1001. *Internuclear Cyclisation. Part XVIII.* Abnormal Cyclisations: Synthesis and Chemistry of Phthalan-1-spiro-1′-cyclohexadiene-3,4′-dione.*

By D. H. Hey, J. A. Leonard, and C. W. Rees.

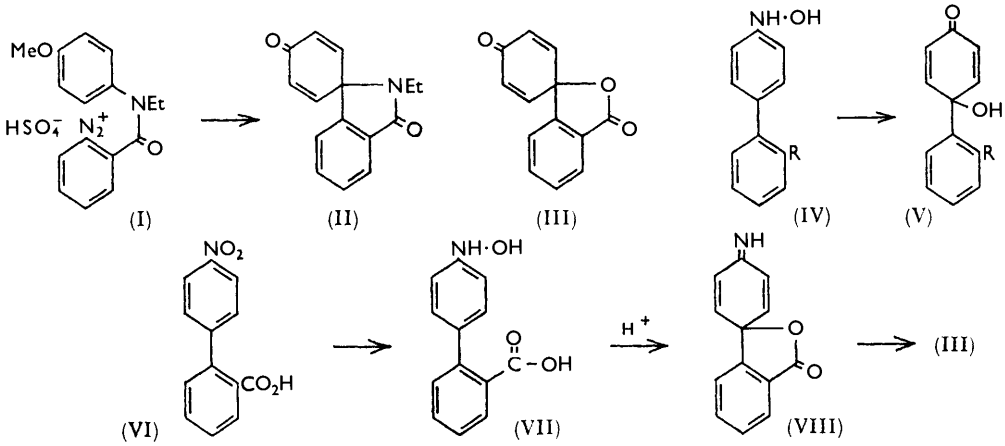
Acid-catalysed rearrangement of 4′-hydroxyaminobiphenyl-2-carboxylic acid (VII) proceeds with intramolecular participation by the carboxylic acid group to give phthalan-1-spiro-1′-cyclohexadiene-3,4′-dione (III), together with five minor products to which structures are assigned. Similar rearrangement of the *N*-ethylamide of the acid (VII) does not yield the corresponding spiro-dienone-lactam (II) but 7-hydroxy-3,4-benzocoumarin (X), together with the dienone-lactone (III). The ready aromatisation of this dienone-lactone (III) and its carbonyl derivatives on mild treatment with acid, alkali, and ethylamine, and on catalytic hydrogenation, is contrasted with the much greater stability of the dienone-lactam (II), obtained previously. The lactone (III) is not converted by ethylamine into the lactam (II), but both are converted into 10-ethyl-2-ethylaminophenanthridone (XXVIII). Mechanisms are proposed for these various reactions.

The abnormal decomposition of *N*-ethyl-4′-methoxybenzanilide-2-diazonium sulphate (I) to give 2-ethylisoindoline-1-spiro-1′-cyclohexadiene-3,4′-dione (II), and the chemical and spectral evidence for the structure of this dienone-lactam (II), were described in Part

* Part XVII, *J.*, 1961, 3873.

XVI.[1] We now describe the synthesis and chemistry of the corresponding dienone-lactone, phthalan-1-spiro-1′-cyclohexadiene-3,4′-dione (III) required as a model for the synthesis of compound (II) and related *N*-substituted lactams, and as a possible precursor to them.

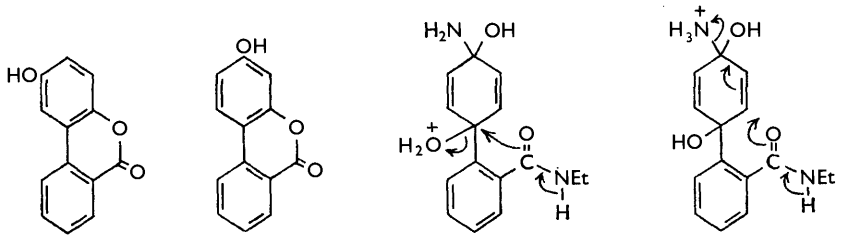
The acid-catalysed Bamberger rearrangement of *para*-substituted phenylhydroxylamines yields cyclohexa-2,5-dienimines, which are readily hydrolysed to the corresponding dienones;[2] *e.g.*, 4-hydroxyaminobiphenyl (IV; R = H) gave 1-hydroxy-1-phenylcyclohexadien-4-one (V; R = H).[3] In a repetition of this reaction the light-sensitive dienone



(V; R = H), which showed strong absorption at 1664 cm.$^{-1}$ characteristic of the cross-conjugated dienone-carbonyl group, was obtained in small yield, the major product being 4,4′-diphenylazoxybenzene. It was envisaged that the rearrangement of a 4′-hydroxyaminobiphenyl with a suitably nucleophilic 2-substituent might proceed by an intramolecular S_N2' reaction with formation of a spiro-dienone system. Thus, the 2-carboxylic acid should yield the required dienone-lactone as shown [(VII) ⟶ (VIII) ⟶ (III)]; and, if the normal intermolecular rearrangement[4] did occur, subsequent lactonisation of the intermediate hydroxy-acid (V; R = CO_2H) would also yield the lactone (III). 4′-Nitrobiphenyl-2-carboxylic acid[5] (VI) was reduced to the hydroxyamino-compound (VII) with zinc and ammonium chloride in ethanol at room temperature. Attempts to isolate and purify this hydroxylamine led only to 4,4′-di-(*o*-carboxyphenyl)azoxybenzene. An aqueous acid solution of the hydroxylamine was therefore continuously extracted with ether; the dienimine (VIII) was not isolated and the dienone (III) was removed from the acid as fast as it was formed. Fractional crystallisation of the extracted material gave the required dienone-lactone (III), m. p. 189°, the structure of which followed from its elementary analysis, reaction with 2,4-dinitrophenylhydrazine, decolorisation of potassium permanganate, strong absorption at 1770 cm.$^{-1}$ (γ-lactone-carbonyl) and 1672 cm.$^{-1}$ (cross-conjugated dienone-carbonyl), and the chemical transformations to be described. Four other crystalline compounds isolated from the ether extract are described below. The aqueous acid solution from the rearrangement was neutralised and continuously extracted with ether to yield, surprisingly, a small amount of the non-basic 6-hydroxy-3,4-benzocoumarin (IX), identical with an authentic specimen.[6] Since acid-catalysed rearrangement of the dienone (III) does not give this isomer (see below) it is thought to arise from a dienone–phenol rearrangement of the hydroxy-acid (V; R = CO_2H), the product of the

[1] Hey, Leonard, Moynehan, and Rees, *J.*, 1961, 232.
[2] Bamberger, *Annalen*, 1921, **424**, 233, 297.
[3] Abe, *Bull. Chem. Soc. Japan*, 1943, **18**, 93.
[4] Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 45.
[5] Hey, Leonard, and Rees, *J.*, 1962, 4579.
[6] Edwards and Lewis, *J.*, 1960, 2833.

intermolecular Bamberger rearrangement mentioned above. Other dienone–phenol rearrangements of 1-alkyl- and 1-aryl-1-hydroxycyclohexadien-4-ones have been shown to involve a similar 1,2-shift of the alkyl or aryl group.[3,7]



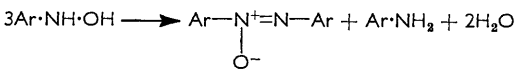
(IX) (X) (XIa) (XIb)

An attempt to extend this hydroxylamine rearrangement to the direct synthesis of the dienone-lactam (II) by starting with *N*-ethyl-4′-nitrobiphenyl-2-carboxyamide was unsuccessful. Reduction to the hydroxylamine, which was not isolated, was effected with a large excess of zinc, but the major product of the acid-catalysed rearrangement was the corresponding azoxy-compound, 4,4′-di-[*o*-(*N*-ethylcarbamoyl)phenyl]azoxybenzene, together with 7-hydroxy-3,4-benzocoumarin (X) (26%) and the dienone-lactone (III) (4%). Inexplicably, the coumarin (X) became the major product (60%) in one small-scale rearrangement. The formation of both products (III) and (X) can be satisfactorily explained in terms of the intermediate (XI), in which the amide group cyclises at the 1′- or 2′-carbon atom *via* its carbonyl-oxygen atom with displacement of water or ammonia (XIa and XIb, respectively). The imino-lactones so formed would rapidly hydrolyse to the products isolated; this scheme involves only acid-soluble intermediates since the reaction mixture was continuously extracted with ether. Formation of a related dienone-lactone by intramolecular nucleophilic displacement by the carbonyl group of an amide has been reported.[8] 7-Hydroxy-3,4-benzocoumarin (X) is the product of the dienone–phenol rearrangement of the dienone (III) but its formation in this way is considered unlikely here since none of this isomer could be detected in the same acid-catalysed rearrangement of 4′-hydroxyaminobiphenyl-2-carboxylic acid (VII), in which the dienone (III) is also formed.

2-Cyano-4′-nitrobiphenyl, prepared by dehydration of the amide of the nitro-acid (VI) with thionyl chloride, was similarly reduced to the impure hydroxylamine (IV; R = CN). Attempts to purify this resulted only in the separation of 4,4′-di-(*o*-cyanophenyl)azoxybenzene, which was also formed from the hydroxylamine in acid solution, together with a small amount of the dienone-lactone (III). The latter presumably arose from the hydroxycyanide (XII) as shown, the linearity of the cyanide group having prevented its intramolecular participation in the Bamberger rearrangement to give a lactam. As to the former, the ready formation of azoxy-compounds from hydroxylamines is well established,[2] being variously reported for aromatic hydroxylamines in the solid state,[9,10] and in neutral,[11,12] alkaline, and acidic media.[3,11] Bamberger recognised the simultaneous formation of the corresponding amine in many cases. Heller, Hughes, and Ingold [13] claim, as a result of a kinetic study of the decomposition of phenylhydroxylamine, that aniline and azoxybenzene are formed in a redox chain reaction, easily started by brief exposure to oxygen, but avoidable if the hydroxylamine has never been exposed to oxygen.

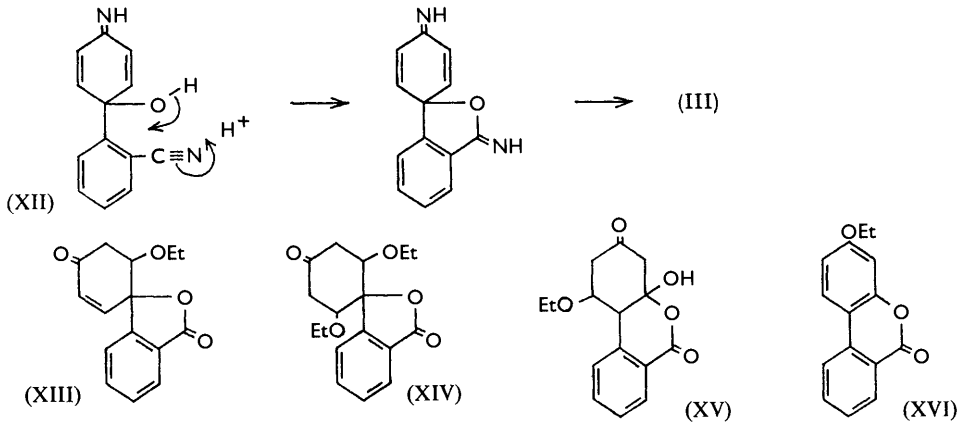
[7] Goodwin and Witkop, *J. Amer. Chem. Soc.*, 1957, **79**, 179.
[8] Corey and Haefele, *J. Amer. Chem. Soc.*, 1959, **81**, 2225.
[9] Sidgwick, " Organic Chemistry of Nitrogen," Oxford Univ. Press, London, 1945, p. **163**.
[10] Sugimori, *Bull. Chem. Soc. Japan*, 1960, **33**, 1599.
[11] Bamberger, *Ber.*, 1894, **27**, 1347, 1548.
[12] Gilman and Kirby, *J. Amer. Chem. Soc.*, 1926, **48**, 2190.
[13] Heller, Hughes, and Ingold, *Nature*, 1951, **168**, 909.

The reduction of 2-cyano-4′-nitrobiphenyl and rearrangement of the resulting hydroxylamine in aqueous acid was, therefore, performed throughout in an atmosphere of oxygen-free nitrogen. The azoxy-compound and the amine were both isolated (*ca.* 70%) in almost equimolecular amounts, consistent with the reaction:



in general agreement with Bamberger's work.[2] In this case, at least, the hydroxylamine disproportionation thus appears to be insensitive to oxygen.

By-products in the Synthesis of the Dienone-lactone (III).—Four crystalline compounds, m. p.s 112·5°, 127°, 177—180°, and 121°, were isolated from the ethereal extracts of the acidic solution of the hydroxylamine (VII), after removal of the dienone-lactone (III). All were nitrogen-free and appeared to be either δ- or γ-lactones resulting from addition of one or two mol. of ethanol to the dienimine (VIII) or the dienone (III), with or without subsequent rearrangement. The chemical and spectral properties of these compounds are consistent with the tentatively proposed structures (XIII), (XIV), (XV), and (XVI),



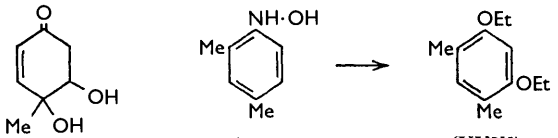
respectively, the formation of which, under the reaction conditions, can be readily rationalised.[14] A by-product (XVII) from the rearrangement [7] of *p*-tolylhydroxylamine presumably resulted from an addition of water analogous to the addition of ethanol to the dienone (III) to give compound (XIII); further addition of ethanol gives compound (XIV). Compound (XVI) would result from addition of ethanol to the C=N bond of the dienimine (VIII) followed by acid-catalysed rearrangement with loss of ammonia. 4,6-Diethoxy-*m*-xylene (XVIII), a minor product of the rearrangement [2] of 4-*m*-xylylhydroxylamine (XIX), could have been formed in precisely the same way.

Reactions of Phthalan-1-spiro-1′-cyclohexadiene-3,4′-dione (III).—The remarkable stability of the dienone-lactam (II) towards acid was described in Part XVI [1] of this series; it was stable to boiling concentrated hydrochloric acid and to acetic anhydride–sulphuric acid at room temperature and required the latter mixture at 100° or phosphoric acid at 170° to effect its rearrangement to 10-ethyl-3-hydroxyphenanthridone. This stability is further illustrated by the recovery of 25% of the lactam after it had been heated with phosphorus pentachloride at 175° for 7 hr. (cf. ref. 15); equal amounts of 3-chloro-10-ethylphenanthridone and 3,9-dichlorophenanthridine were also formed in this reaction.*

* In assigning these two structures it is assumed that the rearrangement had proceeded by a 1,2-aryl shift, as was proved [1] for the rearrangements in acetic anhydride and in phosphoric acid, and not by C–N bond fission.

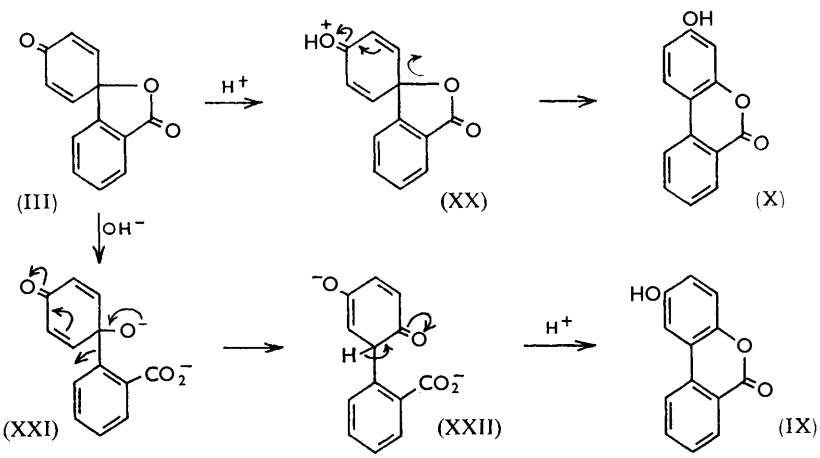
[14] Leonard, Ph.D. Thesis, London, 1962.
[15] Newman and Wood, *J. Amer. Chem. Soc.*, 1959, **81**, 6450.

This stability in acidic media was associated with the presence of the lactam group and was not to be expected in the corresponding dienone-lactone (III), which did, in fact, show the usual lability of cyclohexadienones toward acid. Indeed, all its reactions and those of its carbonyl derivatives were characterised by a great tendency to undergo aromatisation. In hot dilute sulphuric acid it rapidly isomerised to 7-hydroxy-3,4-benzocoumarin (X)



(XVII) (XIX) (XVIII)

(80%), identical with an authentic specimen;[16] thus the dienone–phenol rearrangement had proceeded with C–O bond fission (see the abbreviated scheme, XX), and not with C–C bond fission as for the lactam (II). In hot 10% aqueous sodium hydroxide the lactone (III) very rapidly rearranged to the isomeric 6-hydroxy-3,4-benzocoumarin[6] (IX); a possible mechanism (XXI ⟶ XXII ⟶ IX) is shown, though opening of the lactone ring and aryl migration may be concerted.



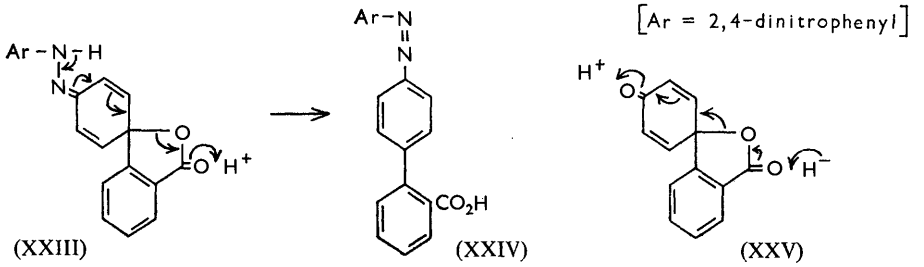
When treated with 2,4-dinitrophenylhydrazine the dienone (III) gave a product with the expected elementary analysis, but the infrared spectrum clearly showed this to be, not the hydrazone-lactone (XXIII), but the isomeric azo-carboxylic acid (XXIV). The ease with which the indicated rearrangement occurred illustrates the lability of this system. The dinitrophenylhydrazone of the dienone-lactam (II) was, by contrast, stable to aqueous acid and alkali.

Similarly, catalytic hydrogenation of the lactone (III) did not give the corresponding tetrahydro-compound, as did the lactam (II),[1] but gave 4'-hydroxybiphenyl-2-carboxylic acid, again illustrating the greater tendency of the former to aromatise. A concerted reduction (as in XXV) appears more probable than formation and reduction of a dienol since none of the corresponding dienol or its rearrangement product was observed in the same reduction of the lactam (II).

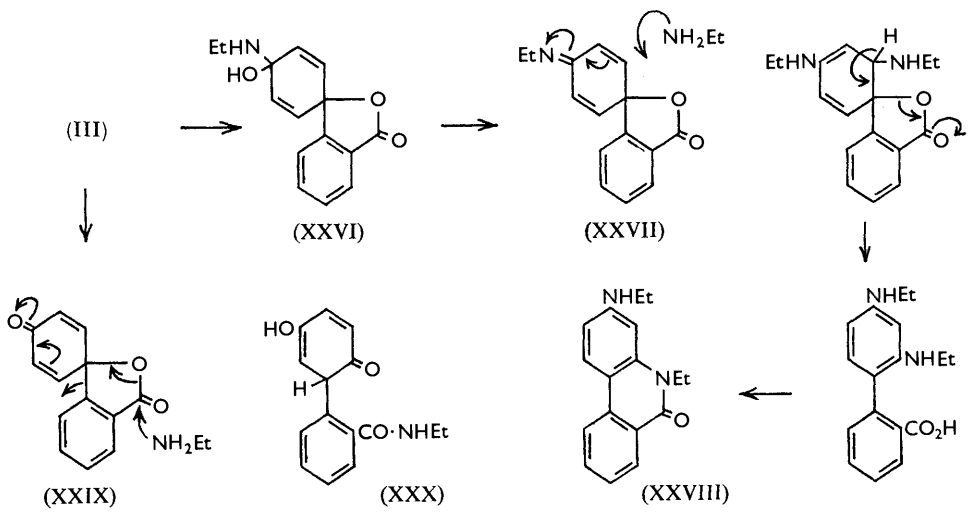
This considerable reactivity of the dienone-lactone (III) has frustrated attempts to convert it into the corresponding lactams, such as (II). Application of the standard reaction with amines gave a complex series of products. The lactone was heated with ethanolic ethylamine in sealed tubes at temperatures from 18° to 210° for periods of from

[16] Ghosh, Todd, and Wilkinson, *J.*, 1940, 1393.

10 to 100 hours, and the products were chromatographed on alumina. No reaction occurred at the lowest temperature, or with pure ethylamine at 5°, but above room temperature 10-ethyl-2-ethylaminophenanthridone (XXVIII) was always isolated and its yield increased with increasing temperature until at 210° it became the sole product. Its



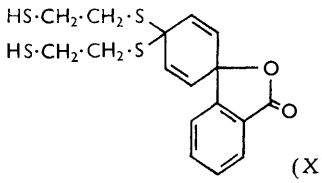
formation must initially involve attack of the dienone-carbonyl group by ethylamine to give the imine (XXVII). In support of this a compound, $C_{15}H_{15}NO_3$, m. p. 124—126°, which has been assigned the structure (XXVI), was isolated in small amount after a reaction at 42° for 10 hours; this compound showed absorption at 1770 (γ-lactone-carbonyl) and 3390 cm.$^{-1}$ (OH) but not in the characteristic dienone-carbonyl region. The subsequent course of the reaction probably involved 1,4-addition of ethylamine to the imine (XXVII), with rearrangement and cyclodehydration as shown, to give the stable phenanthridone (XXVIII).



After longer at 42° the products included this phenanthridone (XXVIII) and a compound, $C_{15}H_{15}NO_3$, m. p. 183°, which was particularly difficult to purify and was isolated in decreasing amounts as the reaction temperature was increased. This compound is considered to be *N*-ethyl-2′,5′-dihydroxybiphenyl-2-carboxyamide (from XXX) on the basis of its infrared spectrum, its solubility in water which is greatly increased by addition of alkali, its decolorisation of potassium permanganate, and its probable formation by a mechanism involving initial attack at the lactone-carbonyl (see XXIX) exactly analogous to the alkaline rearrangement of the dienone-lactone described above.

However, of the two competing processes of nucleophilic attack of the dienone-lactone

(III) by ethylamine at the dienone- or at the lactone-carbonyl group, predominance of the former was evident from the retention of the γ-lactone absorption at 1770 cm.$^{-1}$ in the spectra of product mixtures. Attention was therefore directed to carbonyl derivatives of the dienone. The ethylene ketal could not be obtained as a solid, but treatment with ethanedithiol and boron trifluoride–ether complex in methanol, followed by chromatography, gave a crystalline product, m. p. 85—95°. The molecular formula, $C_{17}H_{18}O_2S_4$, and the γ-lactone absorption (1770 cm.$^{-1}$) suggested structure (XXXI) for this product. The cyclic mono(ethylene thioketal) could not be obtained. This derivative showed enormously enhanced stability compared with the parent dienone, for under all conditions where the latter reacted with ethylamine and also when treated with ethylamine hydrochloride at 155° it, alone, was recovered. Pure ethylamine, with or without ethylamine hydrochloride, at 220° converted it into a yellow oil.



(XXXI)

The stability of the dienone-lactam (II) towards ethylamine under the conditions of its attempted synthesis was briefly investigated. It was largely unaffected at temperatures of up to 100°; at 210° the major product was again 10-ethyl-2-ethylaminophenanthridone (XXVIII), identical with that from the dienone-lactone (III) and probably formed by a similar mechanism.

Alternative procedures employed for the treatment of the lactone (III) with amines included the reaction *in situ* with ammonia from the thermal decomposition of urea and with sodamide in liquid ammonia. The former reaction, and probably the latter, gave 2-aminophenanthridone, presumably formed in a manner similar to that given for its bis-*N*-ethyl derivative (XXVIII).

Experimental

Infrared spectra were determined for Nujol mulls with a Grubb-Parsons double-beam spectrophotometer. Chromatography was on type H alumina (P. Spence Ltd.); organic extracts were dried with anhydrous magnesium sulphate; light petroleum refers to the fraction of b. p. 60—80°. Products were identified by mixed m. p. determination with authentic compounds and by comparison of infrared spectra, wherever possible.

Reduction of 4′-Nitrobiphenyl-2-carboxylic Acid (VI), *and Acid-catalysed Rearrangement of the Hydroxylamine.*—Numerous preliminary experiments with different reducing agents, including zinc and dilute sulphuric acid, zinc and ethanol, and aluminium amalgam, for various reaction times, and at various temperatures, with subsequent acid-catalysed rearrangement, indicated that the optimum conditions were as follows.

A solution of 4′-nitrobiphenyl-2-carboxylic acid (15 g.) in hot ethanol (700 ml.) was allowed to cool. To the stirred solution was added a mixture of ethanol (70 ml.), water (30 ml.), and ammonium chloride (12 g.). Zinc dust (" AnalaR ") (15 g.) was added during 45 min. and the mixture, which had become deep yellow, was stirred for a further 20 min. The filtered solution was evaporated to a small volume under reduced pressure and the yellow azoxy-compound separated. Aqueous 10% sulphuric acid (1·5 l.) was added and the mixture shaken for 15 min. The acid solution (A), after filtration, was continuously extracted with ether for 5 days. The residue (3·4 g.) had an infrared spectrum which indicated the presence of a small quantity of starting material; recrystallisation from ethanol gave *4,4′-di-(o-carboxyphenyl)azoxybenzene* as a yellow powder, m. p. 286—287° (Found: C, 71·6; H, 4·4; N, 6·2. $C_{26}H_{18}N_2O_5$ requires C, 71·2; H, 4·1; N, 6·4%). Several fractions were taken during the extraction. During the

first 10 hr. only the azoxy-compound (0·7 g.) was recovered; subsequently, the fractions were combined. After removal of the solvent, traces of the azoxy-compound remaining were removed by crystallisation from ethanol. Concentration of the mother-liquor gave needles (2·2 g.) which, after crystallisation from ethanol, afforded *phthalan-1-spiro-1′-cyclohexadiene-3,4′-dione* (III) in large blades or needles, m. p. 189° (Found: C, 73·7; H, 4·0; O, 22·6. $C_{13}H_8O_3$ requires C, 73·6; H, 3·8; O, 22·6%), $\nu_{max.}$ 1770, 1672, and 1633 cm.$^{-1}$ (C=C of the dienone), which decolorised aqueous potassium permanganate and reacted with 2,4-dinitrophenylhydrazine reagent. Removal of solvent from the mother-liquor gave an oil (5·3 g.), which, in ether solution, was extracted with aqueous sodium hydroxide, this extract being then acidified; filtration gave 2′-nitrobiphenyl-2-carboxylic acid (0·75 g.), m. p. 169—170°, present as an impurity in the starting material. A solution of the oil in benzene was adsorbed on neutral alumina (2 × 30 cm.) and eluted as follows.

(i) Benzene (2 l.) gave a colourless oil (0·9 g.) which, by fractional crystallisation from benzene–light petroleum, gave needles (XIII) (0·17 g.), m. p. 112·5° (Found: C, 69·7; H, 5·4%; *M*, 236. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%; *M*, 258), $\nu_{max.}$ 1771 (γ-lactone-carbonyl) and 1683 cm.$^{-1}$ (unsaturated-ring ketone), and needles (XIV) (0·1 g.), m. p. 127° (Found: C, 68·2; H, 7·0. $C_{17}H_{20}O_5$ requires C, 67·1; H, 6·6%), $\nu_{max.}$ 1773 (γ-lactone-carbonyl) and 1717 cm.$^{-1}$ (saturated six-membered-ring ketone). Both compounds reacted with 2,4-dinitrophenylhydrazine and were soluble in warm 5% aqueous sodium hydroxide. The compound, m. p. 112·5°, decolorised aqueous potassium permanganate; the compound, m. p. 127°, did not. (ii) Benzene–ether (4 : 1; 2·5 l.) yielded an oil (0·65 g.), which crystallised from light petroleum in needles (0·27 g.), m. p. 121° (Found: C, 75·0; H, 4·9. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%), $\nu_{max.}$ 1739 cm.$^{-1}$. This compound, *7-ethoxy-3,4-benzocoumarin* (XVI), was soluble in hot 10% aqueous sodium hydroxide and was precipitated on acidification. (iii) Ether (1 l.) gave an oil (1 g.) which, on recrystallisation from benzene–light petroleum, gave a powder (0·3 g.), m. p. 177—180° (Found: C, 65·2; H, 5·7. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%), $\nu_{max.}$ 3367 (OH absorption), 1739 (δ-lactone-carbonyl), and 1721 cm.$^{-1}$ (saturated six-membered-ring ketone). This compound, *5-ethoxy-4a,5,6,7,8,8a-hexahydro-8a-hydroxy-7-oxo-3,4-benzocoumarin* (XV), reacted with 2,4-dinitrophenylhydrazine and was soluble in warm aqueous sodium hydrogen carbonate.

The acid solution (A) was neutralised and continuously extracted with ether for 2 days. The solid obtained from the extract crystallised from benzene to give 6-hydroxy-3,4-benzocoumarin (IX) (0·3 g.).

2-Cyano-4′-nitrobiphenyl.—A mixture of 4′-nitrobiphenyl-2-carboxylic acid (10 g.) and thionyl chloride (30 ml.) was boiled under reflux for 30 min. The excess of thionyl chloride was removed under reduced pressure and the solution of the residual oil in acetone (20 ml.) was added to cold aqueous ammonia (*d* 0·88; 20 ml.) with stirring. After 30 min., addition of a large volume of water and filtration gave a solid (9 g.), which was dried; recrystallisation from benzene–ethanol gave 4′-nitrobiphenyl-2-carboxyamide. A mixture of this amide (5 g.) and thionyl chloride (10 ml.) was boiled under reflux for 3 hr. The excess of thionyl chloride was removed with boiling benzene, chloroform (75 ml.) was added, and the resulting solution washed with dilute sodium hydroxide and water, and dried. Removal of the solvent and crystallisation of the residue from ethanol gave *2-cyano-4′-nitrobiphenyl* (3·8 g.) in needles, m. p. 134° (Found: C, 69·8; H, 3·4; N, 12·3. $C_{13}H_8N_2O_2$ requires C, 69·6; H, 3·6; N, 12·5%).

Reduction of 2-Cyano-4′-nitrobiphenyl, and Acid-catalysed Rearrangement of the Hydroxylamine.—(*a*) A stirred solution of 2-cyano-4′-nitrobiphenyl (0·3 g.) in ethanol (60 ml.) and water (2 ml.) was treated with ammonium chloride (0·3 g.), and then zinc powder (" AnalaR ") (1 g.) was added in small portions during 1 hr. After a further 30 min. the mixture was filtered; evaporation of the filtrate gave a yellow powder (0·27 g.). Extraction of the solid with ether left a residue (0·03 g.), which crystallised from acetic acid to give *4,4′-di-(o-cyanophenyl)azoxybenzene* in yellow needles, m. p. 332° (decomp.) (Found: N, 13·6. $C_{26}H_{16}N_4O$ requires 14·0%). Evaporation of the extract afforded the impure hydroxyamino-compound (0·24 g.) (IV; R = CN), which gave a positive Tollen's test; its infrared spectrum had a sharp peak at 3268 cm.$^{-1}$ (N–H) and a broad shoulder at 3205 cm.$^{-1}$ (N–OH). Attempted crystallisation gave only more azoxy-compound.

(*b*) 2-Cyano-4′-nitrobiphenyl (1 g.) in ethanol (200 ml.) and water (8 ml.), with ammonium chloride (1 g.), was reduced with zinc (3·5 g.) as above, but in an atmosphere of " white-spot " nitrogen. Removal of solvent under nitrogen gave the same product (0·91 g.) as in (*a*). Aqueous

10% sulphuric acid (200 ml.) was added and the mixture stirred under nitrogen for 2 days. Filtration yielded the azoxy-compound (0·46 g.). Neutralisation of the filtrate, extraction with ether, and removal of the solvent from the extract gave a solid (0·2 g.), which crystallised from benzene–light petroleum to yield *4'-amino-2-cyanobiphenyl* in pale yellow needles, m. p. 119·5° (Found: C, 79·9; H, 5·6. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2%).

(*c*) The reduction was effected as in (*b*). Ether (150 ml.) was added to the reduction product, and the mixture boiled under reflux for 10 min. in an atmosphere of nitrogen. The azoxy-compound (0·15 g.), m. p. 332°, separated on filtration into 10% sulphuric acid (200 ml.). The ether–acid mixture was stirred under nitrogen for 4 days, with occasional addition of ether. More azoxy-compound (0·31 g.) separated. The ether layer, on evaporation, afforded an oily solid, which on extraction with light petroleum left a residue (0·05 g.), m. p. 186—187°, of phthalan-1-spiro-1'-cyclohexadiene-3,4'-dione (III). Evaporation of the extract gave an oil (0·22 g.). The amine (0·2 g.) was recovered from the neutral solution as in (*b*).

N-Ethyl-4'-nitrobiphenyl-2-carboxyamide.—The acid chloride from 4'-nitrobiphenyl-2-carboxylic acid (20 g.) in acetone (30 ml.) was added to 33% ethanolic ethylamine (50 ml.) with stirring. After 30 min., the mixture was evaporated to a small volume and allowed to cool. Filtration and crystallisation of the residue from benzene–light petroleum gave *N-ethyl-4'-nitrobiphenyl-2-carboxyamide* (12·6 g.) in needles, m. p. 177—177·5° (Found: C, 66·7; H, 5·2; N, 10·8. $C_{15}H_{14}N_2O_3$ requires C, 66·7; H, 5·2; N, 10·4%).

Reduction of N-Ethyl-4'-nitrobiphenyl-2-carboxyamide, and Acid-catalysed Rearrangement of the Hydroxylamine.—Preliminary experiments, under conditions similar to those already described, led to the recovery of large amounts of starting material, and therefore a large excess of zinc was used.

(*a*) *N*-Ethyl-4'-nitrobiphenyl-2-carboxyamide (0·5 g.) in ethanol (25 ml.) and water (2 ml.) was treated with ammonium chloride (0·5 g.), and zinc powder (" AnalaR ") (2 g.) was added with stirring during 1 hr. After a further 30 min., the mixture was filtered, the filtrate was partly evaporated, and 10% sulphuric acid (70 ml.) was added. The mixture was shaken for 15 min., then filtered and extracted continuously with ether for 5 days. The residue (0·032 g.) crystallised from ethanol, to give *4,4'-di-*[*o*-(*N-ethylcarbamoyl*)*phenyl*]*azoxybenzene* in yellow-orange needles, m. p. 270—271° (Found: C, 72·7; H, 5·9. $C_{30}H_{28}N_4O_3$ requires C, 73·1; H, 5·7%). The extracts contained the azoxy-compound (0·008 g.) in suspension. Removal of ether from the combined extracts gave a pale brown solid (0·25 g.), which crystallised from ethanol to give 7-hydroxy-3,4-benzocoumarin (X), m. p. 239—240°. The infrared spectrum of the crude product indicated absorption peaks in addition to those of the main product, namely, at 1770, 952, 929, and 857 cm.$^{-1}$. These coincided with peaks in the infrared spectrum of phthalan-1-spiro-1'-cyclohexadiene-3,4'-dione (III).

(*b*) The nitro-compound (5 g.) was reduced as in (*a*). The concentrated, ethanolic solution was treated with 10% sulphuric acid (500 ml.) and the mixture shaken for 15 min. The azoxy-compound (0·98 g.) was removed by filtration. Fractions taken during the first day of continuous extraction yielded starting material (0·5 g.) and the azoxy-compound (0·43 g.). Subsequent fractions taken during one week gave, after removal of the solvent, a total residue of 1·37 g. The crude product was treated with cold, dilute aqueous sodium hydroxide and filtered. The residue (0·11 g.) was phthalan-1-spiro-1'-cyclohexadiene-3,4'-dione, m. p. 186—187°. Acidification of the alkaline solution gave 7-hydroxy-3,4-benzocoumarin (1 g.), m. p. 239—240°.

Reaction of 2-Ethylisoindoline-1-spiro-1'-cyclohexadiene-3,4'-dione (II) *with Phosphorus Pentachloride.*—The isoindoline (0·5 g.) was heated with phosphorus pentachloride (1·4 g.) and phosphorus oxychloride (1 ml.) at 175° for 7 hr., poured into water, and extracted with chloroform. The solvent was removed and the residual yellow oil in benzene was adsorbed on alumina (1 × 25 cm.) and eluted as follows: (i) Benzene–light petroleum (1 : 1; 500 ml.) gave a yellow oil (0·11 g.), which crystallised from light petroleum (b. p. 40—60°), yielding *3,9-dichlorophenanthridine* in needles, m. p. 69—70° (Found: C, 63·2; H, 3·2. $C_{13}H_7Cl_2N$ requires C, 62·9; H, 2·9%). (ii) Benzene (800 ml.) gave a solid (0·11 g.), which crystallised from benzene–light petroleum, yielding *3-chloro-10-ethylphenanthridone* in needles, m. p. 119° (Found: C, 69·4; H, 4·5. $C_{15}H_{12}ClNO$ requires C, 69·9; H, 4·7%). (iii) Benzene–ether (10 : 1; 400 ml.) gave starting material (0·12 g.).

Reactions of Phthalan-1-spiro-1'-cyclohexadiene-3,4'-dione (III).—(*a*) *With aqueous acid.* The dienone-lactone (0·02 g.) in a mixture of sulphuric acid (1 ml.) and water (5 ml.) was boiled under reflux for 2 hr. On cooling, fine needles (0·016 g.) separated. When recrystallised from

benzene–ethanol, these gave 7-hydroxy-3,4-benzocoumarin (X), m. p. and mixed m. p. 239 240° (Found: C, 73·5; H, 4·0. Calc. for $C_{13}H_8O_3$: C, 73·6; H, 3·8%).

(*b*) *With aqueous alkali.* The dienone-lactone (0·5 g.) in 10% aqueous sodium hydroxide (15 ml.) was heated with stirring on a steam-bath. The brown solution was cooled and acidified. The solid (0·35 g.) which separated crystallised from benzene–ethanol to yield 6-hydroxy-3,4-benzocoumarin (IX), m. p. and mixed m. p. 227—228°.

(*c*) *With* 2,4-*dinitrophenylhydrazine.* The dienone-lactone (0·05 g.) was treated with the reagent in the usual way. Addition of dilute hydrochloric acid gave a deep-red precipitate. The solid was dissolved in chloroform, adsorbed on Celite–bentonite (1 : 4 w/w; 1 × 10 cm.), and eluted with chloroform (50 ml.). Evaporation of the solvent gave red 4′-(2,4-*dinitrophenylazo*)*biphenyl*-2-*carboxylic acid* (XXIV) (0·05 g.), m. p. 192° (Found: C, 57·9; H, 3·5; N, 13·9. $C_{19}H_{12}N_4O_6$ requires C, 58·2; H, 3·1; N, 14·3%). The infrared spectrum of this compound showed no absorption peaks corresponding to N–H, a γ-lactone-carbonyl, or C=C of a cross-conjugated dienimine; it had $\nu_{max.}$ 1692 cm.$^{-1}$, characteristic of an aromatic carboxylic acid.

(*d*) *Hydrogenation.* The dienone-lactone (0·082 g.) in ethanol (20 ml.), containing Adams catalyst (0·1 g.) and saturated with hydrogen, absorbed hydrogen (17·8 ml., 2·06 mol.) in 3 hr. The solution was filtered and evaporated; crystallisation of the residue from ethanol gave 4′-hydroxybiphenyl-2-carboxylic acid (0·05 g.), m. p. 205°.

(*e*) *With ethanedithiol.* The lactone-dienone (0·5 g.) in methanol (10 ml.) and ethane-1,2-dithiol (0·8 ml.) was shaken with boron trifluoride–ether complex (0·6 ml.) at room temperature overnight. After slow dissolution of the dienone-lactone, an oil separated. The mixture was evaporated, benzene added, and the solution adsorbed on alumina (2 × 20 cm.) and eluted as follows: (i) Light petroleum (2 l.) gave a solution of unchanged ethanedithiol. (ii) Ether (2 l.) yielded a colourless oil (0·41 g.), which slowly solidified. Purification of this compound could only be effected by addition of light petroleum to its ethereal solution and washing the precipitate by decantation. Filtration caused immediate reversion to the oil. The product, 4′,4′-*di*-(2-*mercaptoethylthio*)*phthalan*-1-*spiro*-1′-*cyclohexadiene* (XXXI) was obtained as a colourless powder, m. p. 85—95° (Found: C, 53·6; H, 5·1. $C_{17}H_{18}O_2S_4$ requires C, 53·4: H, 4·8%).

Reaction of the Dienone-lactone (III) *with Ethylamine.*—The dienone-lactone (0·1 g.) in ethylamine (1 ml.) was kept at 5° for 10 weeks. Samples taken during this time had identical infrared spectra and no change in the dienone- or lactone-carbonyl absorption was observed. Samples of the dienone-lactone (0·2 g.) in ethanol (12 ml.) and 33% ethylamine in ethanol (1 ml.) were heated in sealed tubes at the temperatures and for the times shown below. The mixtures were evaporated to dryness under reduced pressure and the residues dissolved in benzene, adsorbed on alumina (1 × 10 cm.), and eluted as indicated.

(*a*) *At* 18° *for* 100 *hr.* (i) Benzene–light petroleum (1 : 1; 150 ml.) and benzene (150 ml.) afforded starting material (0·06 g.). (ii) Benzene–chloroform (1 : 1; 300 ml.) gave a solid (0·11 g.). The infrared spectrum indicated a complex mixture which could not be separated by further chromatography and crystallisation.

(*b*) *At* 42° *for* 20 *hr.* (i) Benzene–light petroleum (1 : 1; 100 ml.) gave a solid (0·05 g.) which, after crystallisation from benzene–light petroleum, had m. p. 165·5° alone and mixed with 10-ethyl-2-ethylaminophenanthridone (XXVIII). (ii) Benzene (100 ml.) and benzene–chloroform (3 : 1; 200 ml.) yielded an oil (0·12 g.), which crystallised from ether–light petroleum in prisms, m. p. 183° (Found: C, 69·7; H, 5·8; N, 5·2. $C_{15}H_{15}NO_3$ requires C, 70·0; H, 5·9; N, 5·4%), $\nu_{max.}$ 3195, 1684, 1629, 913, 864, and 762 cm.$^{-1}$. This compound, N-*ethyl*-1′,2′-*dihydro*-5′-*hydroxy*-2′-*oxobiphenyl*-2-*carboxyamide* (XXX), was soluble in water but far more readily soluble in dilute aqueous alkali.

The products and residues from other fractions had infrared spectra which showed a medium peak at 1770 cm.$^{-1}$, indicating either starting material or its Schiff's base with ethylamine. The compound, m. p. 183°, in particular, was difficult to purify.

After 10 hr., only starting material (0·05 g.) and a compound, 4′-*ethylaminophthalan*-1-*spiro*-1′-*cyclohexadien*-4′-*ol* (XXVI) (0·015 g.), m. p. 124—126° (Found: C, 69·6; H, 6·4; N, 5·4. $C_{15}H_{15}NO_3$ requires C, 70·0; H, 5·9; N, 5·4%), were isolated.

(*c*) *At* 80° *for* 20 *hr.* (i) Benzene–light petroleum (1 : 1; 100 ml.) yielded 10-ethyl-2-ethylaminophenanthridone (0·082 g.). (ii) Benzene (200 ml.), benzene–chloroform (5 : 1; 200 ml.) and (3 : 1; 200 ml.), and chloroform (200 ml.) gave the compound, m. p. 183° (0·07 g.), in an impure state.

After 10 hr., 10-ethyl-2-ethylaminophenanthridone (0·03 g.), starting material (0·04 g.), and a complex mixture (0·05 g.) were isolated by chromatography.

(*d*) *At* 100° *for* 20 *hr.* (i) Benzene (300 ml.) yielded 10-ethyl-2-ethylaminophenanthridone (0·095 g.). (ii) Benzene–chloroform (1 : 1; 100 ml.) and chloroform (400 ml.) gave a mixture (0·09 g.), which on crystallisation from methanol afforded 7-hydroxy-3,4-benzocoumarin (X) (0·01 g.). Evaporation of the mother-liquor to dryness gave the impure compound, m. p. 183°.

(*e*) *At* 150° *for* 20 *hr.* (i) Benzene (400 ml.) yielded 10-ethyl-2-ethylaminophenanthridone (0·105 g.). (ii) Benzene–chloroform (1 : 1; 200 ml.) and chloroform (400 ml.) gave the compound, m. p. 183° (0·03 g.).

(*f*) *At* 210° *for* 20 *hr.* (i) Benzene (200 ml.) gave 10-ethyl-2-ethylaminophenanthridone (0·127 g.). (ii) Chloroform (400 ml.) gave only small quantities of tar.

Reactions of the Dienone-lactam (II) *with Ethylamine.*—The dienone-lactam (0·2 g.) was treated with alcoholic ethylamine under the same conditions as the dienone-lactone. The products were separated chromatographically as before.

(*a*) *At* 42° *for* 20 *hr.* (i) Benzene (400 ml.) gave starting material (0·16 g.). At 80° and 100° similar recoveries of the dienone-lactam were achieved.

(*b*) *At* 210° *for* 20 *hr.* (i) Benzene–light petroleum (1 : 1; 100 ml.) gave 10-ethyl-2-ethylaminophenanthridone (XXVIII) (0·107 g.). (ii) Benzene (50 ml.) gave a pale brown solid (0·06 g.), m. p. 104—105° (Found: C, 78·4; H, 9·6%), $\nu_{max.}$ 3436, 3311, 1621, 837, and 767 cm.$^{-1}$. The compound was soluble in aqueous acid. (iii) Chloroform (200 ml.) yielded tars in small amount.

Attempted Reactions of the Dienone-lactone–Ethanedithiol Product (XXXI) *with Ethylamine and Ethylamine Hydrochloride.*—(*a*) The product (0·05 g.) in ethanol (15 ml.) and 33% ethylamine in ethanol (0·25 ml.) was heated in a sealed tube at 40° for 20 hr. The residue, after evaporation, was adsorbed from benzene on alumina (1 × 10 cm.) and eluted with benzene (100 ml.) and ether (400 ml.), to give starting material (0·03 g.) only. A similar experiment at 200° also gave starting material only.

(*b*) The product (0·05 g.) in ethylamine (2 ml.), with and without ethylamine hydrochloride (1 g.), was heated in a sealed tube at 220° for 20 hr. Chromatography, as above, gave only a yellow oil (0·02 g.) and tars.

(*c*) The product (0·05 g.) with ethylamine hydrochloride (0·25 g.) was heated at 155° for 20 hr. Removal of the hydrochloride with water yielded starting material (0·038 g.).

(*d*) The product (0·05 g.) with ethylamine hydrochloride (0·6 g.) was heated at 250° for 20 hr. An oily solid (0·026 g.) was isolated; extraction with ether and evaporation gave an oil with the same infrared spectrum as the product in (*b*). The γ-lactone peak at 1770 cm.$^{-1}$ was absent, but peaks at 3300 (broad, OH) and 1639 cm.$^{-1}$ (amide-carbonyl) indicated the possibility of opening of the lactone ring to give the corresponding hydroxy-amide.

Reaction of the Dienone-lactone (III) *with Urea.*—The dienone-lactone (0·2 g.) with urea (1 g.) was heated at 150°. The temperature was raised to 200° during 30 min. Extraction of the mixture with water left a solid (0·2 g.), which sublimed at 260°/2 mm. to give 2-aminophenanthridone (0·03 g.), m. p. and mixed m. p. 312°.

Ethylation of 1- *and* 2-*Nitrophenanthridone.*—The nitrophenanthridone (1 g.) in acetone (25 ml.) and 10% aqueous sodium hydroxide (12·5 ml.) was boiled under reflux and diethyl sulphate (1·7 ml.) was added dropwise. The solution was boiled for 30 min., cooled, and poured into water.

(*a*) *From* 1-*nitrophenanthridone.* The dried yellow precipitate (0·984 g.) in benzene was adsorbed on alumina (2 × 20 cm.) and eluted as follows: (i) Benzene (150 ml.) gave a yellow solid (0·86 g.) (Found: C, 67·5; H, 4·7; N, 10·3. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%), m. p. and mixed m. p. with 9-ethoxy-1-nitrophenanthridine, 136—137°. This compound was erroneously reported to be 10-ethyl-1-nitrophenanthridone, m. p. 127°, in Part XVI.[1] Further elution did not yield the expected 10-ethyl-1-nitrophenanthridone.

(*b*) *From* 2-*nitrophenanthridone.* The dried yellow precipitate (1·06 g.) in chloroform was adsorbed on alumina (2 × 20 cm.) and eluted as follows: (i) Benzene (150 ml.) gave a yellow solid (0·39 g.), m. p. and mixed m. p. with 9-ethoxy-2-nitrophenanthridine, 174°. (ii) Benzene (300 ml.) gave 10-*ethyl*-2-*nitrophenanthridone* (0·6 g.), which crystallised from benzene in yellow needles, m. p. 225° (Found: C, 67·2; H, 4·4; N, 10·1%), $\nu_{max.}$ 1659 cm.$^{-1}$ (δ-lactam-carbonyl).

9-*Ethoxy*-1- and -2-*nitrophenanthridine.*—These compounds were prepared as for the 3-nitro-isomer [1] and isolated by chromatography on alumina. 9-*Ethoxy*-1-*nitrophenanthridine*, after

crystallisation from ethanol, had m. p. 136—137° (Found: C, 67·1; H, 4·6; N, 10·2. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%). *9-Ethoxy-2-nitrophenanthridine*, after crystallisation from benzene, had m. p. 174° (Found: C, 67·0; H, 4·6; N, 10·4%).

2-Amino-10-ethylphenanthridone.—10-Ethyl-2-nitrophenanthridone (1 g.) in ethanol (600 ml.) containing Adams catalyst (0·1 g.) was shaken in an atmosphere of hydrogen until the required volume had been absorbed. Filtration (Celite), evaporation, and crystallisation of the residue from benzene–light petroleum gave *2-amino-10-ethylphenanthridone* (0·7 g.) in needles, m. p. 178° (Found: C, 74·8; H, 6·3; N, 11·7. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·9; N, 11·8%).

10-Ethyl-2-ethylaminophenanthridone (XXVIII).—The primary amine (0·2 g.), ethyl iodide (0·17 g.), sodium carbonate (0·2 g.), and water (6 ml.) were boiled under reflux for 3 hr. The mixture was extracted with ether; removal of the solvent gave an oily solid (0·13 g.), which was dissolved in benzene, adsorbed on alumina (1 × 10 cm.), and eluted as follows. (i) Benzene–light petroleum (1 : 1; 250 ml.) and (3 : 1; 200 ml.) gave a solid (0·018 g.), which crystallised from light petroleum to yield *10-ethyl-2-diethylaminophenanthridone* in pale yellow needles, m. p. 90—91° (Found: C, 76·9; H, 7·1. $C_{19}H_{22}N_2O$ requires C, 77·5; H, 7·5%). (ii) Benzene–light petroleum (10 : 1; 100 ml.) and benzene (400 ml.) afforded a solid (0·05 g.) which crystallised from ethanol to give *2-ethylamino-10-ethylphenanthridone* in almost colourless needles, m. p. 165·5° (Found: C, 76·4; H, 7·2; N, 10·3. $C_{17}H_{18}N_2O$ requires C, 76·6; H, 6·8; N, 10·5%). (iii) Benzene–chloroform (4 : 1; 200 ml.) gave unchanged starting material (0·05 g.).

10-Ethyl-3-ethylaminophenanthridone.—3-Amino-10-ethylphenanthridone [1] (0·2 g.) was treated as above. Evaporation of the ether extract gave an oily solid (0·15 g.), which was dissolved in benzene, adsorbed on alumina, and eluted as follows. (i) Light petroleum (900 ml.) gave *3-diethylamino-10-ethylphenanthridone* (0·023 g.) which, crystallised from light petroleum, had m. p. 106·5° (Found: C, 77·6; H, 7·6. $C_{19}H_{22}N_2O$ requires C, 77·5; H, 7·5%). (ii) Benzene–light petroleum (2 : 3; 200 ml.) and (3 : 2; 1 l.) yielded *10-ethyl-3-ethylaminophenanthridone* (0·028 g.) which, after crystallisation from benzene–light petroleum, had m. p. 139—140° (Found: C, 76·4; H, 7·0. $C_{17}H_{18}N_2O$ requires C, 76·6; H, 6·8%). (iii) Benzene (600 ml.) and benzene–chloroform (4 : 1; 200 ml.) afforded starting material (0·054 g.).

2-Aminophenanthridone (cf. Walls [17]).—2-Nitrophenanthridone (0·3 g.) in glacial acetic acid (500 ml.) with Adams catalyst (0·3 g.) was hydrogenated with shaking until the required volume had been absorbed. The solution was evaporated at reduced pressure under nitrogen. Extraction of the residue with hot 5N-hydrochloric acid and neutralisation gave the crude product (0·15 g.). The amine sublimed at 260°/2 mm. as a yellow powder which, crystallised from dimethylformamide–benzene, gave *2-aminophenanthridone*, m. p. 312° (Found: N, 12·9. $C_{13}H_{12}N_2O$ requires N, 13·3%). Walls [17] reported m. p. 285° for what was presumably a mixture of the 2- and the 7-isomer (see ref. 18).

3-Aminophenanthridone.—3-Nitrophenanthridone (0·1 g.) in acetic acid (200 ml.) was reduced and the product (0·02 g.) isolated as above. The amine was twice sublimed at 260°/2 mm. The sublimate separated from dimethylformamide–benzene to yield 3-aminophenanthridone, as a yellow powder, m. p. 280° (decomp.), for which a satisfactory elementary analysis could not be obtained.

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[17] Walls, *J.*, 1935, 1407.
[18] Arcus, Coombs, and Evans, *J.*, 1956, 1498.