Internuclear Cyclisation. Part XXIX.[1] Oxidation of Some *N*-Methylbiphenyl-2-carboxamides with Persulphate

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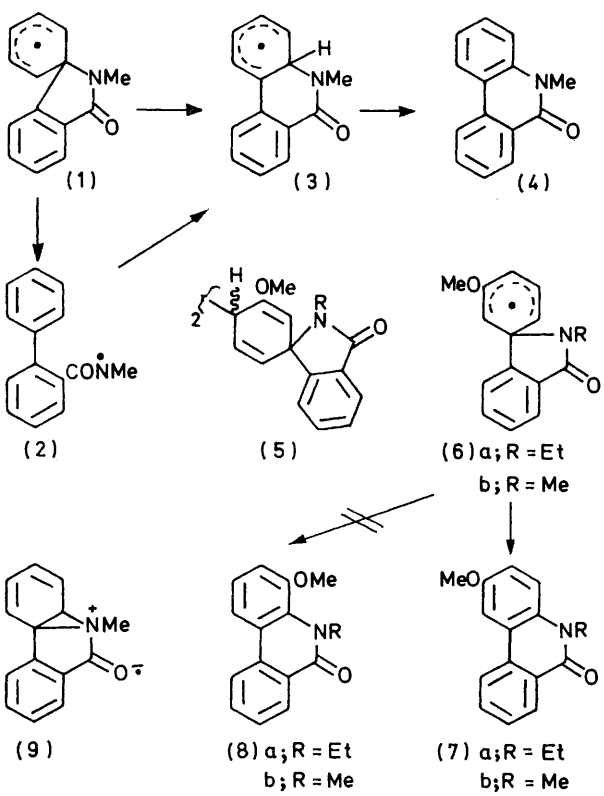
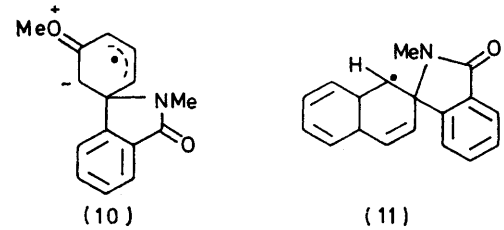
Oxidations of 2'-, 3'-, and 4'-methoxy-*N*-methylbiphenyl-2-carboxamides by potassium persulphate have been studied. Cyclisation to γ-lactams as well as the expected phenanthridinones is found to be important, particularly in alkaline solution. Similar oxidation of *N*-methylbiphenyl-2-carboxamide itself in alkaline solution in the presence of oxygen gives some of the γ-lactam-dienone (16) in addition to *N*-methylphenanthridinone. Persulphate oxidation of 3-methoxy-*N*-methylphenanthridinone gives the biphenanthridinone (20).

In Parts XXVII [2] and XXVIII [1] isomerisation reactions of the spirocyclohexadienyl radical (1) and related species have been discussed. Some evidence has emerged which supports rearrangement by way of the ring-opened intermediate (2),[2] but the high regioselectivity [3] found in the rearrangement of (6a) formed by pyrolysis of (5) [2] seems difficult to interpret on this basis. Furthermore, in only one instance was it possible to isolate a product which might have arisen by scavenging of the ring-opened radical.[2] Therefore serious consideration has been given to an alternative mechanism involving a

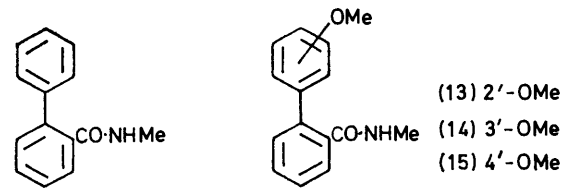


sigmatropic [1,2]-shift of nitrogen, in the bridged transition state (intermediate?) for which, the unpaired electron might be accommodated in a relatively low-lying carbonyl π* orbital, *e.g.* (9). No precedent appears to exist for this type of rearrangement, however, and in the present system where the migration terminus is a relatively stable cyclohexadienyl radical, the possibility seems energetically unlikely. Furthermore, if the selectivity in the rearrangement of (6) is a consequence of such a mechanism, perhaps as a result of partial localisation of the unpaired electron [*e.g.* (10)], then selectivity might reasonably also be expected in the rearrangement of (11). The experimental result [2] is contrary to this.

In an attempt to differentiate between these alternatives, a study has been made of the oxidation of the ring-



opened amides (12)—(15). The oxidation of (12) with lead tetra-acetate–iodine has previously been found to give a good yield of *N*-methylphenanthridinone (4), and the reaction was considered to proceed *via* (2).[4] The same intermediate has been suggested for the oxidation of (12) to (4) by means of aqueous persulphate.[5] The lead tetra-acetate–iodine method was of little value with the methoxylated amides (13)—(15), but it has now been found that persulphate does oxidise these amides to give cyclisation products in good yield. However, the proportions and nature of these have failed to throw light on the mechanism of the spirodienyl rearrangements, and have created several new problems.



The persulphate-oxidation reactions were carried out in hot (usually boiling) dilute aqueous solution, in which

[1] Part XXVIII, D. H. Hey, G. H. Jones, and M. J. Perkins, preceding paper.
[2] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 105.
[3] A. Hassner, *J. Org. Chem.*, 1968, **33**, 2684.
[4] D. H. Hey, G. H. Jones, and M. J. Perkins, *J. Chem. Soc.* (*C*), 1971, 116.
[5] P. M. Brown, P. S. Dewar, A. R. Forrester, A. S. Ingram, and R. H. Thomson, *Chem. Comm.*, 1970, 849.

the amides were completely soluble. The progress of persulphate oxidations in initially neutral solutions is accompanied by a reduction in pH. In view of the acid-sensitive nature of possible products of these reactions, experiments were duplicated in the presence of an excess of potassium carbonate. The experimental results are summarised in Table 1. With the unsubstituted amide (12) (*cf.* ref. 5) and the 3′-methoxy-derivative (14), the major products in the absence of potassium carbonate were the expected *N*-methylphenanthridinones. A high selectivity was noted in the latter case, with 2-methoxy-*N*-methylphenanthridinone (7b) exceeding the 4-methoxy-isomer (8b) by 8 : 1. Nevertheless, this contrasts with the apparently exclusive formation of (7a) in the pyrolysis of the cyclohexadienyl dimer (5) [2] (at a temperature some 100° higher).* The qualitative observation was made that the presence of potassium carbonate retarded these oxidations, particularly that of (14), but had no effect on the nature of the products. However,

TABLE 1

Products of persulphate oxidation of some *N*-methylbiphenyl-2-carboxamides

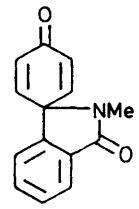
		Products [b]	
Amide	Conditions [a]	Phenanthridinones [%]	Other [%]
(12)	100°; K_2CO_3 absent	(4) [86]	
(12)	100°; K_2CO_3	(4) [n.e.]	
(12)	80°; K_2CO_3; O_2	(4) [40]	(16) [10]
(14)	100°; K_2CO_3 absent	(7b) [73]; (8b) [9]	
(14)	100°; K_2CO_3	(7b) [n.e.]; (8b) [n.e.] [c]	
(15)	100°; K_2CO_3 absent [d]	(17) [47]	(16) [14]; (18) [n.e.]
(15)	100°; K_2CO_3 absent [e]	(17) [5]	(16) [n.e.] (18) [3] (20) [*ca.* 35]
(15)	100°; K_2CO_3	(17) [9]	(16) [70]
(13)	100°; K_2CO_3 absent	(4) [10]	(21) [45]
(13)	100°; K_2CO_3	None detected (≪1%)	(24) [20]; (23) [25]

[a] All reactions in aqueous solution at reflux or at lower temperatures under N_2, except where stated to be under O_2. For full details, see Experimental. [b] n.e. = Not estimated. A blank entry means that no additional products were identified. [c] Reaction incomplete; ratio of products unchanged from that in the absence of carbonate. [d] *Ca.* 15% conversion. [e] 100% conversion.

with potassium carbonate and molecular oxygen at 80° (all other reactions were in oxygen-free conditions), oxidation of (12) gave a reduced yield of phenanthridinone, together with some of the cross-conjugated dienone (16). This provides a clear indication that cyclisation of (12) to a γ-lactam can occur under the persulphate-oxidation conditions. The source of carbonyl oxygen may be the molecular oxygen, but other possibilities cannot be excluded on present evidence. The presence of oxygen was without effect on the products of oxidation of (14), under the conditions which yielded some (16) from (12).

* The effect of changing the *N*-alkyl substituent from methyl to ethyl in the *meta*-methoxy-series is expected to be unimportant.

Different and unexpected results were obtained when the 4′- and 2′-methoxy-amides (15) and (13) were oxidised by persulphate. With the 4′-methoxy-derivative (15) in the presence of carbonate, a low yield of the expected



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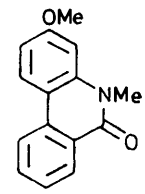

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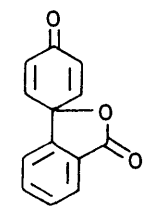
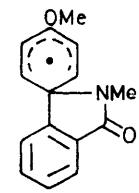


(18)

3-methoxy-*N*-methylphenanthridinone (17) was accompanied by a high yield of the spirodienone-lactam (16). The latter could reasonably be formed by way of a spirodienyl radical (19), oxidation of which to the corresponding carbonium ion, followed by hydrolysis, giving (16).

Repetition of the oxidation in the absence of carbonate gave, after a short reaction time (*ca.* 20% conversion), 3-methoxy-*N*-methylphenanthridinone (17), in *ca.* 50% yield. This was accompanied by smaller amounts of the dienone-lactam (16) and the dienone-lactone (18). However, as the reaction progressed a new component



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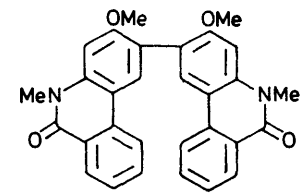
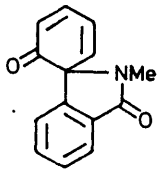


(20)

became dominant among the products, and spectroscopic evidence (n.m.r., m.s.) leaves little doubt that this is the biphenanthridinone (20). At first sight this would appear to be the product of dimerisation of the cyclohexadienyl radical precursor of (17) followed by dehydrogenation. However, in no other persulphate oxidations in this series were significant amounts of dimers of any kind observed. Furthermore, the dimer (30) can be produced in high yield by persulphate oxidation of the phenanthridinone (17), and presumably this is its origin also in the oxidation of (15). The oxidation of (15) thus introduces several problems: (i) the nature of the oxidation process which converts (17) to dimer (20); (ii) the role of carbonate in altering the proportions of the γ- and δ-lactam in the products, and (iii) the origin of the lactone (18). In no other reaction in this series have γ-lactones been detected, nor have benzocoumarins been found.

The oxidation of the amide (13) in the absence of potassium carbonate gave the linear dienone (21), together with unsubstituted *N*-methylphenanthridinone (4) but no 1-methoxy-*N*-methylphenanthridinone (22). In the presence of carbonate it gave instead the methoxydienone (23) and the methoxydienols (24) as the only

identifiable products. When the deuteriated amide (25) was oxidised with persulphate in the absence of carbonate, the n.m.r. spectrum of the resulting *N*-methylphenanthridinone was consistent only with structure (26), thus eliminating the possibility of its formation by way of a dienol–benzene rearrangement of (24) with (the expected) phenyl migration. The possibility of such a route, but with nitrogen migration, cannot be ruled out, although treatment of dienol (24) with aqueous hydrochloric acid gives a good yield of the dienone (21), and no phenanthridinones.



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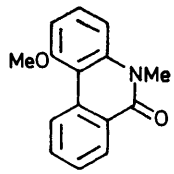

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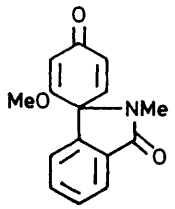

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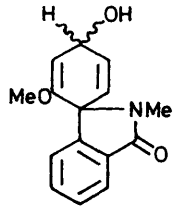

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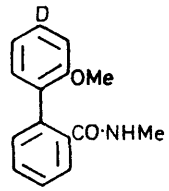

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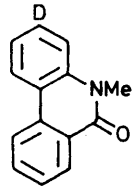
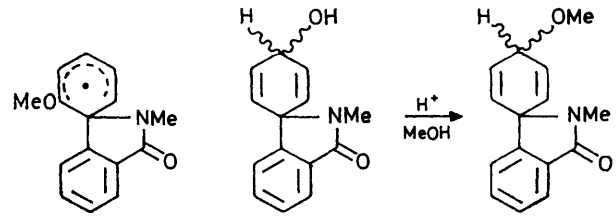


(26)

The mixture of dienols (24) is oxidised to the dienone (23) under the basic reaction conditions, and this is probably the origin of (23) in the persulphate oxidation of (13). Two routes to the mixture of dienols merit consideration. The first involves oxidation of a methoxyspirocyclohexadienyl radical (27) to the corresponding cation and interception by water. The second step of this type of reaction finds analogy in the acid-catalysed epimerisation of the dienols (28);[6] similarly, with acid in methanol, (28) gives the methanolysis products (29).[6] Both of these reactions are believed to involve spirocyclohexadienyl cations. Precedent also exists in the literature.[7] However, we have failed to effect epimerisation or alcoholysis of the dienol (24), which is instead very readily converted into (21) in the presence of acid.[6] In the alternative mechanism, interception of the methoxyspirocyclohexadienyl radical (27) could take place by an oxygen-centred radical ($SO_4^{\cdot-}$) followed by hydrolysis. (·OH itself is too reactive to appear in a major radical coupling product).



(27) (28) (29)

In those of the above reactions in which more than one phenanthridinone can be formed [*i.e.* from (13) and (14)], the relative yields are quite different from those found in the corresponding dimer pyrolyses (see Table 2), and the simplest interpretation of this would be in terms

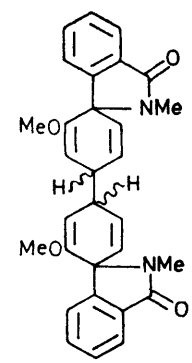
TABLE 2

Yields of phenanthridinones from amide oxidation and dimer pyrolysis

Reaction	Conditions	Phenanthridinones [%] [a]
Persulphate oxidn. of (14)	H_2O reflux; K_2CO_3 absent	(7a) [73]; (8b) [9]
Pyrolysis of (5)	1,2,4-$C_6H_3Cl_3$ reflux	(7a) [80]; (8a n.d.) [≪1%]
Pyrolysis of (5)	$HOCH_2CH_2OH$ reflux	n.d. [≪1%]
Persulphate oxidn. of (13)	H_2O reflux; K_2CO_3 absent	(4) [10]; (22) n.d. [≪1%]
Pyrolysis of (30)	1,2,4-$C_6H_3Cl_3$ reflux	(4) [19]; (22) [23]
Pyrolysis of (30)	$HOCH_2CH_2OH$ reflux	(4) [25]; (22) [11]

[a] n.d. = Not detected.

of a major difference in mechanism. However, the temperatures and particularly the solvents are very different. An amido-radical might reasonably be expected to exhibit noticeably different reactivity patterns in water and in hydrocarbon (or hydrocarbon-like) solvents. In an attempt to test this point, pyrolyses of (30) and (5) were repeated in refluxing ethylene glycol as a



(30)

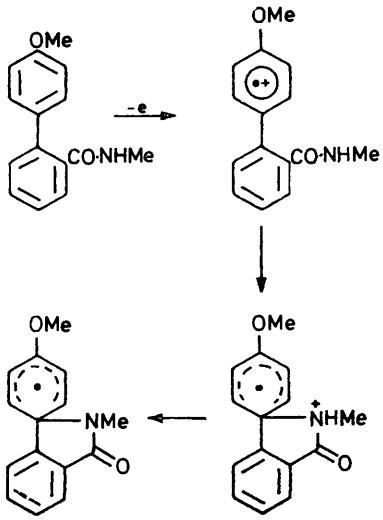
high-boiling hydroxylic solvent. Under these conditions (5) yielded no detectable phenanthridinones. However, (30) gave both (4) and (22), and although the proportion of (22) was substantially reduced compared with the

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

[7] E. C. Friedrich and S. Winstein, *Tetrahedron Letters*, 1962, 475.

result in trichlorobenzene, this is still very different from the situation which obtains in the persulphate oxidation of (13) from which only (4) is formed.

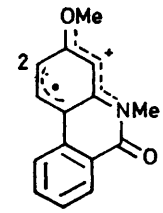
The results described here have not cast any light on the mechanisms of the dimer pyrolysis reactions. It seems probable that the two series of reactions do not involve amido-radicals akin to (2) as common intermediates, but this has not been conclusively established. It is possible that amido-radicals are involved in neither reaction system. One plausible mechanism which circumvents amido-radical participation in the persulphate oxidations, at least in those cases where methoxy-substitution is present, merits serious consideration. This involves one-electron oxidation of the aromatic moiety (as is believed to occur in the persulphate oxidation of anisole [8]), followed by internal nucleophilic capture by the amide function and subsequent de-



protonation. Intermolecular capture of an aromatic radical cation by a nucleophile was recently established in an anodic oxidation reaction,[9] and has been extensively discussed in the context of other anodic substitutions,[10] This type of mechanism affords an alternative route to the cyclohexadienyl radical intermediates, which are probably further oxidised very rapidly, thus preventing dimerisation. A measure of support for an electron-transfer initiated mechanism is found in the formation of (20), which is most easily interpreted in terms of dimerisation of the radical cation of 3-methoxy-*N*-methylphenanthridinone, the valence structure (31) of which suggests a high spin density at C-2. Electrophilic attack of a dication on a neutral molecule cannot, however, be ruled out as an alternative mechanism for the formation of this dimer. Such a mechanism has been proposed, for example, to explain the formation of dimethoxybiphenyls during oxidation of anisole by lead tetra-acetate.[11]

[8] P. M. Brown, J. Russell, R. H. Thomson, and A. G. Wylie, *J. Chem. Soc.* (*C*), 1968, 842.
[9] V. D. Parker and L. Eberson, *J. Amer. Chem. Soc.*, 1970, **92**, 7488.

Clearly there remains much to be understood regarding the mechanism of the oxidations described here. The role of base seems to be more than one of merely inhibiting acid-catalysed reactions of the primary products, though this must be important. One possible difference between the reactions in the presence and absence of carbonate might be the participation, in the



(31)

former, of hydroxyl radicals,[12] though we have no evidence which requires this.

EXPERIMENTAL

Treatment of reaction mixtures, analytical procedures, and instrumentation were as described in Part XXVI.[4]

Preparation of the Carboxamides.—N-*Methylbiphenyl-2-carboxamide*. This compound was prepared from biphenyl-2-carboxylic acid following conventional procedures. It had m.p. 168—170° (lit.,[4] m.p. 168—170°).

4′-*Methoxy*-N-*methylbiphenyl-2-carboxamide*. 2-Methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (16) (5 g) in ethanol (100 ml) was reduced with sodium borohydride (300 mg). The reaction mixture was stirred for 30 min and then solvent was removed until the residual volume was 10 ml. Aqueous sodium hydroxide (100 ml, 10%) was added, and the mixture was then boiled under reflux for 15 h, cooled, and acidified (aqueous HCl). The mixture was extracted with chloroform, the extract was washed with water, dried ($MgSO_4$), and the solvent was removed. The residual crude phenol was dissolved in acetone (20 ml), the solution was boiled, and aqueous sodium hydroxide (50 ml) and dimethyl sulphate (5 ml) were added dropwise. When addition was complete, the mixture was refluxed for a further 5 min, cooled, and extracted with chloroform. The extract was washed with water, dried ($HgSO_4$), and the solvent was removed. Mesityl oxide was removed by co-distillation with added toluene. The residual pale yellow oil crystallised from ethanol to give 4′-*methoxy*-N-*methylbiphenyl-2-carboxamide* as colourless prisms (3·6 g) m.p. 131—133° (Found: C, 74·3; H, 6·1; N, 5·8. $C_{15}H_{15}NO_2$ requires C, 74·7; H, 6·2; N, 5·8%), $\nu_{max.}$ 3320 and 1640 cm^{-1} (secondary amide), τ 2·2—3·2 (8H, m), 4·6 (1H, broad s, NH), 6·15 (3H, s, OCH_3), and 7·3 (3H, d, $NHCH_3$).

3′-*Methoxy*-N-*methylbiphenyl-2-carboxyamide*. 2-Methyl-3′-methoxy-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (prepared by the copper-catalysed decomposition of 3′-methoxy-*N*-methylbenzanilide-2-diazonium fluoroborate in the presence of oxygen [6]) (1 g) in ethanol (20 ml) was reduced with sodium borohydride (60 mg). After the mixture had been stirred for 30 min, the bulk of the solvent

[10] R. N. Adams, *Accounts Chem. Res.*, 1969, **2**, 175.
[11] R. O. C. Norman, C. B. Thomas, and J. S. Willson, *J. Chem. Soc.* (*B*), 1971, 518.
[12] R. O. C. Norman, P. M. Storey, and P. R. West, *J. Chem. Soc.* (*B*), 1970, 1087.

was removed, and aqueous sodium hydroxide (50 ml, 10%) was added. The mixture was refluxed overnight, cooled, acidified (HCl), and extracted with chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and the solvent was removed. The crude 4'-hydroxy-3'-methoxy-*N*-methylbiphenyl-2-carboxamide was dissolved, together with 2-chlorobenzoxazole (700 mg) in dry acetone (15 ml), and the solution was heated to boiling point and stirred under reflux with anhydrous potassium carbonate (1·5 g) for 24 h.[13] The mixture was cooled, filtered, and the solvent was removed. The residual *4'-benzoxazol-2-yloxy-3'-methoxy-*N*-methylbiphenyl-2-carboxamide* crystallised from benzene as needles, m.p. 157—159° (Found: C, 73·0; H, 4·8; N, 8·1. $C_{21}H_{16}N_2O_3$ requires C, 73·2; H, 4·65; N, 8·15%), $\nu_{max.}$ 3320 and 1625 cm^{-1} (secondary amide). This product (1·2 g) and palladium on charcoal (400 mg 10%) were suspended in benzene (100 ml) and shaken with hydrogen at atmospheric pressure and 50° overnight.[12] Filtration and removal of solvent left a colourless oil. Chromatographic purification then gave *3'-methoxy-*N*-methylbiphenyl-2-carboxamide* as colourless crystals, m.p. 92—94° from benzene (700 mg) (Found: C, 74·6; H, 6·2; N, 5·6. $C_{15}H_{15}NO_2$ requires C, 74·4; H, 6·2; N, 5·8%), $\nu_{max.}$ 3300 and 1630 cm^{-1} (secondary amide), τ 2·2—3·3 (8H, m), 4·55 (1H, broad s, NH), 6·2 (3H, s, OCH_3), and 7·35 (3H, d, $NHCH_3$).

*2'-Methoxy-*N*-methylbiphenyl-2-carboxamide.* A synthesis of this compound has been given in Part XXVII.[2] It has also been obtained by a route similar to that described above for the 3'-methoxy-derivative, except that the initial borohydride reduction of 2'-methoxy-2-methyl-3-oxoisoindoline-1-spiro-1'-cyclohexa-2',5'-dien-4'-one (prepared by copper-catalysed decomposition of 2'-methoxy-*N*-methylbenzanilide-2-diazonium fluoroborate [6]), gave, in addition to the desired cyclohexadienol, a substantial quantity of a cyclohexenol. The products of the reduction were refluxed with 10% aqueous sodium hydroxide overnight, as described above, and the reaction mixture was extracted with chloroform to remove the unchanged cyclohexenols. These were demethylated on treatment with ethanolic hydrochloric acid, to give *2-methyl-3-oxoisoindoline-1-spiro-1'-cyclohex-3'-en-2'-one*, as pale yellow crystals, m.p. 140—141° from ethanol (Found: *M*, 227·0943. $C_{14}H_{13}NO_2$ requires *M*, 227·0946), τ 2·0—2·9 (5H, m, 4 aromatic CH and 4'-H), 3·7 (1H, broad d, *J* 10 Hz, 3'-H), 7·0 (3H, s, $N{-}CH_3$), and 7·0—8·3 (4H, m). The alkaline solution, after extraction with chloroform, was acidified (HCl) and extracted with chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and the solvent was removed leaving crude 4'-hydroxy-2'-methoxy-*N*-methylbiphenyl-2-carboxamide as a pale yellow solid (700 mg from 1 g of dienone). This was treated with 2-chlorobenzoxazole as before, to give the benzoxazolyl derivative as a colourless oil after chromatography on alumina.[13] Hydrogenation after palladium on charcoal at 50° gave the desired 2'-methoxy-*N*-methylbiphenyl-2-carboxamide, m.p. 113—115°, indistinguishable from that prepared previously. Repetition of this experiment using deuterium gas in place of hydrogen for the last step gave *4'-deuterio-2-methoxy-*N*-methylbiphenyl-2-carboxamide*, although this was found to contain *ca.* 30% of undeuteriated material (m.s.).

Oxidation of the Carboxamides.—General procedure. The concentrations of amides were such that complete dissolution in water was achieved at the reaction temperature employed. Persulphate (used in excess) was not added until dissolution of the amide was complete, and the reactions were quenched by cooling before the starting material was completely consumed. This was followed immediately by extraction of the organic products into chloroform. To accomplish this, the progress of prolonged reactions was monitored by t.l.c. and/or g.l.c. Whenever possible, product analysis was by g.l.c. (*cf.* ref. 4 for details); where this was not possible, products were estimated by weighing, usually after separation by chromatography on neutral aluminal (*cf.* ref. 4). Reactions were conducted in the absence of oxygen (N_2) except where specified to the contrary. Percentage yields are based on starting material consumed. Characterisation of reference compounds has been described in earlier papers in this series, with the exceptions of 1-, and 3-methoxy-*N*-methylphenanthridinone,[6] and where otherwise detailed.

Oxidation of N-*methylbiphenyl-2-carboxamide.* (i) A solution of the amide (42 mg) in water (30 ml) was boiled under reflux, and potassium persulphate (100 mg) in water (5 ml) was added to it. After the mixture had been boiled for a further 10 min, g.l.c. analysis showed a trace of starting material (*ca.* 2 mg), and *N*-methylphenanthridinone (*ca.* 35 mg, 86%). Chromatography over alumina gave a colourless solid (36·2 mg) indistinguishable from authentic *N*-methylphenanthridinone.

(ii) A solution of potassium persulphate (100 mg) in water (5 ml) was added to a stirred solution of the amide (21 mg) and potassium carbonate (22 mg) in water (60 ml), which was maintained at 80°, and through which was bubbled a stream of oxygen. The mixture was stirred for 2 h at 80°, after which time g.l.c. revealed a trace of starting material (*ca.* 1 mg), *N*-methylphenanthridinone (40%), and 2-methyl-3-oxoisoindoline-1-spiro-1'-cyclohexa-2',5'-dien-4'-one (16).[14] The formation of this product, which was confirmed by g.l.c. on two different columns, and by t.l.c. on both alumina and silica gel, was shown, in a series of control experiments, to require the presence of both oxygen and potassium carbonate.

Oxidation of 3'-*methoxy-*N*-methylbiphenyl-2-carboxamide.* A solution of the amide (43 mg) in water (15 ml) was boiled under reflux, and potassium persulphate (70 mg) in water (5 ml) was added to it. The mixture was boiled under reflux for 1 h, after which extraction into chloroform and analysis by g.l.c. revealed unchanged starting material (15·5 mg), 2-methoxy-*N*-methylphenanthridinone (73%), and 4-methoxy-*N*-methylphenanthridinone (9%). The ratio of phenanthridinones was found to be independent of the extent of reaction, and it was also found in separate experiments that the presence of potassium carbonate or oxygen either individually or together had no effect on product composition. However, in the presence of these substances it was qualitatively observed that a longer reaction time was required.

Oxidation of 4'-*methoxy-*N*-methylbiphenyl-2-carboxamide.* (i) A solution of the amide (57 mg) in water (15 ml) was boiled under reflux, and potassium persulphate (100 mg) in water (5 ml) was added to it. The mixture was refluxed for 1 min, and rapidly cooled. The organic products were extracted into chloroform, and g.l.c. analysis revealed the presence of unchanged amide (47 mg), together with 3-methoxy-*N*-methylphenanthridinone (*ca.* 47%) and the

[13] W. J. Musliner and J. W. Gates, *J. Amer. Chem. Soc.*, 1966, **88**, 4271.

[14] D. H. Hey, J. A. Leonard, and C. W. Rees, *J. Chem. Soc.*, 1963, 5266.

dienone (16) (*ca.* 14%). Traces of the dimer (20), and lactone (18) [15] were detected by t.l.c. (see below).

(ii) In an experiment similar to (i), the reaction mixture was heated for 5 min. After this time oxidation was *ca.* 50% complete, but the yield of methoxyphenanthridinone had fallen to 30%.

(iii) A solution of the amide (150 mg) in water (50 ml) was boiled under reflux, and potassium persulphate (500 mg) in water (15 ml) was added to it. The mixture was refluxed for 30 min, cooled, and extracted with chloroform. Evaporation of the dried ($MgSO_4$) chloroform solution to small bulk deposited a pale brown solid (50 mg) which crystallised from chloroform as colourless needles, m.p. 340° (Found: *M*, 476·1722. $C_{30}H_{24}N_2O_4$ requires *M*, 476·1736), $\nu_{max.}$ 1660 (δ-lactam) and 1610 cm^{-1} (3-substituted *N*-alkylphenanthridinone). The n.m.r. spectrum showed a low field singlet (τ 1·92) for protons on C-1 and C-1′, and a second singlet (τ, 3·14) for protons on C-4 and C-4′, which, by analogy with the spectrum of 3-methoxy-*N*-methylphenanthridinone, defined the position of substitution in this dimeric product, and permitted its formulation as 3,3′-*dimethoxy*-NN′-*dimethyl*-2,2′-*biphenanthridine*-6,6′-(5H,5′H)-*dione*. The remaining organic products from this reaction was examined by g.l.c., which showed the complete disappearance of starting amide, and the formation of the dienone (16) (not estimated) and 3-methoxy-*N*-methylphenanthridinone (5%). The products were then chromatographed on neutral alumina. The first product eluted was identified as the dienone-lactone (18) (3·5 mg), white needles from ethanol, m.p. 182—184° (lit.,[15] m.p. 189°), $\nu_{max.}$ 1775 (γ-lactone), 1665, and 1633 cm^{-1} (cyclohexadienone) (*cf.* ref. 15).

(iv) A solution of the amide (46 mg) and potassium carbonate (60 mg) in water (15 ml) was boiled under reflux and potassium persulphate (100 mg) in water (5 ml) was added to it. The mixture was refluxed for 5 min. T.l.c. showed the absence of the dimer and of the dienone-lactone (18). G.l.c. analysis showed the presence of starting amide (11 mg), the spirodienone (16) (70%), and 3-methoxy-*N*-methylphenanthridinone (9%). The spirodienone was isolated by chromatography and was identified by comparison with an authentic sample.

(v) A solution of the amide (41 mg) and potassium carbonate (60 mg) in water (30 ml) was heated to reflux and cooled to 80°. Potassium persulphate (100 mg) in water (5 ml) was added to the mixture which was stirred under nitrogen at 80° for 2 h. T.l.c. showed the absence of the dimer (20) and the dienone-lactone (18). G.l.c. analysis, showed the presence of unchanged starting material (*ca.* 1 mg), the spirodienone (16) (68%), and 3-methoxy-*N*-methylphenanthridinone (9%). Experiments with larger amounts of potassium carbonate failed to reduce the yield of phenanthridinone, but inhibited disappearance of starting material.

(vi) A solution of 3-methoxy-*N*-methylphenanthridinone (52 mg) in water (50 ml) was boiled under reflux, and potassium persulphate (150 mg) in water (5 ml) was added to it. The mixture was refluxed for 5 min and extracted into chloroform. T.l.c. showed the presence of starting material and the dimeric phenanthridinone (20). Removal of the bulk of the solvent was accompanied by separation of the crude dimer (20), which, after crystallisation from chloroform, was indistinguishable from that obtained in (iii) above (18 mg; 60% based on unrecovered starting material). The mother liquors, after chromatography to remove residual dimer, yielded unchanged methoxyphenanthridinone (22 mg).

(vii) When the isomeric 1-, 2-, and 4-methoxy-*N*-methylphenanthridinones were subjected to the oxidation conditions of (vi), each was recovered unchanged (*ca.* 90% recovery).

(viii) Repetition of (vi) in the presence of potassium carbonate (125 mg) gave no trace of dimeric phenanthridinone (20). 3-Methoxy-*N*-methylphenanthridinone was recovered unchanged (*ca.* 80%).

Oxidation of 2′-*methoxy*-N-*methylbiphenyl*-2-*carboxamide*. (i) A solution of the amide (42 mg) in water (15 ml) was boiled under reflux and potassium persulphate (100 mg) in water (5 ml) was added. The mixture was refluxed for 10 min, and then extracted into chloroform. Analysis of the dried ($MgSO_4$) chloroform solution by g.l.c. indicated the presence of unchanged amide (7 mg) and *N*-methylphenanthridinone (10%). There was no component of the reaction mixture with the retention characteristics of 1-methoxy-*N*-methylphenanthridinone. The major product (t.l.c.) was the linear dienone (21),[16] which cannot be estimated by g.l.c. Therefore the products were chromatographed on alumina and a fraction comprising all the monomeric product (27 mg) was collected. Examination of this by n.m.r. with careful comparison of the intensity of the O–CH_3 resonance of unchanged starting material and the N–CH_3 resonance of (21) indicated a total yield of (21) of 45% based on starting material consumed. The total product was then dissolved in ethanol and reduced with sodium borohydride. Chromatography to remove the hydroxylic reduction products of the dienone gave an oil (12 mg). The weight of material lost in this reduction (15 mg) again corresponds to a yield of dienone of *ca.* 45%. No evidence could be found for the formation of a spirodienone-lactone in this oxidation (absence of absorption at 1770 cm^{-1}).

(ii) Repetition of the above reaction at 80°, employing similar analytical procedures to estimate the products, gave very similar results.

(iii) A solution of the amide (40 mg) and potassium carbonate (60 mg) in water (30 ml) was deoxygenated at 70° (N_2 passage). Potassium persulphate (100 mg) in oxygen-free water (5 ml) was added, and the mixture was heated to boiling and refluxed for 5 min. The reaction mixture was cooled and extracted into chloroform. Examination of the product by g.l.c. and t.l.c. revealed the presence of unchanged starting material (11 mg), and the absence of *N*-methylphenanthridinone, 1-methoxy-*N*-methylphenanthridinone, and of the linear dienone (21). The analysis also showed the formation of the methoxydienone (23) [6] (25%). Chromatography of the products gave a fraction containing unchanged starting material and methoxydienone, followed by a fraction containing the more-polar stereoisomeric cyclohexadienols (24) (12·5 mg), characterisation of which will be described elsewhere.[6] This fraction was treated with ethanolic hydrochloric acid [known to convert (24) into linear dienone (21) in almost quantitative yield [6]]. Chromatography of the products gave the dienone (21) (5·5 mg). The yield of this corresponds to a yield of *ca.* 20% of dienols (24) (based on starting material consumed). In several repetitions of this

[15] D. H. Hey, J. A. Leonard, and C. W. Rees, *J. Chem. Soc.*, 1963, 5251, 5263.

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

experiment, the total yield of (23) plus (24) was *ca.* 40—50%. However the proportions of the two compounds varied. In a control experiment, (24) was found to be oxidised to (23) by persulphate.

(iv) A solution of 4′-deuterio-2′-methoxy-*N*-methylbiphenyl-2-carboxamide (100 mg) in water (40 ml) was boiled under reflux, and potassium persulphate (200 mg) in water (10 ml) was added to it. The solution was refluxed for 10 min, cooled, and extracted into chloroform. The combined products of this and a second, identical, reaction were chromatographed to give deuteriated *N*-methylphenanthridinone (15 mg) and a fraction (119 mg) consisting of a 2 : 1 mixture of the linear dienone (21) and unchanged starting material (by n.m.r. and t.l.c.). The mass spectrum of the *N*-methylphenanthridinone confirmed the retention of *ca.* 70% of one deuterium atom, and its n.m.r. spectrum revealed that the low-field signal at τ 1·75 due to 1-H showed a large *ortho*-splitting consistent with the presence of a proton at C-2. The larger splitting of the signal due to 2-H at τ 2·70 had however simplified from a triplet to a doublet, consistent with its proximity with only one *ortho*-proton (on C-1). The *N*-methylphenanthridinone formed in this reaction is, therefore, considered to be deuteriated at C-3.

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