Internuclear Cyclisation. Part XXXII.[1] Dienol–Benzene and Related Rearrangements of Some Spirocyclohexadiene-lactams

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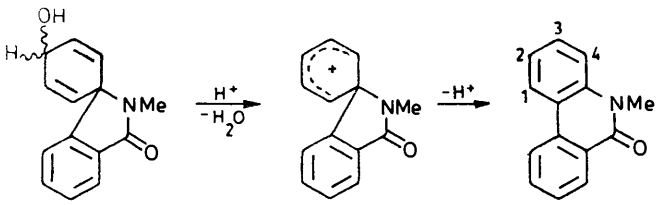
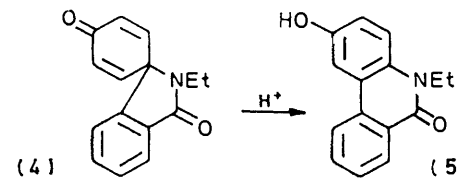
The stereoisomeric 4'-hydroxy-2-methylisoindoline-1-spiro-1'-cyclohexadien-3-ones (1) rearrange with acid to give *N*-methylphenanthridinone (3) by migration of the aryl group and not of the nitrogen atom. However, similar reactions of the 2',3'-benzo- and 6'-hydroxy-4',5'-benzo-analogues [(21) and (7)] occur with predominant nitrogen migration. Brief exposure of compound (1) or (21) to methanolic acid results in the formation of cyclohexadienyl methyl ethers, presumably by way of intermediate cyclohexadienyl cations. It has not, however, been possible to identify a similar process in the acid-catalysed methanolysis of compound (7). The cyclohexadienyl ethers are also obtained when the corresponding cyclohexadienyl iodides are exposed to methanolic silver nitrate. Treatment of the stereoisomeric 4',5'-benzo-6'-iodo-compounds (34) with methanolic silver nitrate leads to one stereoisomer of the 6'-methyl ether (26) and to *N*-methylbenzo[*c*]phenanthridin-6-one (9). Stereospecific formation of the same isomer of (26) was observed when 2-(*N*-methyl-2-naphthylcarbamoyl)benzenediazonium sulphate was decomposed by heating in methanol. Possible factors controlling stereoselection in these reactions, and the competition between aryl and nitrogen migration, are briefly discussed.

THE dienol–benzene rearrangement,[2,3] although less well documented than the related dienone–phenol rearrangement,[4] has been extensively explored in steroid systems,[5] and has found synthetic utility in the alkaloid field.[6] In Part XXI [7] of this series an example of this reaction was reported in which a mixture of the stereoisomeric cyclohexadienols (1), on treatment with acid, gave *N*-methylphenanthridinone (3). By analogy with the dienone–phenol rearrangement of compound (4), which gives the hydroxyphenanthridinone (5), the reaction



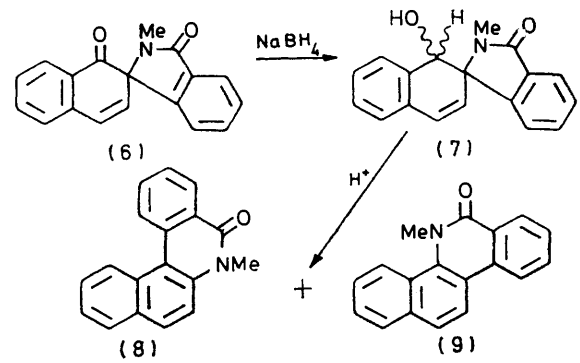
(1) (2) (3)



(4) (5)

was thought to involve an aryl shift in the spirocyclohexadienyl intermediate (2). We were therefore surprised to find that an attempted synthesis of the benzophenanthridinone (8) by acid-catalysed dehydration of the dienol (7) gave instead the isomeric benzophenanthridinone (9) as the major product.

The alcohol (7) was readily obtained by reduction of the ketone (6);[1] closer examination of the reaction of this alcohol with acid under a variety of conditions showed that the benzophenanthridinones (8) and (9) were formed in high yield, with the isomer (8) (resulting



(6) (7) (8) (9)

from phenyl migration) accounting for only *ca.* 15% of the product. Migration of an amide nitrogen atom to an electron-deficient centre has been reported before,[8] but this appears to be the first instance in which it has been encountered in the rearrangement of a cyclohexadienyl system. The result prompted further investigations of the reactions of various spirocyclohexadienyl precursors which were to hand. One serious complicating factor is undoubtedly protonation of the amide grouping. Thus in the closely related dienone–phenol rearrangement of (4), exceptionally vigorous conditions are required (P_2O_5–H_3PO_4; 170°), presumably because amide protonation prevents nitrogen migration and at the same time inhibits phenyl migration.[4a] The rearrangement of (4) has been repeated in the present work, and the total reaction product examined by g.l.c.,

[1] Part XXXI, D. H. Hey, G. H. Jones, and M. J. Perkins, preceding paper.

[2] *E.g.*, M. J. Perkins and P. Ward, in 'Mechanisms of Molecular Migrations,' ed. B. S. Thyagarajan, vol. 4, Interscience, New York, 1971, p. 55.

[3] H. J. Hansen, B. Sutter, and H. Schmid, *Helv. Chim. Acta*, 1968, **51**, 828.

[4] (*a*) B. Miller in 'Mechanisms of Molecular Migrations,' ed. B. S. Thyagarajan, vol. 1, Interscience, New York, 1968, p. 248; (*b*) A. J. Waring, *Adv. Alicyclic Chem.*, 1966, **1**, 131.

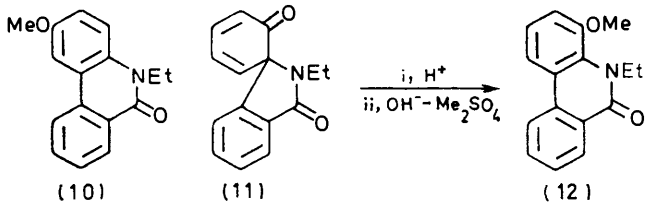
[5] *E.g.*, E. S. Caspi, D. M. Piatak, and P. K. Grover, *J. Chem. Soc.* (*C*), 1966, 1034; E. Caspi and P. K. Grover, *Steroids*, 1963, **1**, 39; H. Dannenberg and H.-G. Neumann, *Annalen*, 1961, **646**, 148.

[6] *E.g.*, A. R. Battersby, T. H. Brown, and J. H. Clements, *J. Chem. Soc.*, 1965, 4550; A. R. Battersby, T. J. Brucksom, and R. Ramage, *Chem. Comm.*, 1969, 464; see also ref. 4*b*.

[7] D. H. Hey, J. A. Leonard, T. M. Moynehan, and C. W. Rees, *J. Chem. Soc.*, 1961, 232.

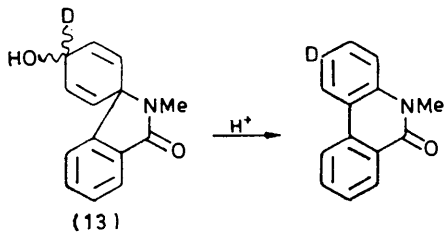
[8] J. W. Huffman and T. Kamiya, *Tetrahedron Letters*, 1966, 1857.

after methylation (Me_2SO_4). Only a single methoxy-*N*-ethylphenanthridinone (10), was detected. Likewise it was demonstrated that compound (11) rearranges under similar conditions to give the phenanthridinone (12), albeit in low yield. In neither reaction was the product of nitrogen migration detected.



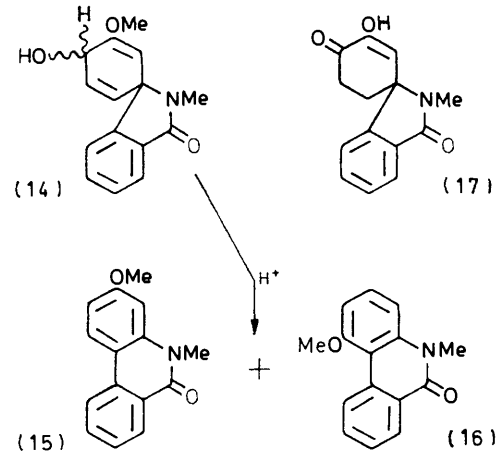
Reduction of the cyclohexadienones reported in Part XXXI [1] afforded a simple route to a series of cyclohexadienols whose acid-catalysed rearrangements have now been investigated.

The rearrangement of the unsubstituted dienols (1) was further investigated by studying the deuteriated analogue (13). On treatment with acid, this gave *N*-methyl[2-^{2}H]phenanthridinone, identified by n.m.r. spectroscopy which provided no evidence for the presence of isomerically labelled species (< *ca.* 5%).



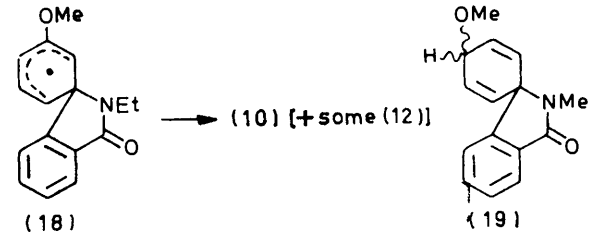
A methoxy-derivative of compound (1), namely the dienol (14) (two stereoisomers), was found to give (15) and (16) as the only detectable phenanthridinone products. Here again, only aryl migration has apparently occurred, and there appears to be a clear distinction between the behaviour of the simple cyclohexadienols, such as (1) and (14), and that of the benzo-analogues of (1) [see also the reactions of compound (21) described later]. In the initial experiments with (14), which employed aqueous or aqueous alcoholic mineral acid, the yields of compounds (15) and (16) were low (*e.g.* 16% in aqueous sulphuric acid).

Spectroscopic examination revealed that the major products from these reactions had suffered *O*-demethylation, and retained the γ-lactam ring. The diosphenol structure (17) has been assigned to one of these, obtained crystalline from the reaction in aqueous sulphuric acid. This formulation is based on spectroscopic evidence, and the deep colouration obtained with iron(III) chloride solution. When, however, the dienols (14) were dissolved in the relatively non-nucleophilic trifluoroacetic acid, demethylation was no longer a major reaction path, and a mixture of products (15) and (16) was obtained in *ca.* 70% yield. Migration of the aryl group occurred predominantly towards the position *para* to the methoxy-substituent (*ca.* 17 : 1), and this parallels a similar *para* regioselectivity in the rearrangement of radical (18) in which, however, it is the nitrogen



atom which migrates.[9] In related rearrangements, preference for migration either to the position *ortho*, or to the position *para* to a methoxy-substituent has been encountered.[6]

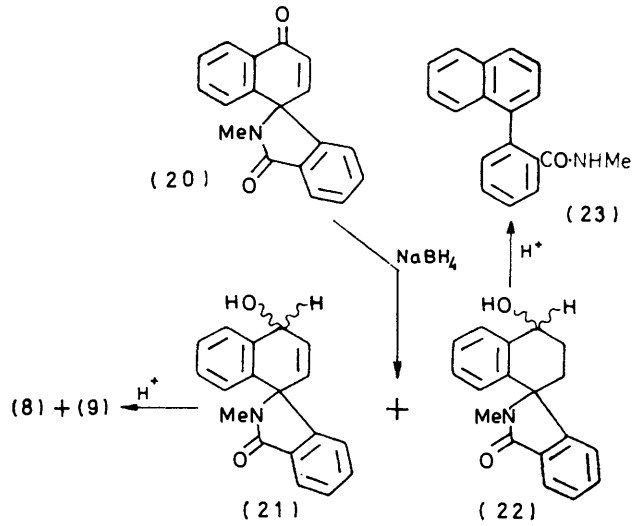
Brief exposure of the dienols (1) to methanolic sulphuric acid gave the epimeric ethers (19). Similarly, with aqueous acid, either stereoisomer of (1) could be transformed into an equilibrium mixture of the two



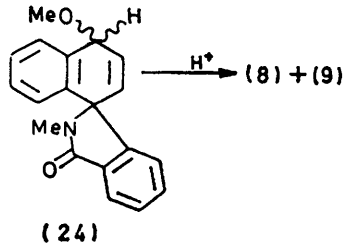
forms. Clearly, therefore, nucleophilic capture of the intermediate spirocyclohexadienyl cation (2) is faster than its rearrangement. This observation has been utilised in an investigation of the rearrangement of the reduction products of the spirodienone (20).[1] This compound was reduced by borohydride to a mixture of epimeric spirodienols (21) and their epimeric dihydro-derivatives (22), which could not be separated. Treatment of the mixture with acid gave the two benzophenanthridinones (8) and (9), together with the naphthylbenzamide (23). This last product presumably arose from the acid-catalysed dehydration and ring-opening of compounds (22). No over-reduction had been detected in the preparation of the dienols (1), (7), or (14), either spectroscopically or by production of analogues of (23) following exposure to acid. Brief exposure of the total reduction product from (20) to methanolic sulphuric acid converted the spirodienols (21) into the corresponding methyl ethers (24). The spiro-enols

[9] D. H. Hey, G. H. Jones, and M. J. Perkins, (*a*) *Chem. Comm.*, 1970, 1438; (*b*) *J.C.S. Perkin I*, 1972, 105.

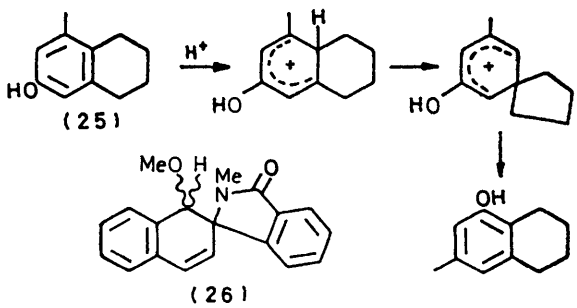
(22) were unaffected, and the product mixture was now readily fractionated chromatographically. The methoxydiene fraction was employed in the subsequent rearrangement studies. More vigorous



treatment of these ethers with acid gave a mixture of the benzophenanthridinones (8) and (9), in which the product of nitrogen migration predominated.



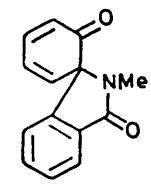
However, the precise ratio of the two products varied according to the acid system employed (see Experimental section). No systematic study of the acid-dependence of this rearrangement has been made, but evidence could not be found for an acid-catalysed interconversion of the isomeric products. Such a reaction seemed unlikely but not impossible in view of the known phenol ⟶ phenol rearrangement of (25).[10]



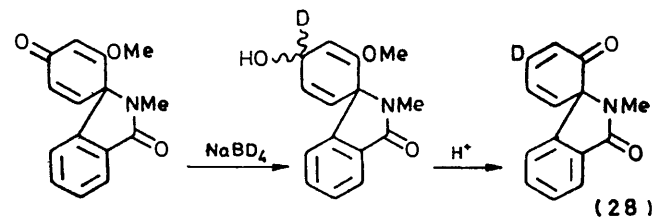
Nitrogen migration had first been encountered with the dienols (7). The acid-catalysed rearrangement of a single methyl ether (26) of unknown stereochemistry (see later) was also examined under a variety of conditions. It was found, however, that in this case the ratio of aryl to nitrogen migration was independent of the acid system employed, and was equal to that recorded for the dienols themselves. Furthermore, when the progress of a reaction in deuteriochloroform containing trifluoroacetic acid was followed by n.m.r. spectroscopy, the proportions of products were unchanged throughout the reaction.

The possibility that, in the reaction of compound (26), rearrangement is concerted with loss of alcohol is rendeted unlikely by this result, for a single methyl ether would be expected to give a single product by migration of the group *trans* to the methoxy-group. On the other hand, in the rearrangement of the corresponding dienol (7), no evidence has been found for nucleophilic capture of an intermediate cyclohexadienyl cation by solvent after only brief exposure to acid.

A number of other results which bear on those already described have also been obtained, but for various experimental reasons these have to be evaluated with caution. For example, although the linear conjugated dienone (27) gave, on borohydride reduction, a product which on treatment with acid yielded *N*-methylphenanthridinone, the overall yield was poor, and spectroscopic examination of the intermediate reduction product showed that some over-reduction of the dienone had taken place. However, the dienols could not be isolated from the mixture. Furthermore, no evidence was found for the formation of the expected methyl ethers (19) when the reduction products were exposed to methanolic sulphuric acid. If

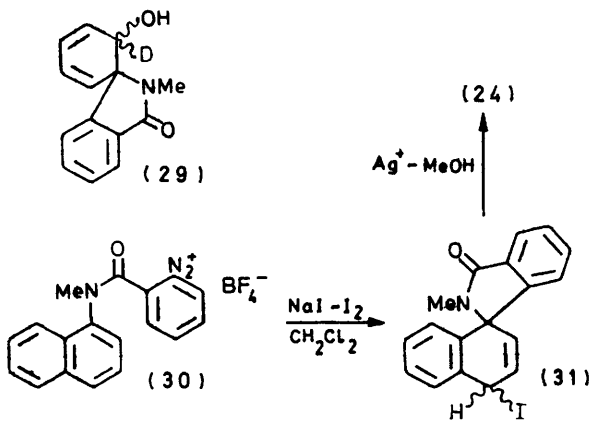


we suppose that the phenanthridinone arises solely from the dienol component of the reduction mixture, the last result reopens the possibility that rearrangement occurs in concert with loss of water from the protonated dienol and the reaction by-passes a cyclohexadienyl cation. In spite of the experimental difficulties with this system, two further investigations were made. In the first, the deuteriated dienone (28), obtained by the sequence of

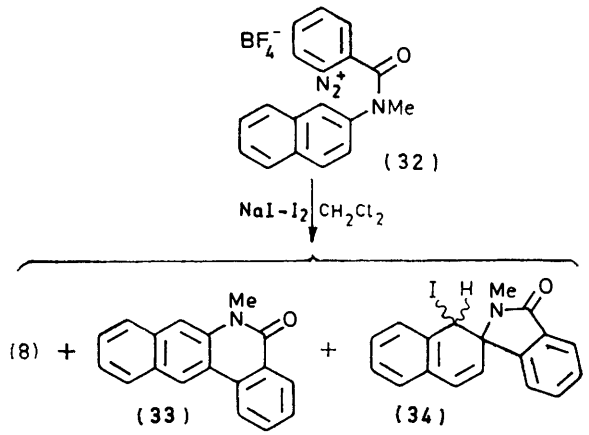


[10] W. H. Hopff and A. S. Dreiding, *Angew. Chem. Internat. Edn.*, 1965, **4**, 690.

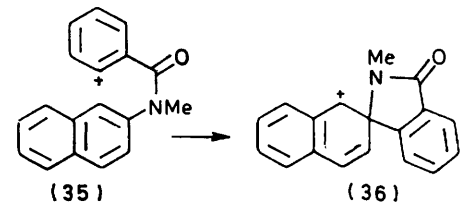
reactions shown, was reduced with sodium borohydride and the reaction products were treated with acid. The phenanthridinone which was obtained was deuteriated exclusively (n.m.r. >95%) at C-2, again suggesting that only aryl migration had occurred. In the second, the dienone (27) was reduced with sodium borodeuteride, and the product was rearranged with acid. Significantly, less than 50% of the molecules of *N*-methylphenanthridinone contained a deuterium atom (mass spectrum). Rate-limiting rearrangement of a cyclohexadienyl cation intermediate should give 50% deuterium retention, and rate-limiting deprotonation (following a reversible rearrangement) should give more than 50% retention of deuterium.[11] Two alternatives remain. Either some, at least, of the rearrangement is concerted with loss of water from the protonated dienol, or the phenanthridinone can also be derived from one or more of the reduction products other than the dienols (29), in a reaction in which deuterium loss is favoured.



As noted in Part XXXI,[1] it has been possible in some instances to obtain iodospirodienes from the decomposition of diazonium salts such as (30) promoted by sodium iodide in methylene chloride. These iodo-compounds constitute alternative precursors to the spirodienyl cations. Thus (31), on treatment with methanolic silver nitrate, gives a mixture of the epimeric methoxy-dienes (24).[1] When the diazonium salt (32) was exposed to sodium iodide in methylene chloride, the products included the expected benzophenanthridinones (8) and (33), and a 3 : 2 mixture of epimeric iodides (34). The products of this reaction were identified by a combination of chromatographic and spectroscopic techniques, and no attempt was made to separate them. The iodo-dienes (34) have not been isolated. The mixture of products [(8) + (33) + (34)] was dissolved in methanol containing silver nitrate, whereupon the iodides were replaced by a mixture of the benzophenanthridinone (9) and a single methyl ether (26), in the same 3 : 2 ratio. The possibility that some of the benzophenanthridinone (8) was also formed from the iodo-compounds could not be verified, as this compound was already present in the reaction mixture. Nevertheless, the correspondence between the proportions of products and proportions of epimeric iodides raises the possibility that the two iodides might behave differently under these conditions, the two proceeding to different products. Once again,



this hints at rearrangement in concert with the departure of the leaving group. The silver ion-catalysed methanolysis of (34) afforded the first instance of phenanthridinone formation in the absence of a Brønsted acid, and an alternative explanation for this result may simply involve a particularly high tendency for rearrangement under these conditions.



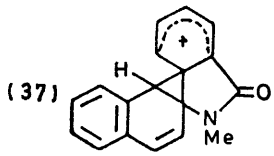
In an attempt to generate the cation (36) by an alternative route, the diazonium sulphate corresponding to (32) was heated in methanol. This reaction depends on initial formation of the aryl cation (35), and subsequent cyclisation.[12] In the event, the reaction gave the two benzophenanthridinones (8) and (33), and the single isomer of (26), previously isolated from methanolysis of the spirodienyl iodide. The benzophenanthridinone (9) was absent; we therefore conclude that if the immediate precursor of the methyl ethers is common to both reactions in which it has been formed, then this is not the precursor to the benzophenanthridinone (9) from the silver-catalysed methanolysis of (34). This supports the earlier suggestion that the epimeric iodides (34) proceed to different products when treated with methanolic silver nitrate.

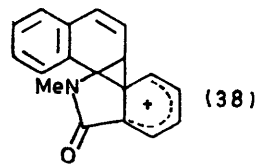
Two separate problems are raised by this work. These are: (i) the identification of the factors responsible for the stereospecific formation of only one methyl ether in the reactions believed to involve the spirodienyl cation (36), and (ii) the elucidation of the factors which differentiate between the rearrangements of the simple

[11] V. P. Vitullo and N. Crossman, *Tetrahedron Letters*, 1970, 1559.
[12] R. A. Abramovitch, *Adv. Free Radical Chem.*, 1967, **2**, 87.

cyclohexadienyl systems in which exclusive aryl migration occurs, and those of their benzo-analogues in which nitrogen migration predominates.

If it is assumed that migration of aryl or nitrogen is by a direct [1,2] sigmatropic shift, one interesting possibility is that the intermediate bridged structure, *e.g.* (37), is unusually stable with respect to the spirocyclohexadienyl structure (36). Compared with a phenyl shift in an acyclic system this might be the case, in view of partial relief of angle strain in the γ-lactam ring of (37) compared with (36). If such a bridged ion did correspond to a significant energy minimum along the reaction co-ordinate, it might be the precursor to the methyl ether (26), of which only one stereoisomer would then be expected. In the methanolysis of the iodides (34), compound (37) would be the expected product from that isomer with iodine *cis* to nitrogen, and nitrogen





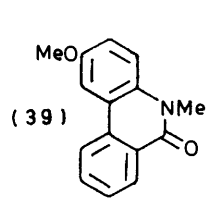
migration should occur with the corresponding *trans*-isomer. No evidence was obtained for the participation of relatively stable bridged species in other instances, however. For example, had (38) (say) been the immediate precursor to (24) in the silver nitrate-catalysed methanolysis of (31), substantial stereoelectronic control would probably have been relayed to the site of nucleophilic capture by methanol. No evidence was found for this.

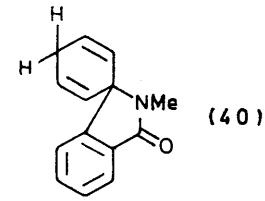
An alternative rationalisation for stereospecific capture of (36) might be based on the very different ordering of solvent molecules on opposite faces of the cation, due to the presence, on one side only, of the dipolar amide link.

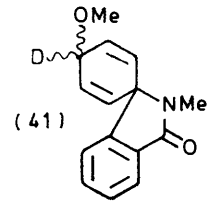
It is more difficult to find any plausible explanation for the second point. Presumably factors influencing aryl migration will also affect nitrogen migration, and in the same fashion. The exception is amide protonation, which would presumably retard nitrogen migration much more strongly than aryl migration. If rearrangement of spirodienyl cations can occur both with and without amide protonation, and if in the unprotonated species nitrogen migration predominates whilst in the protonated species aryl migration predominates, then it is possible to devise a scheme which, assuming that rearrangement in the naphthalene series is more rapid, might give the observed results. Whilst it seems certain that the lactams are substantially protonated under the acid conditions employed, the remainder of the argument is purely speculative and requires detailed examination of the acid-dependence of the rearrangement of both the spirocyclohexadienyl systems themselves and their benzo-analogues.

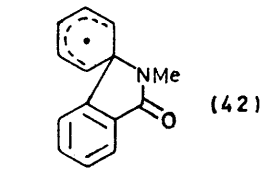
[13] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 1150.

Reactions of the Methoxy-dienes (19) *with Hydrogen Iodide and with Iodine.*—In Part XXX [13] it was noted that the products of u.v. irradiation of a benzene solution of the spirocyclohexadienyl methyl ethers (19) and iodine included the methoxyphenanthridinone (39). The results of further control experiments pertinent to this reaction and to the photochemistry of 2-iodo-4′-methoxy-*N*-methylbenzanilide are noted here.



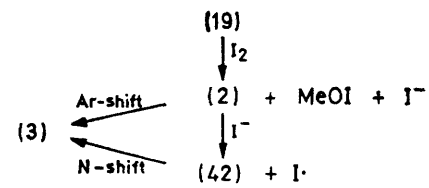






The methoxy-dienes (19) were dissolved in benzene and the solution was saturated with hydrogen iodide at room temperature. Rapid work-up gave an almost quantitative yield of the reduction product (40).[14,15] Delayed (15 h) work-up gave, instead, *N*-methylbiphenyl-2-carboxamide, by acid-catalysed rearrangement of (40).

The thermal reaction between compounds (19) and iodine was investigated by heating in boiling chlorobenzene. The major product was *N*-methylphenanthridinone (3). When the deuteriated analogue (41) was similarly oxidised, n.m.r. examination of the product indicated it to be a mixture of the 2-deuterio- (*ca.* 70%) and 3-deuterio-derivatives. In view of the earlier demonstration that spirodienyl radicals such as (42) rearrange exclusively by nitrogen migration,[9] and the present evidence that the corresponding cation (2) rearranges by aryl migration, it seems probable that two competing reaction pathways are involved in the formation of *N*-methylphenanthridinone in the reaction of (19) with iodine, as indicated below. On the other hand,



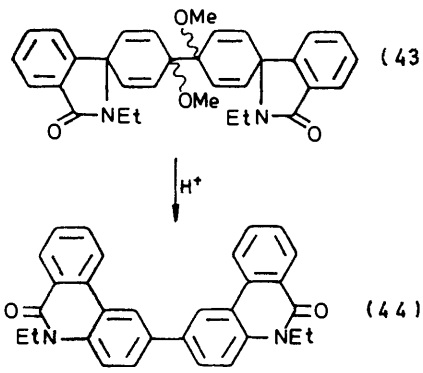
the conditions (solvent, extent of amide protonation) of this reaction are far removed from those of the

[14] D. H. Hey, G. H. Jones, and M. J. Perkins, *Chem. Comm.*, 1969, 1375.

[15] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 113.

cationic rearrangements of the cyclohexadienols, and mechanistic alternatives cannot be discounted.

Rearrangement of the Spirocyclohexadienyl Dimer (43).—The spirocyclohexadienyl dimer (43) obtained as described in Part XXVII [9b] was briefly exposed to polyphosphoric acid. This gave a product considered to be the expected biphenanthridinone (44), which was required for comparison with an isomeric compound isolated in the course of a study of hydrogen abstraction from some spirocyclohexadienes.[15]



(43)

(44)

EXPERIMENTAL

The general experimental and analytical procedures employed are indicated in Part XXVI.[16] Reference compounds for this work have been described in earlier Parts of this series.

Preparation of Cyclohexadienols.—The following general procedure was adopted. The dienone [1] was dissolved or suspended in a little absolute ethanol at room temperature, the mixture was stirred, and a slight excess of sodium borohydride in ethanol was added. Reactions were usually complete in *ca.* 10 min (t.l.c.). The bulk of the solvent was removed, and the residue was poured into water and extracted into chloroform. The extract was dried and evaporated and the residue was examined by n.m.r. spectroscopy.

Formation of the unsubstituted dienols (1) was apparently uncomplicated by over-reduction. The product was separated chromatographically (neutral alumina; elution with methylene dichloride) into two stereoisomers, m.p. 126—130° (from benzene) and 197—198° (from benzene), in approximately equivalent amounts. Both showed $\nu_{max.}$ 3300 (OH) and 1670 cm^{-1} (γ-lactam), and had n.m.r. spectra consistent with the dienol formulation. The *deuteriated analogue* (13) of (1) was similarly obtained by use of sodium borodeuteride in ethanol. The mixture of stereoisomers was not, in this case, separated (Found: M^+, 228·1013. $C_{14}H_{12}DNO_2$ requires M, 228·1009).

The stereoisomeric *4′-hydroxy-3′-methoxy-2-methylisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-3-ones* (14), were obtained as an oil; the n.m.r. spectrum again indicated the absence of over-reduction: τ 1·9—2·9 (4H, m), 3·7 (1H, dd, J 10 and 3 Hz, H-5′), 4·6 (1H, d, J 10 Hz, H-6′), 5·2 (1H, m, H-4′), 5·6 (1H, s, H-2′), 6·55br (1H, s, OH), 6·4 (3H, s, OMe), and 7·05 and 7·15 (3H, 2 × s, NMe of isomers).

The *1,2-dihydro-1-hydroxy-2′-methylnaphthalene-2-spiro-1′-isoindolin-3-ones* (7) separated from chloroform as a white powder, m.p. 247—266°. Although the melting range is suggestive of a mixture of stereoisomers, only a single *N*-methyl resonance was evident in the n.m.r. spectrum (Found: C, 77·8; H, 5·3; N, 5·0. $C_{18}H_{15}NO_2$ requires C, 78·0; H, 5·4; N, 5·0%), $\nu_{max.}$ 3320 (OH) and 1680 cm^{-1} (γ-lactam).

Solvolysis Reactions and Rearrangements of the Cyclohexadienols.—(i) A mixture of the stereoisomeric dienols (1) (105 mg) in ethanol (1 ml) and concentrated aqueous hydrochloric acid (5 ml) was boiled for 1 h, and then poured into water. The product which separated was extracted into chloroform and, after removal of solvent, was identified as *N*-methylphenanthridinone, m.p. 106—107° formed in essentially quantitative yield.

(ii) Solutions of each of the isomeric dienols (1) (50 mg) in methanol (1 ml) and hydrochloric acid (2 ml) were separately boiled for 30 s, and cooled rapidly. The mixtures were treated as in (i); t.l.c. of the chloroform solutions showed, in each case, the formation of *N*-methylphenanthridinone, *both* isomeric dienols, and two additional products subsequently identified as the methyl ethers (19).

(iii) A solution of the deuteriated spirodienols (13) (200 mg) in ethanol (2 ml) and hydrochloric acid (10 ml) was boiled under reflux for 1 h. The product was worked up as before, and crystallised from ethanol to yield *N-methyl-[2-²H]phenanthridinone*, m.p. 106—107°, identified by the absence of the triplet in the n.m.r. spectrum at τ 2·73, and the presence of a broad singlet at τ 1·79 (H-1) replacing the doublet centred here in the spectrum of the undeuteriated molecule. The spectrum showed no evidence of the presence of the isomeric 3-deuterio-derivative.

(iv) A solution of the mixture of dienols (1) (3·4 g) in methanol (50 ml) and sulphuric acid (5 g) was refluxed for 3 min, cooled, poured into chloroform, and washed with water. The dried chloroform solution was evaporated and the residual oil was chromatographed on neutral alumina. The major fraction, eluted with benzene–methylene chloride, and obtained as an oil (2·43 g) which slowly solidified, comprised a mixture of the stereoisomeric *4′-methoxy-2-methylisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-3-ones* (19). These crystallised together from benzene with m.p. 110—130° (Found: C, 74·6; H, 6·2; N, 5·8. $C_{15}H_{15}NO_2$ requires C, 74·7; H, 6·2; N, 5·8%), $\nu_{max.}$ 1700 cm^{-1} (γ-lactam), τ 2·0—2·9 (4H, m), 3·6 and 4·45 (each 2H, m, major splitting J 10 Hz), 5·45 (1H, m), 6·55 (3H, 2 × s, OMe of two isomers), and 7·1 (3H, 2 × s, NMe of two isomers).

(v) The 4′-deuterio-dienols (13) were similarly converted into the *4′-deuterio-analogues* of (19) [*i.e.* (41)].

(vi) A solution of the 3′-methoxy-dienols (14) (250 mg) in water (5 ml) was boiled, and hot 50% aqueous sulphuric acid (2 ml) was added. The mixture was refluxed for 5 min and cooled. After extraction into chloroform, the organic products were chromatographed on neutral alumina. Elution with benzene gave a mixture of phenanthridinones (38 mg) as an oil, which was shown (g.l.c.; n.m.r. spectrum) to consist of 3-methoxy-*N*-methylphenanthridinone and 1-methoxy-*N*-methylphenanthridinone in a ratio of 10 : 1. Elution with methylene chloride gave an oil (153 mg), $\nu_{max.}$ *ca.* 1690 cm^{-1}, consistent with retention of the γ-lactam structure. The n.m.r. spectrum showed the absence of the *O*-methyl group. Crystallisation from methylene chloride yielded one component, needles (33 mg), m.p. 195—199°, which gave a red colour with ferric chloride,

[16] D. H. Hey, G. H. Jones, and M. J. Perkins, *J. Chem. Soc.* (*C*), 1971, 116.

and was identified as *3′-hydroxy-2-methylisoindoline-1-spiro-1′-cyclohex-2′-ene-3,4′-dione* (17) (Found: M^+, 243·0896. $C_{14}H_{13}NO_3$ requires M, 243·0895), $\nu_{max.}$ 3300—3000 (OH) and 1690—1650 cm^{-1}, τ 1·8—2·7 (4H, m), 3·4 (1H, s, OH, removed by shaking with D_2O), 4·3 (1H, s), 6·85 (3H, s, NMe), and 6·9—8·2 (4H, m).

(vii) A solution of the dienols (14) (100 mg) in trifluoroacetic acid (2 ml) was warmed at 50° for 5 min, cooled, diluted with chloroform, and washed with aqueous 10% sodium hydroxide. Solvent was removed from the dried chloroform solution and the residue was chromatographed on alumina. Elution with benzene gave a mixture of 3-methoxy- and 1-methoxy-*N*-methylphenanthridinone (68%) as an oil. The ratio of isomers was *ca.* 17 : 1 (g.l.c.).

(viii) As repetition of experiment (vi) with alcoholic solvents again led to *O*-demethylation, a solution of the dienols (14) (50 mg) in acetone (2 ml) and aqueous 10% sodium hydroxide (2 ml) was treated with dimethyl sulphate (100 mg), and the mixture was stirred at room temperature overnight. Dilution with water followed by extraction with chloroform gave an oil which was chromatographed to give a mixture of stereoisomeric *3′,4′-dimethoxy-2-methylisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-3-ones* (14; OH replaced by OMe) as an oil (47 mg), $\nu_{max.}$ 1680 cm^{-1} (γ-lactam), τ 2·0—3·0 (4H, m), 3·8 (1H, overlapping doublets, H-5′ of two isomers, J 10 Hz), 4·5 (1H, d, J 10 Hz, H-6′), 5·0. (1H, m, H-4′), 5·5 (1H, s, H-2′), 6·35 (3H, s, 3′-OMe), 6·45 and 6·35 (3H, 2 × s, 4′-OMe for two isomers), and 7·0 and 7·1 (3H, 2 × s, NMe for two isomers). It was the same as the product of silver nitrate-catalysed methanolysis of the corresponding spirodienyl iodide (14; OH replaced by I).[1]

(ix) A solution of the dienols (7) (100 mg) in ethanol (5 ml) and hydrochloric acid (15 ml) was refluxed overnight. Work-up as before [see (i)] gave a mixture of *N*-methylbenzo[*c*]phenanthridinone and *N*-methylbenzo[*a*]phenanthridinone (*ca.* 7 : 1 by g.l.c. and n.m.r. spectrum) in almost quantitative yield. A similar result was obtained by use of ethanolic hydrochloric acid (ratio *ca.* 6 : 1). No dienyl ethyl ethers could be isolated after short reaction times.

Formation and Rearrangement of the Methoxy-dienes (24).—The dienone (20) was reduced with sodium borohydride by the general procedure. The n.m.r. spectrum of the product was consistent with formation of the desired dienols and further reduction products, τ *ca.* 7·7 (m). This was examined as follows. (i) The product (100 mg) was refluxed with aqueous ethanolic hydrochloric acid to give a mixture [*ca.* 40% based on ketone (24)] of *N*-methylbenzo[*a*]phenanthridinone and *N*-methylbenzo[*c*]phenanthridinone (*ca.* 3 : 1 by g.l.c.) together with unidentified products and *N-methyl-2-(1-naphthyl)benzamide* (23), m.p. 139—140° (from ethanol) (Found: C, 82·5; H, 5·6; N, 5·5. $C_{18}H_{15}NO$ requires C, 82·8; H, 5·7; N, 5·4%), identical with material obtained from t-butoxide-catalysed isomerisation of 1,4-dihydro-2′-methylnaphthalene-1-spiro-1′-isoindolin-3′-one [9b] (21; OH replaced by H).

(ii) The product (1500 mg) was crystallised from ethanol to give a solid (630 mg). This was dissolved in methanol (20 ml) and sulphuric acid (1 g), and the solution was heated to boiling, cooled at once, and poured into water. The organic products were extracted into chloroform and chromatographed on neutral alumina. The major fraction, obtained as an oil (520 mg), crystallised from benzene–light petroleum to give a mixture (m.p. 120—150°) of the stereoisomeric *1,4-dihydro-4-methoxy-2′-methylnaphthalene-1-spiro-1′-isoindolin-3′-ones* (24) (Found: C, 78·1; H, 5·7; N, 5·0. $C_{19}H_{17}NO_2$ requires C, 78·3; H, 5·8; N, 4·8%), $\nu_{max.}$ 1690 cm^{-1} (γ-lactam), τ 1·9—3·4 (8H, m), 3·45 (1H, 2 overlapping dd, major splitting 10 Hz), 4·23 (1H, d, J 10 Hz), 4·65br and 4·8br (together 1H, each s), 6·5 and 6·55 (3H, 2 × s, OMe of two isomers), and 7·15 and 7·25 (3H, 2 × s, NMe). These dienyl methyl ethers (100 mg) were dissolved in ethanol (3 ml) and sulphuric acid (1·5 g), and the mixture was boiled under reflux overnight. Examination of the organic products (g.l.c.; n.m.r. spectrum) after the usual work-up indicated the formation of a mixture (52 mg) of *N*-methylbenzo[*a*]phenanthridinone and *N*-methylbenzo[*c*]phenanthridinone in a ratio of *ca.* 5 : 1. Exposure of the dienols (100 mg) to boiling ethanol (1 ml) and hydrochloric acid (10 ml) for 15 min yielded a similar mixture of phenanthridinones (57 mg; *ca.* 4 : 1). The carboxamide (23) was not formed in these reactions. After 1 h in trifluoroacetic acid (1 ml) at 35°, the dienols (100 mg) again gave the same two phenanthridinones (61 mg) but in a ratio of 1·5 : 1. These yields were reproducible, and in control experiments both phenanthridinones were shown to be stable to the acidic conditions employed.

Reduction of the Linear Dienone (27) *and Reaction of the Products with Acid.*—(i) The dienone (27) [17] on reduction with sodium borohydride gave a complex mixture of products (n.m.r.). (No evident improvement in this situation was obtained by employing either lithium aluminium hydride or aluminium hydride.) The total product from the dienone (800 mg) and sodium borodeuteride (40 mg) in ethanol (5 ml) and hydrochloric acid (20 ml) was refluxed for 1 h, and the products were extracted into chloroform as before. The solvent was removed and the product chromatographed on neutral alumina to give *N*-methylphenanthridinone (m.p. 106—107°) (83 mg). Mass spectroscopic examination of this product indicated a ratio of undeuteriated to deuteriated phenanthridinone of *ca.* 1·7 : 1.

(ii) Reduction of 2′-methoxy-2-methylisoindoline-1-spiro-1′-cyclohexa-2′,5′-diene-3,4′-dione [1] (1500 mg) in ethanol (40 ml) with sodium borodeuteride (150 mg) was effected by boiling under reflux for 10 min. (The unusually vigorous conditions required are consistent with the vinylogous ester constitution of the dienone.) The organic products were found to contain some over-reduced material (n.m.r.). Nevertheless, the total product (an oil) was dissolved in ethanol (5 ml), and treated with hydrochloric acid (5 ml). The mixture immediately became yellow and was poured into water and extracted into chloroform. The extract was dried and evaporated; the n.m.r. spectrum of the residue suggested the presence of both the desired 4′-deuteriated dienone (28), and the corresponding 5′,6′-dihydro (dideuterio) derivative (the dihydro-compound has been reported previously [18]). The total product was reduced with sodium borohydride (80 mg) in ethanol, and the organic products from this reaction were dissolved in ethanol (5 ml) and hydrochloric acid (20 ml) and refluxed for 1 h. Work-up as before gave *N*-methylphenanthridinone (35 mg) (m.p. 106—107°) which had an n.m.r. spectrum identical with that of the 2-deuterio-derivative already described.

Dienone–Phenol Rearrangements.—(i) A mixture of the dienone (4) (500 mg) and polyphosphoric acid (3 g) was

[17] D. H. Hey, J. A. Leonard, C. W. Rees, and A. R. Todd, *J. Chem. Soc.* (*C*), 1967, 1513.

[18] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 122.

heated with shaking at 180° for 5 min and cooled. The products were distributed between chloroform and water, and the chloroform solution was washed with water and extracted with aqueous 10% sodium hydroxide. The alkaline extract was diluted with a little acetone, heated to boiling, and treated with dimethyl sulphate (200 mg). The mixture was cooled and extracted with chloroform, and the extract was examined by g.l.c. and t.l.c. The only product detected by g.l.c. was *N*-ethyl-2-methoxyphenanthridinone.

(ii) The linear dienone (11) was treated similarly; the only product detected by g.l.c. was *N*-ethyl-4-methoxyphenanthridinone.

Methanolysis of the Spirodienyl Iodides (34).—The formation and characterisation of the iodides (34) is reported in Part XXXI.[1] These compounds were obtained admixed with *N*-methylbenzo[*a*]phenanthridinone and *N*-methylbenzo[*b*]phenanthridinone. The composition of the mixture was such that the two isomeric iodides constituted *ca.* 30%, and were present in a ratio of *ca.* 3 : 2. The total mixture from 1 g of the amine hydrochloride precursor of (32) was dissolved in methanol and treated with silver nitrate solution. The n.m.r. spectrum of the organic products suggested that in addition to the two phenanthridinones, a third isomer, *N*-methylbenzo[*c*]phenanthridinone, was present, as well as a spirodienyl methyl ether, the latter two products being present in a ratio of 2 : 3. Chromatography of the products gave an initial fraction comprising the three phenanthridinones, in which the presence of all three isomers was confirmed by g.l.c., and a second fraction which crystallised from ethanol to give *1,2-dihydro-1-methoxy-2'-methylnaphthalene-2-spiro-1'-isoindolin-3'-one* (26) as needles, m.p. 134—135° (Found: C, 78·2; H, 5·6; N, 4·8. $C_{19}H_{17}NO_2$ requires C, 78·3; H, 5·8; N, 4·8%), $\nu_{max.}$ 1675 cm^{-1} (γ-lactam), τ 1·9—3·0 (8H, m), 3·08 and 4·42 (each 1H, d, *J* 10 Hz), 5·3 (1H, s), 6·9 (3H, s, OMe), and 7·25 (3H, s, NMe). The spectra of the total product revealed no evidence for the presence of the stereoisomer of (26).

Decomposition of 2-(N-Methyl-2-naphthylcarbamoyl)benzenediazonium Sulphate in Methanol.—A solution of 2-(*N*-methyl-2-naphthylcarbamoyl)aniline (2 g) in methanol (40 ml) and sulphuric acid (1 g) was diazotised at 0° with sodium nitrite (600 mg) in water (3 ml). The mixture was stirred at 0° for 5 min and then at 50° for 2 h (evolution of nitrogen had then ceased), cooled, poured into chloroform, and washed with water. Removal of solvent from the dried chloroform solution left a red oil which was dissolved in methylene chloride; the solution was filtered through a bed of neutral alumina. Examination of the filtrate by g.l.c. and t.l.c. revealed the presence of four major products, subsequently identified by chromatographic isolation. These were *N*-methylbenzo[*a*]phenanthridinone, *N*-methylbenzo[*b*]phenanthridinone, *o*-(*N*-methyl-2-naphthylcarbamoyl)anisole, and the methyl ether (26). A combination of n.m.r. spectroscopy and g.l.c. indicated the yields of these products to be 20, 5, 23 and 16%, respectively. There was no evidence for the formation of either *N*-methylbenzo[*c*]phenanthridinone or the stereoisomer of (26). The anisole derivative was obtained as an oil, $\nu_{max.}$ 1640 cm^{-1} (tert. aromatic amide), τ 2·1—3·7 (11H, m) and 6·45 and 6·50 (6H, 2 × s, NMe and OMe).

Rearrangement of the Dienyl Methyl Ether (26) *with Acid.*—(i) A solution of the ether (26) (52 mg) in ethanol (4 ml) and sulphuric acid (1 g) was refluxed overnight. Examination of the organic products by g.l.c. and n.m.r. spectroscopy indicated the formation of *N*-methylbenzo[*c*]phenanthridinone and *N*-methylbenzo[*a*]phenanthridinone in a ratio of *ca.* 6 : 1.

(ii) A solution of the ether (26) (50 mg) in trifluoroacetic acid (1 ml) was warmed at 35° for 1 h. The ratio of the phenanthridinones produced was again *ca.* 6 : 1.

Reaction of the Methoxy-dienes (19) *with Hydrogen Iodide and Iodine.*—(i) *With hydrogen iodide.* Hydrogen iodide was bubbled into an oxygen-free solution of the methoxy-dienes (19) (50 mg) in benzene (10 ml). The solution was set aside for 1 min and was then diluted with benzene and washed with aqueous sodium thiosulphate. Removal of benzene from the dried solution and examination of the residue by n.m.r. spectroscopy revealed almost quantitative conversion into the diene-lactam (40). If, however, the benzene solution was left overnight before treatment with aqueous sodium thiosulphate, the product was *N*-methylbiphenyl-2-carboxamide, m.p. 167—168°, again formed in essentially quantitative yield.

(ii) *With iodine.* A solution of the 4'-deuterio-4'-methoxy-dienes (41) (240 mg) and iodine (100 mg) in chlorobenzene (5 ml) was boiled under reflux for 5 min under nitrogen. After removal of iodine, the organic products were examined by g.l.c. and found to comprise *N*-methylphenanthridinone, together with traces of *N*-methylbiphenyl-2-carboxamide and the spirodienone (4; Et replaced by Me). Chromatography over neutral alumina gave the phenanthridinone (165 mg), which was crystallised from ethanol. Its n.m.r. spectrum showed major peaks similar to those of the 2-deuterio-derivative already described, but also revealed a broad doublet (*ortho*-splitting) centred at τ 2·73 and a broad singlet at τ 2·65, attributed to H-2 and H-4 respectively of *N*-methyl[3-^{2}H]phenanthridinone. It was estimated that the 2'- and 3'-deuterio-derivatives were present in the ratio 7 : 3.

Acid-catalysed Rearrangement of the Dimer (43).—The spirocyclohexadienyl dimer (43) [9b] (100 mg) and polyphosphoric acid (1 g) were heated to 150° with shaking, until a homogeneous solution was obtained. This was cooled and distributed between water and chloroform. The chloroform layer was dried and diluted with ethanol, and the bulk of the solvent was removed. A white crystalline solid separated (77 mg), m.p. 306—308°, which is considered to be *2,2'-bis-N-ethylphenanthridinone* (44) (Found: M^+, 444. $C_{30}H_{24}N_2O_2$ requires *M*, 444), $\nu_{max.}$ 1640 cm^{-1}, τ 3·50 (H-1 and H-1') (signals for the protons on C-2 of an *N*-alkylphenanthridinone were absent).

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