and washed with ethanol. The combined filtrate and washings were evaporated and the residue was crystallised to give *1-amino-3,4,7-triphenylpyrazolo*[3,4-d]*pyridazine* (176 mg, 87%), m.p. 207—208° (from benzene) (Found: C, 76.2; H, 4.8; N, 19.2. $C_{23}H_{17}N_5$ requires C, 76.0; H, 4.7; N, 19.3%); *m/e* 363 (M^+, base).

4,5,8-Triphenylpyridazino[4,5-d]*triazine* (8).—The pyrazolopyridazine (7) (205 mg) was stirred in dry dichloromethane (5 ml) and lead tetra-acetate (275 mg) was added in portions. The mixture was stirred for 10 min and was then rapidly percolated through a short silica column. Elution with ethyl acetate and trituration of the product with ether gave *4,5,8-triphenylpyridazino*[4,5-d]*triazine* (161 mg, 81%), m.p. 246—248° (bright yellow needles from ethanol) (Found: C, 76.1; H, 4.3; N, 19.3. $C_{23}H_{15}N_5$ requires C, 76.4; H, 4.2; N, 19.4%); $\lambda_{max.}$ (EtOH) 240 (ε 13 350) and 324 nm (8 900); *m/e* 361 (M^+) and 202 (base).

Pyrolysis of 4,5,8-Triphenylpyridazino[4,5-d]*triazine.*—The triazine (33 mg) was pyrolysed by heating at 200—210 °C and 0.05 mmHg and passing the vapour through a tube heated at 420 °C. The pyrolysis product, a yellow solid (22 mg), was triturated with ether to give yellow crystals (10 mg), m.p. 199—201°, which were recrystallised to give *1,4-diphenyl-5H-indeno*[1,2-d]*pyridazin-5-imine* (9), m.p. 213—215° (from ethyl acetate), $\nu_{max.}$ 3 260 (NH), 1 634, and 1 558 cm^{-1}; *m/e* 333 (M^+), 332 (base), 305, 304, 152, and 151. The substance was characterised further by its hydrolysis in dil. aqueous HCl for 10 min at 80 °C, to give *1,4-diphenyl-5H-indeno*[1,2-d]*pyridazin-5-one*, m.p. 213—216° (from ether) (Found: M^+, 334.113. $C_{23}H_{14}N_2O$

[11] R. Stollé and F. Helwerth, *Ber.*, 1914, **47**, 1132.

requires *M*, 334.111); $\nu_{max.}$ ($CHCl_3$) 1 713 (C=O), 1 607, and 1 550 cm^{-1}. Layer chromatography of the remaining mixture from the pyrolysate gave diphenylbutadiyne, m.p. and mixed m.p. 86—88°.

4,5-Dibenzoyl-1H-1,2,3-*triazole*.— Dibenzoylacetylene (2.34 g, 0.01 mol) in dimethylformamide (20 ml) was added dropwise during 20 min to a vigorously stirred suspension of finely powdered sodium azide (0.65 g, 0.01 mol) in dimethylformamide (20 ml) at −30 °C. The pale yellow solution was stirred at −30 °C for a further 20 min, then diluted to 100 ml with water, and acidified (dil. HCl); the pale yellow precipitate (2.7 g, 98%) was filtered off. Crystallisation gave 4,5-dibenzoyl-1,2,3-triazole, m.p. 165—167° (from ethanol) (lit.,[12] 164—165°).

1- *and* 2-*Amino*-4,5-*dibenzoyl*-1,2,3-*triazole*.— 4,5-Dibenzoyltriazole (5.0 g, 0.018 mol) in dry ether (250 ml) containing sufficient dioxan to cause complete dissolution, was converted into its sodium salt by addition of sodium hydride (0.95 g of a 50% dispersion). A solution of *O*-mesitylsulphonylhydroxylamine (4.3 g, 0.02 mol) in ether (50 ml) was added dropwise to the rapidly stirred suspension of the sodium salt. After 2 h the mixture was filtered and the filtrate evaporated to leave a gum (3.5 g). A portion (0.75 g) of the gum was separated into two major components by column chromatography (silica; ether–petroleum, 1 : 2). The first to be eluted was 1-*amino*-4,5-*dibenzoyl*-1H-1,2,3-*triazole* (0.08 g), m.p. 158—160° (from ether–hexane) (Found: C, 65.9; H, 4.2; N, 19.0. $C_{16}H_{12}N_4O_2$ requires C, 65.8; H, 4.1; N, 19.2%); $\nu_{max.}$ 3 320, 3 220 (NH), 1 675, 1 648, and 1 595 cm^{-1}; *m/e* 292 (M^+), 277, 264, and 105 (base). The second component was 2-*amino*-4,5-*dibenzoyl*-2H-1,2,3-*triazole* (0.30 g), m.p. 100—102° (from benzene–hexane) (Found: C, 66.1; H, 4.3; N, 19.0%); $\nu_{max.}$ 3 320, 3 250, 3 170w (NH), 1 673, 1 640, and 1 597 cm^{-1}; *m/e* 292 (M^+), 263, 248, and 105.

1-*Amino*-4,7-*diphenyl*-1H-*triazolo*[4,5-d]*pyridazine* (11).— 1-Amino-4,5-dibenzoyltriazole (0.150 g) was heated under reflux in ethanol (4 ml) with hydrazine hydrate (0.20 g) for 20 min, and gave 1-*amino*-4,7-*diphenyl*-1H-*triazolo*[4,5-d]-*pyridazine* (0.127 g, 86%), m.p. 182—184° (from ethanol) (Found: C, 65.8; H, 4.4; N, 29.0. $C_{16}H_{12}N_6$ requires C, 66.6; H, 4.2; N, 29.1%); $\nu_{max.}$ 3 385, 3 340, and 3 120 (NH) cm^{-1}; *m/e* 288 (M^+), 260, and 216 (base).

2-*Amino*-4,7-*diphenyl*-2H-*triazolo*[4,5-d]*pyridazine* (12).— By the procedure described for the 1-amino-isomer, 2-amino-4,5-dibenzoyltriazole gave *compound* (12), m.p. 221—223° (from ethanol) (Found: C, 66.6; H, 4.2; N, 28.9%); $\nu_{max.}$ 3 230 and 3 040 cm^{-1} (NH); *m/e* 288 (M^+, base) and 259.

In subsequent experiments involving the oxidation of the triazolopyridazines it was found convenient to prepare a mixture of the two isomers by reaction of the mixture of 1- and 2-amino-4,5-dibenzoyltriazoles with hydrazine hydrate. The mixture was then used in the oxidation experiments.

Oxidation of 1- *and* 2-*Amino*-4,7-*diphenyltriazole*[4,5-d]-*pyridazine*.—(a) The mixture of triazolopyridazines (50 mg) in dichloromethane (5 ml) containing calcium oxide (100 mg) was treated with lead tetra-acetate (90 mg) in portions. Evaporation of the filtrate and trituration of the residue with ether gave *benzoyl cyanide azine* (15) (18 mg), m.p. 205—206° (from ethanol) (Found: M^+, 258.090. $C_{16}H_{10}N_4$ requires *M*, 258.090); $\nu_{max.}$ 2 230w (C≡N); $\lambda_{max.}$ (EtOH) 240 (ε 8 920), 244sh (8 670), and 356 nm (31 200). No other products were isolated.

(b) *With tetracyclone*. The procedure described in (a) was repeated in the presence of tetraphenylcyclopentadienone (0.20 g). Layer chromatography (silica; ether–petroleum, 3 : 1) gave 1,4,5,6,7,8-*hexaphenylphthalazine* (13) (22 mg), m.p. 249—251° (from ethanol–petroleum) (Found: M^+, 586.240. $C_{44}H_{30}N_2$ requires *M*, 586.241); $\lambda_{max.}$ (EtOH) 270sh (ε 19 900) and 294sh nm (15 800).

(c) *With furan*. The mixture of aminotriazolopyridazines (0.35 g) was stirred in dichloromethane (5 ml) and furan (10 ml) with calcium oxide (1.0 g). Lead tetra-acetate (0.65 g) was added in portions. Chromatography of the product on silica (50 g) gave (i) benzoyl cyanide azine (0.138 g) and (ii) (with ether–petroleum, 1 : 3) 5,8-*epoxy*-5,8-*dihydro*-1,4-*diphenylphthalazine* (14) (0.157 g), m.p. 245—248° (from ethanol) (Found: M^+, 298.112. $C_{20}H_{14}N_2O$ requires *M*, 298.111); $\lambda_{max.}$ (EtOH) 266 nm (ε 26 500); τ ($CDCl_3$) 3.87 (2 H), 2.61 (2 H), and 1.9—2.5 (10 H, m); *m/e* 298 (M^+) and 202 (base).

Pyrolysis of the Furan Adduct (14).—The adduct (40 mg) was pyrolysed by sublimation at 200 °C and 0.05 mmHg and passage of the vapour through an oven at 550 °C. The crude pyrolysate (26 mg) was triturated with ether to give a substance tentatively identified as 1,4-*diphenylphthalazin*-5-*ol* (10 mg), m.p. 296—298° (from benzene); $\nu_{max.}$ 3 430w cm^{-1} (OH); $\lambda_{max.}$ (EtOH) 267 and 340 nm; *m/e* 298 (M^+), 297 (base), 202, and 84. Diphenylbutadiyne (3 mg), m.p. 86—88°, was isolated after layer chromatography of the remaining material.

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[12] J. J. Looker, *J. Org. Chem.*, 1965, **30**, 638.