Internuclear Cyclisation.   Part XXVIII.[1]   Free Radical Reactions of Some Spirocyclohexadiene Lactams

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Abstraction of hydrogen from the spirocyclohexadiene lactam (1) and related compounds gives cyclohexadienyl radicals. at low temperatures (60°), dimerise ; at higher temperatures rearrangement may give *N*-alkylphenanthridinones : the effect of substituents in the cyclohexadiene ring on the case of this rearrangement is considered.   The abstraction of hydrogen from the cyclohexadienyl radical dimers leads to dehydrodimers : the nature of these is also temperature dependent.

In Part XXVI,[2] reference was made to the isolation of the spirodiene lactam (1) from the products of the photolysis of 2-iodo-*N*-methylbenzanilide in benzene. It had been considered that hydrogen abstraction from this lactam should constitute an unambiguous route to the spirodienyl radical (2),[3] and that investigations of such reactions should enhance the understanding of the thermal decomposition of the spirodienyl dimer (3) and related compounds.   Previous attempts to synthesise (1) had failed, but the isolation of this compound from the photochemical reaction [2] prompted further work, and a successful synthesis of this diene has now been developed.[4]   Routes to several closely related dienes have also been established,[1,5] and some reactions of these dienes with selected free-radical reagents are now described.   The results afford further insight into the factors which govern the competition between rearrangement and recombination of spirodienyl radicals formed during the pyrolysis of the dimer (3) and analogous compounds.

Although the diene (1) was first isolated from the photolysis of 2-iodo-*N*-methylbenzanilide (4) in benzene,[2] the yield was very low (*ca.* 5%).   It seemed probable that in this system spirodienyl radicals were being scavenged by a good hydrogen donor, possibly hydrogen
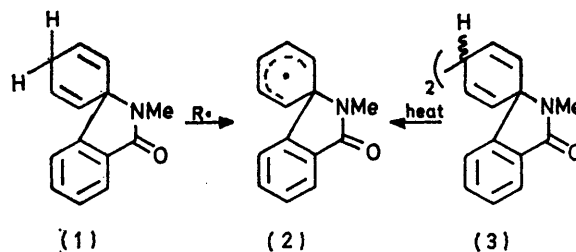
iodide,[6] and when hydrogen iodide was bubbled through the benzene solution during photolysis, a high yield of (1) was evident at the outset of the reaction.   However, continuation of the reaction for a longer period resulted in a reduction of the yield of the diene, and the methylamide of biphenyl-2-carboxylic acid (6) became a major product, presumably by acid-catalysed rearrangement

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

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

[3] D. M. Collington, D. H. Hey, and C. W. Rees, *J. Chem. Soc.* (C), 1968, 1017.

[4] A preliminary report of this synthesis has been given : D. H. Hey, G. H. Jones, and M. J. Perkins, *Chem. Comm.*, 1969, 1375.

[5] D. H. Hey, G. H. Jones, and M. J. Perkins, manuscript in preparation.

[6] *E.g.*, A. S. Rodgers, D. M. Golden, and S. W. Benson, *J. Amer. Chem. Soc.*, 1967, **89**, 4578.

of (1).[2] Attempts were then made to generate the spiro-dienyl radical (2) in the presence of hydrogen iodide employing the diazonium salt (5) as precursor. It was found that hydrogen iodide not only scavenged the intermediate radical, but also induced the decomposition of the diazonium salt. The most useful solvent was found to be methylene chloride, and, on a small scale, yields of

iodine and hydrogen iodide; in some instances spiro-cyclohexadienyl iodides have been isolated. The formation and reactions of these compounds will be discussed more fully elsewhere.[5] However, the dienes (8) * and (9) were made available by the pyrolyses of the appropriate spirodienyl dimers in the presence of 9,10-di-hydroanthracene,[1] and the stereoisomeric dienes (10)

(4) X = I
(5) X = N$_2^+$ BF$_4^-$

(6)
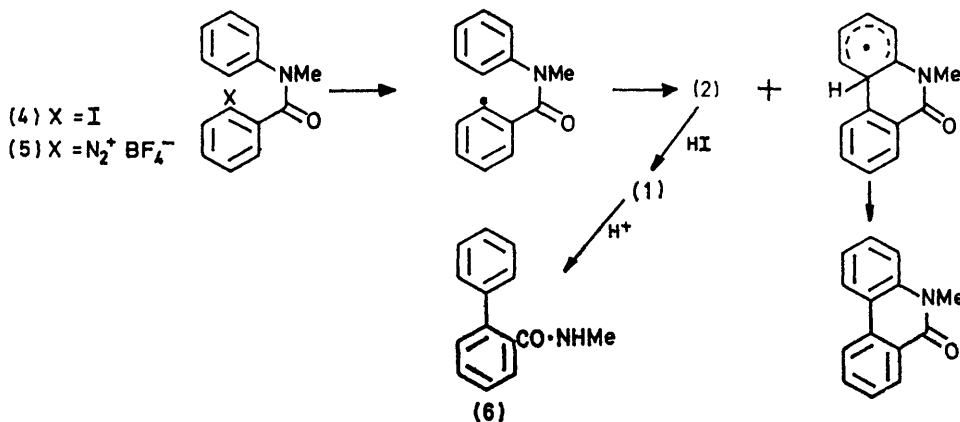
(1) of ca. 45% were attained with very little isomerisation to (6).

It was independently observed by Chauncy and Gellert [7] that synthetically useful internuclear cyclisation reactions can be brought about by inducing diazonium salt decomposition by means of sodium iodide in acetone. Both of these reactions probably involve electron-transfer reduction of the diazonium ion by iodide. $(ArN_2^+ + I^- \longrightarrow Ar\cdot + N_2 + I\cdot).$[8] The sodium iodide procedure afforded a particularly satisfactory means of obtaining spiro-dimers [e.g. (3)] in the present work,[2,8a] and it is significant that the yields of (3) from the sodium iodide-induced [1] or copper-catalysed decomposition of (5),[5] or from photolysis of (4),[2] were ca. 40—45%. This is very similar to the yield of diene obtained in the hydrogen iodide experiments and is considered to reflect the proportion of initially-formed aryl radical which cyclises to a γ-lactam structure. The similarity between the yields of the two types of product (i.e. diene and dimer) indicates efficient scavenging of the spirodienyl radicals by hydrogen iodide. In these room-temperature cyclisation reactions there is no evidence for conversion of spirodienyl radicals (2) into N-methylphenanthridin-one.

The diene (1) was obtained as a crystalline solid, and was characterised by analysis, spectroscopy, and by its acid- and base-catalysed isomerisations to (6). There was no evidence for the formation of the conjugated diene (7).

Attempts to extend the hydrogen iodide method for the preparation of other spirodienes met with limited success. One complication which manifested itself was the competition for the spirodienyl radical between

* An inefficient syntheses of (8) by the hydrogen iodide-catalysed decomposition of the appropriate diazonium salt is described in the experimental section.

were available from the acid-catalysed methanolysis of the corresponding dienols.[5]

(7)

(8)

(9)

(10)
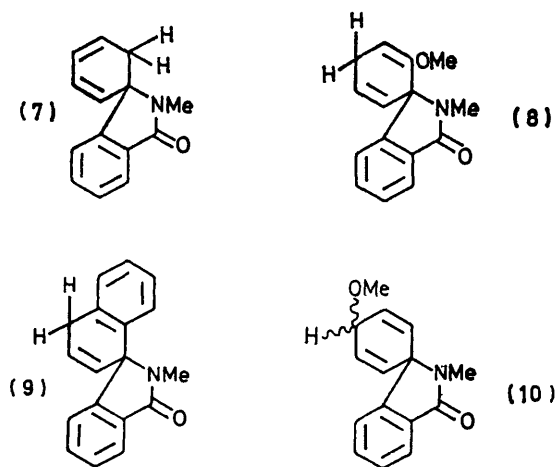
Hydrogen abstraction from the four dienes [(1) and (8)—(10)] was investigated using di-t-butyl peroxy-oxalate [9] (at 60° in benzene) and di-t-butyl peroxide (in boiling chlorobenzene). In the former case the principal hydrogen-abstracting species is very probably the butoxyl radical. In the latter, however, methyl radicals may play a significant role. No attempt has been made to quantify this, for example by determination of butanol/acetone ratios. The identity of the products was sufficient, in each case, to define the major reaction path as involving cyclohexadienyl radicals.

[7] B. Chauncy and E. Gellert, Austral. J. Chem., 1969, 22, 993; see also B. Chauncy and E. Gellert, ibid., 1970, 23, 2503.

[8] (a) D. H. Hey, G. H. Jones, and M. J. Perkins, Chem. Comm., 1970, 1438; (b) W. A. Waters, J. Chem. Soc., 1942, 266.

[9] P. D. Bartlett, E. P. Benzing, and R. E. Pincock, J. Amer. Chem. Soc., 1960, 82, 1762.

With peroxyoxalate at 60°, none of the four dienes gave any phenanthridinones; they gave instead a mixture of stereoisomeric spiro-dimers [*e.g.* (3)] as the major primary product. This was best demonstrated with the diene (10), the dimers from which were less susceptible to removal by secondary radical reactions (see below) than were those from the other dienes, and were spectroscopically similar to those formed from photolysis of 2-iodo-4'-methoxy-*N*-methylbenzanilide.[5]

Hydrogen abstraction at *ca.* 130° by means of radicals from di-t-butyl peroxide gave different results. Both the diene (1), and dienes (10), gave phenanthridinones in good yield (*ca.* 90 and 80% respectively). The phenanthridinone formed from (10) was exclusively 3-methoxy-*N*-methylphenanthridinone (11), *i.e.* the product of nitrogen migration in the spirodienyl intermediate. In contrast, the dialin (9) and diene (8) both gave high yields of dimeric products unaccompanied by phenanthridinones.


(11)
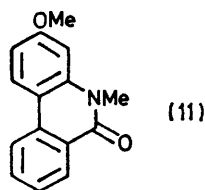
These observations are interpreted as reflecting a relatively low tendency for the spirodienyl radicals derived from (8) and (9) to undergo rearrangement. Hence in these cases bimolecular dimerisation competes more effectively with unimolecular rearrangement. Similar conclusions have been drawn from the dimer pyrolyses (Part XXVII). Hydrogen abstraction from (10) at 100° gives dimers and a little 3-methoxy-*N*-methylphenanthridinone (11). In this case the spirodienyl dimers decompose slowly at 100°,[1] and the phenanthridinone may, therefore, arise indirectly. Certainly, dimerisation still competes effectively with rearrangement at this temperature. However, decomposition of the unsubstituted dimer (3) is very slow at 130°, yet the predominant product of hydrogen abstraction from (1) at this temperature is *N*-methylphenanthridinone. In this case, therefore, the unimolecular rearrangement must be competing successfully with the bimolecular dimerisation. The competition would be expected to be concentration dependent, but this point has not been investigated.

The present results are consistent with a stepwise mechanism for phenanthridinone formation involving two discrete isomeric cyclohexadienyl radicals [*e.g.* (2) and (13)], as already discussed for the dimer pyrolysis reactions.[2] They do not, however, distinguish between a direct [1,2]shift of amide nitrogen and the alternative mechanism involving ring-opened intermediates such as (12), which found some support in Part XXVII when it was noted that the ring-opened amide (15) could be isolated from pyrolysis of the dimer (14) in the presence of 9,10-dihydroanthracene.[1]

In those instances where cyclohexadienyl dimers are formed, these products are themselves susceptible to further attack by butoxyl radicals. This could occur by addition to the double bonds, but a much more serious
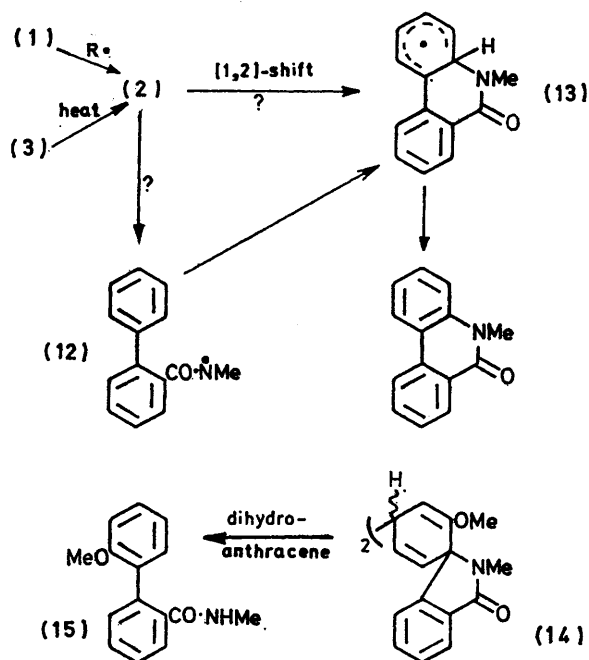

complication involves abstraction of the doubly allylic hydrogen atoms. Not surprisingly, therefore, the chromatographic 'dimer fraction' was usually more complex than would be expected for a mixture of stereoisomeric spiro-dimers. The exception to this was the dimeric product obtained by hydrogen abstraction from (10), for in this case, (16), the allylic hydrogen atoms are replaced by methoxy-groups.

(16)
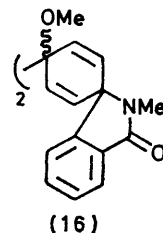
The consequences of hydrogen abstraction from the dimers were further investigated in the case of the unsubstituted dimer (3). The product of allowing this to react with butoxyl radicals from the decomposition of di-t-butyl peroxyoxalate at 60° was found by n.m.r. to be similar to that from the analogous reaction of (1). In addition a small amount of a product m.p. 170—180° was isolated from the reaction of (3), which, from the 1690 cm⁻¹ carbonyl absorption (γ-lactam) and the strong parent ion at *m/e* 418, is thought to be the dehydro-dimer (17) (*cf.* ref. 10) presumably as a mixture of

[10] D. J. Atkinson, M. J. Perkins, and P. Wood, *J. Chem. Soc.* (C), 1971, 3240.

geometrical isomers. The major components in the remaining product, as judged from its i.r. spectrum, had retained the γ-lactam structure; n.m.r. spectroscopy showed aliphatic protons, suggesting that addition to the double bonds of (17) [and perhaps also of (3)] had occurred.

(17)

(18) R = Me
(19) R = Et
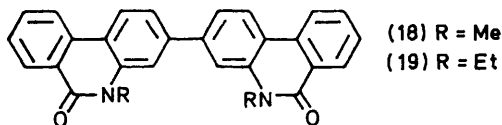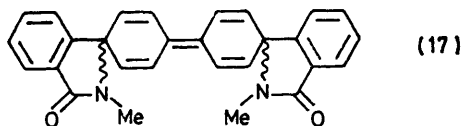
At 130°, with di-t-butyl peroxide, a substantial yield of a high melting (>300°) yellow crystalline solid was obtained from (3). This contained two hydrogen atoms less than (7), (m.s.) and its i.r. spectrum showed a doublet at 1650 and 1610 cm⁻¹, which is characteristic of 3-substituted N-alkylphenanthridinones.[1] The product has, therefore, been assigned structure (18). The formation of (18) is readily interpreted in terms of hydrogen abstraction followed by rapid migration of amide nitrogen, as occurs in the reactions of (1) at this temperature.[1] The absence of γ-lactam absorption in the i.r. region and the mass spectral data are consistent with rearrangement having occurred in both halves of the molecule. A trace of the same compound was identified among the products of reaction (1) with di-t-butyl peroxide at 130°.

A product (19), m.p. 315—320°, similar to (18), was obtained from the reaction of di-t-butyl peroxide with the NN'-diethyl analogue of (3). A possible alternative structure (20) for this compound, which might have arisen by hydrogen abstraction from a hydroaromatic dimer already containing the rearranged δ-lactam rings, seems to be excluded by the assignment of this structure to a compound, m.p. 306—308°, isolated from acid-

(20)

(21)
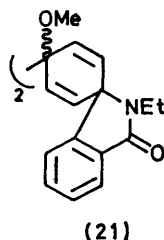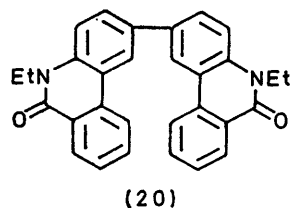
catalysed isomerisation of (21).[5] The two products were spectroscopically distinct, only (19) exhibiting the split carbonyl absorption characteristic of 3-substituted-N-alkylphenanthridinones.[1]

[11] D. H. Hey, C. W. Rees, and A. R. Todd, J. Chem. Soc., 1967, 1518.

EXPERIMENTAL

Treatment of reaction mixtures, analytical procedures, and instrumentation were as described in Part XXVI.[2]

Preparation of the Spirodiene-lactam (1).—Hydrogen iodide was generated by the dropwise addition of a solution of iodine in hydriodic acid onto an excess of dry powdered red phosphorus. The gas thus liberated was passed, without prior purification, into a suspension of N-methyl-benzanilide-2-diazonium fluoroborate [11] (500 mg) in dry oxygen-free methylene chloride (200 ml). Decomposition of the diazonium salt was complete within a few seconds, and the reaction was rapidly quenched by shaking with water. The methylene chloride was washed with aqueous sodium thiosulphate, and then again with water, dried, and filtered, and the solvent was removed. Examination of the residue both by t.l.c. and by g.l.c. indicated the presence of two major products, namely N-methylphenanthridinone and the diene (1). These were readily separated by column chromatography to give the diene as a colourless oil which crystallised from a small volume of light petroleum containing a little benzene; it had m.p. 63—65°. Spectral characteristics and analytical figures for this product were reported in Part XXVI.[2] In a repetition of the reaction, the product mixture was allowed to stand overnight before being quenched with water. The products of this reaction were N-methylphenanthridinone (35%) and N-methylbi-phenyl-2-carboxamide (45%). These were separated by chromatography, and the amide, m.p. 168—170°, was identified by comparison with an authentic specimen. The amide presumably results from acid-catalysed rearrangement of the diene. In attempts to scale up the synthesis of the diene, much reduced yields were obtained as a consequence of competing side reactions, the nature of which will be discussed elsewhere.[5]

Preparation of the 2'-Methoxy-N-methylspirodiene-lactam (8).—A suspension of 2'-methoxy-N-methylbenzanilide-2-diazonium fluoroborate [11] (1 g) in methylene chloride was treated with hydrogen iodide and the reaction mixture was immediately worked-up as described above. The major product was shown by t.l.c. to be the yellow 2-methyl-3-oxoisoindoline-1-spiro-1'-cyclohexa-3',5'-diene-2'-one.[12] Chromatography over alumina removed 4-methoxy-N-methyl-2-iodobenzanilide. Further elution gave a colourless oil (73 mg) which crystallised from a small quantity of light petroleum containing a little benzene, m.p. 85—86°. This was identified as the required 2-*methyl*-2'-*methoxy*-3-*oxoisoindoline*-1-*spiro*-1'-*cyclohexa*-2',5'-*diene* (8) (Found: C, 74·9; H, 6·0; N, 5·5. $C_{15}H_{15}NO_2$ requires C, 74·7; H, 6·2; N, 5·8), $\nu_{max.}$ 1690 (γ-lactam) and 1650 cm⁻¹ (olefin); τ 2·1—3·0 (4H, m), 3·8 (1H, d of t), 4·8 (1H, d of t), 4·87 (1H, m), 7·0 (2H, m), 6·67 (3H, s), and 7·25 (3H, s). The n.m.r. spectrum of the total chromatographic fraction was indistinguishable from that of the crystalline material, and non-crystalline product was employed in the hydrogen-abstraction experiments described below. Further elution gave the yellow dienone. Attempts to scale up this experiment were unsuccessful.

Hydrogen Abstraction from the Cyclohexadienes.—Preparation of dienes. The 4'-methoxyspirodienes (10), obtained from the corresponding dienols by brief treatment with acidified methanol,[5] consisted of a mixture of two stereo-isomers m.p. 110—130°. The dialin (9), m.p. 132—133°,

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

was obtained from the pyrolysis of the corresponding cyclohexadienyl dimer.[1]

Hydrogen abstraction experiments. (All experiments were conducted in an atmosphere of nitrogen). (i) A solution of the diene (1) (50 mg) and di-t-butyl peroxyoxalate [9] ($t_{\frac{1}{2}}{}^{60°} = 6.8$ min [9]) (50 mg) in benzene (1 ml), was warmed at 60° for 1 h under an atmosphere of nitrogen. N-Methylphenanthridinone could not be detected among the reaction products. Chromatography gave a dimer fraction of some complexity (t.l.c. and n.m.r.). However, when a mixture of stereoisomeric cyclohexadienyl dimers (3) (120 mg) and di-t-butyl peroxyoxalate (60 mg) were similarly heated in benzene (1 ml) at 60°, a comparable product mixture was obtained. The reaction mixture from the dimer reaction deposited a small amount of white solid, m.p. 170—180° (5 mg). This had $\nu_{max.}$ 1690 cm^{-1} (γ-lactam), and its mass spectrum showed a strong parent ion peak at $m/e = 418$. It is considered to be the *dehydro-spirodimer* (17). The remaining product had spectra (i.r. and n.m.r.) very similar to those of the dimeric product formed following hydrogen abstraction from (1). These featured $\nu_{max.}$ 1690 (γ-lactam) and τ 8.5—9.5 (saturated C–H).

(ii) A solution of the diene (1) (70 mg) and di-t-butyl peroxide ($t_{\frac{1}{2}}{}^{130°} = 8$ h) in chlorobenzene (1 ml) was refluxed overnight. Examination of the reaction products by g.l.c. and t.l.c. revealed the formation of N-methylphenanthridinone (87%) and a trace of the dimeric substance, m.p. 315—321°. This same substance was produced as the major product of a reaction of the spirocyclohexadienyl dimers (3) (300 mg) and di-t-butyl peroxide (300 mg) in boiling chlorobenzene (5 ml) for 15 h. A yellow crystalline solid was precipitated from the reaction mixture. This was separated, washed with benzene, and dried (305 mg). It is considered to be NN'-*dimethyl-3,3'-biphenanthridine*-6,6'-(5H,5'H)-*dione* (18), m.p. 318—322° [Found: C, 79.9; H, 5.1; N, 6.6%; M, 416 (m.s.). $C_{28}H_{20}N_2O_2$ requires C, 80.4; H, 4.8; N, 6.7%; M, 4.6], $\nu_{max.}$ 1650 (δ-lactam) and 1610 cm^{-1} (3-substituted N-alkylphenanthridinone).

(iii) Hydrogen abstraction from the dimer as reported in (ii) above was repeated with a specimen of the NN'-diethyl analogue of (3). The compound used was a single crystalline stereoisomer, m.p. 224—229°, isolated from the photolysis of N-ethyl-2-iodobenzanilide in benzene.[5] Progress of the reaction was similar, a yellow crystalline solid with m.p. 315—320° being obtained. This is considered to be NN'-*diethyl*-3,3'-*biphenanthridine*-6,6'-(5H,5'H)-*dione* (19) [Found: M, 444 (m.s.). $C_{30}H_{24}N_2O_2$ requires M, 444], $\nu_{max.}$ 1650 (δ-lactam) and 1610 cm^{-1} (3-substituted N-alkylphenanthridinone). The n.m.r. spectrum (100 MHz, CDCl$_3$, 80°) showed that the signals due to the protons at C-1 and C-1' (τ 1.67) experienced a large *ortho* splitting, consistent with a 3,3'-link between the phenanthridinone nuclei. The product was readily distinguished spectroscopically from an NN'-diethylphenanthridinone dimer believed to have a 2,2'-link.[5]

(iv) A solution of the diene (10) (60 mg) and di-t-butyl peroxyoxalate (60 mg) in benzene (1 ml) was maintained at 60° overnight. The white precipitate which had formed was separated, and shown by chromatographic and spectroscopic examination to be similar to the mixture of stereoisomers of the dimer (16), previously isolated from the photolysis of 2-iodo-4'-methoxy-N-methylbenzanilide in benzene. The mother liquors contained further dimer together with unchanged starting material; 3-methoxy-N-methylphenanthridinone could not be detected.

(v) A solution of the diene (10) (70 mg) and di-t-butyl peroxide (70 mg) in chlorobenzene (1 ml) was refluxed overnight. Examination of the products by g.l.c. and t.l.c. revealed the formation of 3-methoxy-N-methylphenanthridinone (78%). This was isolated by chromatography, and its identity confirmed by comparison with authentic material.

(vi) and (vii) In experiments similar to (v), the diene (8), and dialin (9) were found not to give detectable (g.l.c. and t.l.c.) quantities of phenanthridinones. Instead complex mixtures of dimeric products were indicated by t.l.c. [*cf.* (i) and (ii) above].