N-Iodo-amides: Cyclisation of Substituted Biphenyl-2-carboxamides

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Homolysis of *N*-iodo-amides leads to 2'-, 3'-, and 4'-substituted biphenyl-2-carboxamidyl radicals which cyclise intramolecularly to give γ- and δ-lactams in parallel processes. The proportion of Ar_1-5 and Ar_2-6 cyclised products is in accord with the steric and electronic effects of the substituents. 4'-Iodo-4'-methoxy-*N*-methyl-3-oxoisoindoline-1-spiro-1'-cyclohexa-2',5'-dienes have been identified as spiro-intermediates in the cyclisation of *N*-methyl-4'-methoxybiphenyl-2-carboxamide.

THE intramolecular cyclisation of biphenyl-2-carboxamides has been effected by persulphate oxidation [1,2] and irradiation or thermolysis of the corresponding *N*-iodo-amides.[3-5] The thermal persulphate oxidations of substituted biphenyl-2-carboxamides gave amongst other products phenanthridones, dibenzopyranones (through oxygen cyclisation), nitrogen dealkylation products, and products arising from displacement of 2'-substituents by both nitrogen and oxygen. Hey *et al.*[1] also illustrated the pH dependence of the product distribution, basic media favouring spiro- or Ar_1-5 cyclisation.

Recently, it was reported [4] that treatment of biphenyl-2-carboxamides with t-butyl hypoiodite, and irradiation or heating in t-butyl alcohol, afforded a method of trapping intermediate spirodienyl radicals as spirodienyl t-butyl ethers and dienones and it has been proposed [5] that the Ar_1-5 and Ar_2-6 cyclisations occur by reaction of the amido-radical in the Σ and Π electronic states respectively. The effect of substituents on the course of cyclisation has now been investigated.

RESULTS AND DISCUSSION

The results of irradiation of 4'-substituted biphenyl-2-carboxamides with t-butyl hypoiodite in t-butyl alcohol at room temperature are given in Table 1. The cyclisations were not effected in the dark at this temperature.

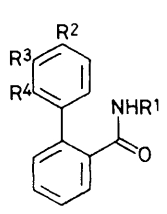
TABLE 1

Time (h)	Amide	Phenanthridone [%]	Spirodienone [%]
2.5	(1a)	(2a) [17]	(3a) [65]
2.5	(1b)	(2b) [n.e.] [a]	(3b) [68]
4	(1c)	(2c) [17]	(3a) [70]
8	(1d)	(2d) [17]	(3a) [40] [b]
3	(1e)	(2e) [15]	
3	(1f)		

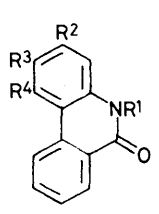
[a] n.e. = Not estimated; fraction with $\nu_{max.}$ 1 670 cm^{-1} isolated. [b] Yields based on n.m.r. *N*-methyl signals.

4'-Methyl-*N*-methylbiphenyl-2-carboxamide (1e) also afforded an intractable mixture of spiro-components while the 4'-nitrile substrate (1f) failed to react under the reaction conditions.

A detailed study of the cyclisation of 4'-methoxy-*N*-methylbiphenyl-2-carboxamide (1a) at room temperature showed (n.m.r.) that after one hour of irradiation the mixture contained, in addition to 3-methoxy-*N*-methylphenanthridone [(2a), 14%] and the spirodienone [(3a), 17%], another Ar_1-5 cyclised product (56%) which rearranged slowly to the dienone. This rearrangement



(1)



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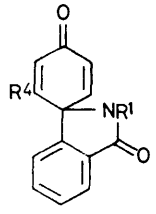
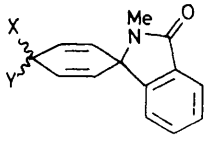


(3)

a; R^1 = Me, R^2 = OMe, R^3 = R^4 = H
b; R^1 = R^3 = R^4 = H, R^3 = OMe
c; R^1 = Me, R^2 = I, R^3 = R^4 = H
d; R^1 = Me, R^2 = Cl, R^3 = R^4 = H
e; R^1 = Me, R^2 = Me, R^3 = R^4 = H
f; R^1 = Me, R^2 = CN, R^3 = R^4 = H
g; R^1 = Me, R^2 = R^4 = H, R^3 = OMe
h; R^1 = Me, R^2 = R^3 = H, R^4 = OMe
i; R^1 = R^2 = R^3 = H, R^4 = OMe
j; R^1 = Me, R^2 = R^3 = R^4 = H

a; R^1 = Me, R^4 = H
b; R^1 = H, R^4 = H
c; R^1 = Me, R^4 = OMe
d; R^1 = H, R^4 = OMe

was accelerated by irradiation. N.m.r. data of this labile product were consistent with 4'-iodo-4'-methoxy-*N*-methyl-3-oxoisoindoline-1-spiro-1'-cyclohexa-2',5'-dienes (4a). The two isomeric spirodienyl iodides (4a)



(4)

a; X = OMe, Y = I
b; X = OH, Y = H
c; X = OMe, Y = H

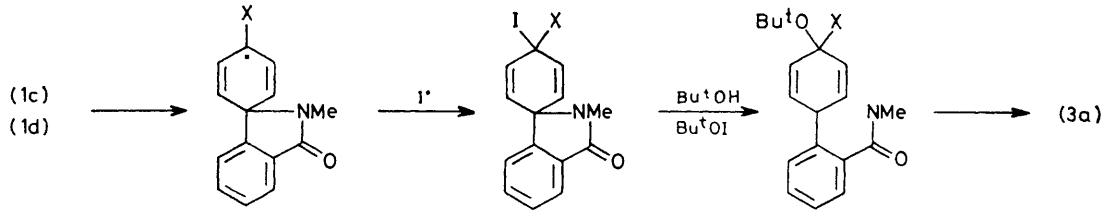
were rapidly converted into the dienone (3a) with methanolic silver nitrate in contrast to the methanolysis products obtained by similar treatment of other spirodienyl iodides.[6] In an attempt to dimerise (4a) the mixture, in dry benzene, was irradiated with a medium-pressure mercury lamp [6a] through quartz. However, only the dienone (3a) was formed. The transformation was likewise effected by addition of molecular iodine to (4a) in $CDCl_3$. The isomeric spirodienyl iodides (4a) were synthesised from the spirodienone (3a) by sodium

[1] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 118.
[2] A. R. Forrester, A. S. Ingram, and R. H. Thomson, *J.C.S. Perkin I*, 1972, 2847.
[3] S. A. Glover, A. Goosen, and H. A. H. Laue, *J.C.S. Perkin I*, 1973, 1647.
[4] S. A. Glover and A. Goosen, *J.C.S. Perkin I*, 1974, 2353.
[5] S. A. Glover and A. Goosen, *J.C.S. Perkin I*, 1977, 1348.
[6] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, (*a*) 1155; (*b*) 1162.

borohydride reduction to the dienols (4b) which in methanol–sulphuric acid afforded the methoxy-dienes (4c) whose n.m.r. spectra were consistent with reported data.[6b] Irradiation of the methoxy-dienes (4c) in the presence of t-butyl hypoiodite gave a mixture (n.m.r.) of dienone (3a), unchanged methoxydienes (4c), and spirodienyl iodides (4a). The detection of methoxy-spirodienyl iodides as intermediates in the cyclisation of (1a) and the failure to isolate 4′-t-butoxy-spirodienyl iodides from our earlier cyclisations of *N*-methyl-biphenyl-2-carboxamide,[4,5] are in accord with the more favourable dealkylation of the corresponding t-butoxy-spirodienyl iodides to give (3a).

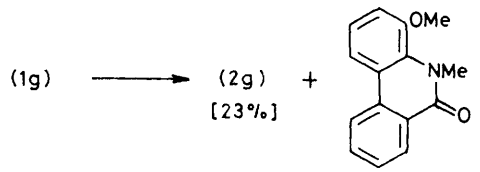
The mode of cyclisation was altered dramatically when a 3′-methoxy group was present (1g). The mixture contained only Ar_2-6 cyclisation products, 2-methoxy-*N*-methylphenanthridone (2g) and 4-methoxy-*N*-methyl-phenanthridone (6), formed in similar yields, thus providing evidence for a considerable electronic effect in the radical cyclisation process. The lack of selectivity in this experiment contrasts with that found by Hey *et al.* in the persulphate oxidation of (1g).[1]

2′-Methoxy-substituted amides [(1h) and (1i)] gave nearly quantitative yields of 2′-methoxy-spirodienones [(3c) and (3d)] in accord with the electronic effect of the 2′-substituent. However, with this substrate the steric



(5) X = I or Cl

The formation of the spirodienone (3a) from the 4′-iodo- and 4′-chloro-*N*-methylcarboxamides [(1c) and (1d)] is proposed to arise from the corresponding t-



(6)
[17%]

butoxy-spirodienyl halides (5) which rapidly decompose to the dienone (3a).

Comparative rate studies showed that, like the parent amide, *N*-methylbiphenyl-2-carboxamide,[5] the cyclisation of 4′-substituted amides (1a, c, and d) gave products by pseudounimolecular parallel reactions. The relative rate constants at 26 °C (Table 2) indicate that

TABLE 2

Rate constants for cyclisation at 26 °C

Substrate	10^4k(overall) / s^{-1}	$10^4k(Ar_1\text{-}5)$ / s^{-1}	$10^4k(Ar_2\text{-}6)$ / s^{-1}	$k(Ar_1\text{-}5)/k(Ar_2\text{-}6)$
(1a)	6.7	5.80	1.00	6.0
(1j)	1.5	1.00	0.50	2.0
(1c)	0.53	0.45	0.10	4.7
(1d)	0.25	0.21	0.04	4.9

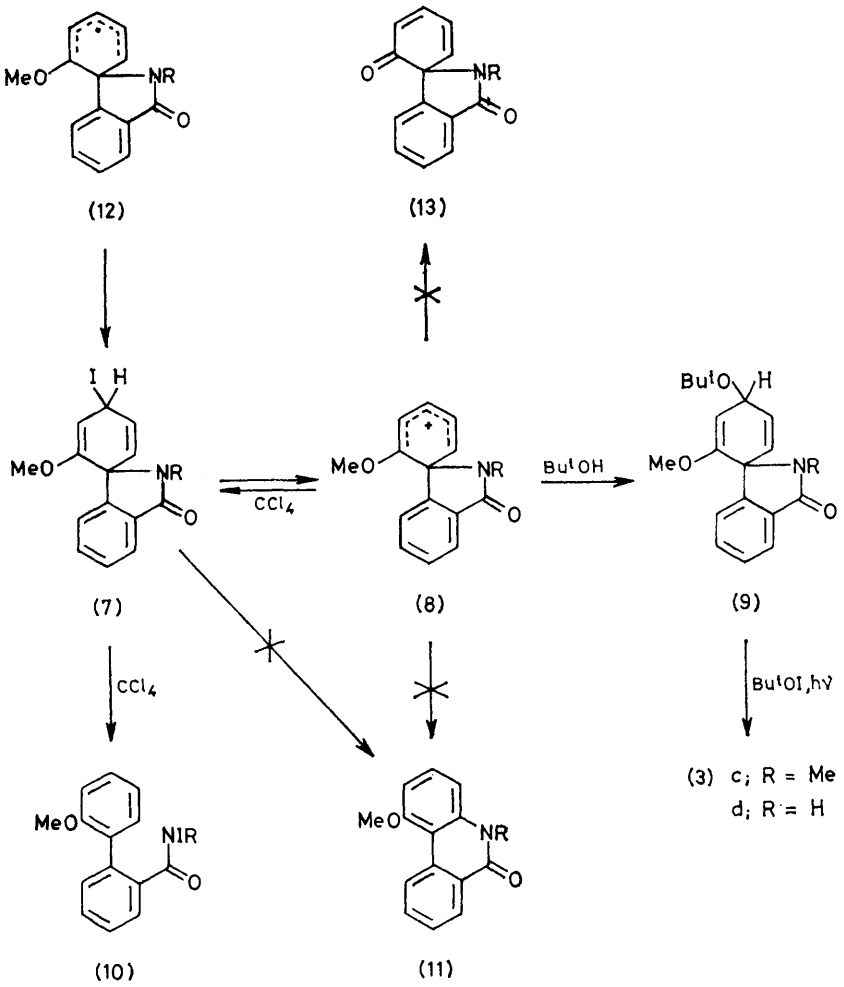
the 4′-substituents facilitate cyclisation at the 1′-position in the expected order for substitution involving an electrophilic [7] radical. Further, radical stability in the transition state is not a dominant effect.

effect of the 2′-substituent also favours orthogonality of the aryl rings. A similar steric effect was found in the cyclisation of *cis-o*-methoxy-*N*-methylcinnamamide.[5] The formation of the methoxy-spirodienones [(3c) and (3d)] is consistent with the ready formation of the resonance-stabilised carbocation (8; R = H or Me) which is solvolysed to give the diether (9; R = H or Me). Conversion to the methoxy-dienone [(3c) and (3d)] upon irradiation with t-butyl hypoiodite [4,5] is due to the easier elimination of the t-butyl group as opposed to the methyl group from the intermediate diether carbocations. In an attempt to synthesise the linear dienone (13; R = H) [(13; R = Me) was obtained by Hey *et al.* from persulphate oxidation of (1h) [1]], (1i) was irradiated with t-butyl hypoiodite (from potassium t-butoxide and iodine monochloride [4,5])–iodine in carbon tetrachloride, which unlike t-butyl alcohol could not solvolyse the intermediate (8; R = H). Only starting material was recovered whereas in a control experiment,with t-butyl alcohol as solvent, the same reagents effected complete conversion into dienone (3d). In addition, although biphenyl-2-carboxamide and *N*-methylbiphenyl-2-carboxamide showed a preference for Ar_2-6 cyclisation in non-trapping media (benzene or CCl_4) [3,4] the absence of 1-methoxy-phenanthridone (11; R = H) in the reaction of the 2′-methoxy-amide (1i) supports our proposal [5] that Ar_2-6 cyclisation requires a planar conformation of the aromatic rings. The Ar_1-5 cyclisation in this case is probably reversible in non-trapping media and a heterolytic ring opening of (7; R = H) is suggested. The 2′-methoxy-*N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dienyl radical (12; R = Me) does not rearrange even at high temperatures (130 °C).[8] The

[7] R. S. Neale, *Synthesis*, 1971, **1**, 1; S. A. Glover, A. Goosen, D. Graham, and J. Lovelock, *J. S. African Chem. Inst.*, 1976, **29**, 46.

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

difference in reactivity in t-butyl alcohol and carbon tetrachloride was not due to different solubilities of the oxidant, iodine, in the two solvents since the formation of the dienone (3d) from (1i) in t-butyl alcohol with t-butyl



hypoiodite was relatively unaffected when the reaction was carried out with or without additional iodine.

In contrast to the results obtained from the analogous persulphate oxidations [1,2] no demethoxylation of the 2'-methoxy substrates was observed and cyclisation was in all cases through nitrogen. The mode of cyclisation of all the substrates was predictable on the basis of electronic and steric effects.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were run on Unicam SP 200G and SP 1 000 spectrometers. Hydrogen-1 n.m.r. spectra (60 MHz) were recorded with a Perkin-Elmer R12A spectrometer, with tetramethylsilane as internal standard and mass spectra (A.E.I. MS 9 instrument) were recorded at the N.C.R.L./C.S.I.R. laboratories in Pretoria. Irradiations were performed with a 1000 W tungsten lamp unless otherwise specified. Silica gel for preparative t.l.c. was Merck HF 254 + 366 type 60 (nach Stahl).

Preparation of Carboxylic Acids and Carboxamides.—The following were prepared from 4'-aminobiphenyl-2-carboxylic acid, synthesised by reduction (H_2–PtO) of 4'-nitrobiphenyl-2-carboxylic acid,[9] by standard procedures. (a) *4'-Methoxybiphenyl-2-carboxylic acid*, δ($CDCl_3$) 3.78 (3 H, s), 6.83 [2 H, d, *J*(AB) 10 Hz], 7.1—7.6 (5 H, m), and 7.77—7.97 (1 H, m); $\nu_{max.}$ ($CHCl_3$) 840, 1 625, 1 712, and 3 000br cm^{-1}. The amide (1b) (plates from benzene–light petroleum, b.p. 40—60 °C) had m.p. 112—114 °C (lit.,[10] 114—115 °C). The *N*-methylamide (1a) (prisms from ethanol) had m.p. 130—132 °C (lit.,[1] 131—133 °C).

(b) *4'-Iodobiphenyl-2-carboxylic acid* [11,12] (plates from benzene), m.p. 189—193 °C, M^+ 324, δ($CDCl_3$) 7.0—8.15 (8 H, m), and 10.1 (1 H, broad s); $\nu_{max.}$ ($CHCl_3$) 830, 1 710, and 3 600br cm^{-1}. The *N*-methylamide (1c) (prisms from benzene) had m.p. 168—172 °C, M^+ 337; δ($CDCl_3$) 2.71 (3 H, d), 5.55 (1 H, broad s), 7.17 [2 H, d, *J*(AB) 9 Hz], 7.3—7.7

[9] R. L. Dannley and M. Sternfield, *J. Amer. Chem. Soc.*, 1954, **76**, 4543.
[10] T. Muroi, *Nippon Kagaku Zasshi*, 1956, **77**, 1084 (*Chem. Abs.*, 1959, **53**, 5250a).
[11] A. H. Blatt, *Org. Synth.*, 1963, Coll. Vol. II, p. 355.
[12] W. J. Hickenbottom, ' Reactions of Organic Compounds,' Longmans, 3rd edn., 1959.

(4 H, m), and 7.78 [2 H, d, J(BA) 9 Hz]; $\nu_{max.}$ ($CHCl_3$) 1 660 and 3 465 cm^{-1}.

(c) *4′-Chlorobiphenyl-2-carboxylic acid* [12,13] (needles after sublimation), m.p. 162—164 °C (lit.,[10] 162—164 °C). The *N*-methylamide (1d) (needles from benzene) had m.p. 147—150 °C, M^+ 226; δ($CDCl_3$) 2.69 (3 H, d), 5.6 (1 H, broad s), and 7.29—7.69 (8 H, m); $\nu_{max.}$ ($CHCl_3$) 842, 1 663, and 3 465 cm^{-1}.

(d) *4′-Cyanobiphenyl-2-carboxylic acid* [12] (prisms from ethanol), m.p. 215—218 °C, M^+ 223; $\nu_{max.}$ ($CHCl_3$) 846, 1 712, 2 245, and 3 600br cm^{-1}. The *N-methylamide* (1f) [needles from chloroform–benzene–light petroleum (b.p. 40—60 °C)] had m.p. 167—168 °C, M^+ 236; δ($CDCl_3$) 2.76 (3 H, d), 5.55 (1 H, broad s), and 7.32—7.86 (8 H, m); $\nu_{max.}$ ($CHCl_3$) 850, 1 668, 2 245, and 3 465 cm^{-1} (Found: C, 75.7; H, 5.1; N, 11.9. $C_{15}H_{12}N_2O$ requires C, 76.25; H, 5.1; N, 11.85%).

(e) *4′,N-Dimethylbiphenyl-2-carboxamide* (1e). 4′-Cyano-*N*-methylbiphenyl-2-carboxamide (2g) was reduced to the 4′-formyl analogue (1.2 g) (sodium dihydrogen phosphite over Raney nickel [14]) which crystallised from benzene–light petroleum (b.p. 40—60 °C), m.p. 166—167 °C, M^+ 239; δ($CDCl_3$) 2.75 (3 H, s), 5.5 (1 H, broad s), 7.4—8.07 (8 H, m), and 10.13 (1 H, s); $\nu_{max.}$ ($CHCl_3$) 848, 1 665, 1 710, and 3 465 cm^{-1}. Clemmensen reduction of 4′-formyl-*N*-methylbiphenyl-2-carboxamide (1.2 g) gave *4′,N-dimethylbiphenyl-2-carboxamide* (1e) [prisms from benzene–light petroleum (b.p. 60—80 °C)], m.p. 107—109 °C, M^+ 225; δ($CDCl_3$) 2.37 (3 H, s), 2.65 (3 H, d), 5.5 (1 H, broad s), and 7.15—7.80 (8 H, m); $\nu_{max.}$ 830, 1 660, and 3 465 cm^{-1}.

(f) *3′-Methoxy-N-methylbiphenyl-2-carboxamide* (1g). A mixture of methyl 3′-nitrobiphenyl-2- and 4-carboxylates (12 g; 47 and 38%, respectively), isolated by column chromatography from the Gomberg reaction of *m*-nitroaniline (50 g) with methyl benzoate (1 l),[15] was saponified (aqueous 10% sodium hydroxide) to give, after acidification, a component soluble in CH_2Cl_2, 3′-nitrobiphenyl-2-carboxylic acid (5 g), m.p. 154—155 °C [plates from $CHCl_3$–ether–light petroleum (b.p. 40—60 °C)] (lit.,[15] m.p. 155—157 °C). The *N-methylamide* crystallised from benzene–light petroleum (b.p. 80—100 °C) as needles, m.p. 118—120 °C, M^+ 256; δ($CDCl_3$) 2.29 (3 H, s), 6.1 (1 H, broad m), 7.26—7.8 (6 H, m), and 8.03—8.2 (2 H, m); $\nu_{max.}$ ($CHCl_3$) 1 552, 1 680, and 3 500 cm^{-1} (Found: C, 66.0; H, 4.9; N, 10.8. $C_{14}H_{12}N_2O_3$ requires C, 65.6; H, 4.9; N, 10.8%). The amide (2 g) was reduced (H_2–PtO) to *3′-aminobiphenyl-2-carboxylic acid* (plates from benzene), m.p. 162—164 °C, M^+ 226 (Found: C, 73.8; H, 6.2; N, 12.4. $C_{14}H_{14}N_2O$ requires C, 74.3; H, 6.25; N, 12.4%). The corresponding diazonium sulphate was converted into 3′-methoxy-*N*-methylbiphenyl-2-carboxyamide (prisms from benzene), m.p. 91—93 °C (lit.,[1] 92—94 °C).

(g) *2′-Methoxybiphenyl-2-carboxamides* (1h *and* i). Biphenyl-2-carboxylic acid (10 g) was oxidised to benzocoumarin (5 g) [15] which, after refluxing in alkaline dimethyl sulphate, afforded 2′-methoxybiphenyl-2-carboxylic acid (2.71 g), δ($CDCl_3$) 3.64 (3 H, s), 6.7—8.0 (8 H, m), and 11.61 (1 H, s); $\nu_{max.}$ ($CHCl_3$) 1 702 and 3 060br cm^{-1}. The *N*-methylamide [plates from benzene–light petroleum (b.p. 40—60 °C)] had m.p. 113—115 °C (lit.,[1] 113—115 °C). The *amide* had m.p. 107—108.5 °C, M^+ 227, δ($CDCl_3$) 3.65 (3 H, s); $\nu_{max.}$ ($CHCl_3$) 1 685, 3 425, and 3 550 cm^{-1} (Found: C, 73.3; H, 5.7; N, 6.2. $C_{14}H_{13}NO_2$ requires C, 73.9; H, 5.75; N, 6.2%).

Reactions. General procedure. Cyclisation of Substituted Amides.—t-Butyl hypochlorite (1.28 g, 11.9 mmol), potassium t-butoxide (1.33 g, 11.9 mmol), and the amide (2.37 mmol) were added in the dark at 15 min intervals to a stirred mixture of iodine (3 g, 11.9 mmol) and t-butyl alcohol (25 ml). The mixture was irradiated at room temperature, then shaken with excess of aqueous sodium thiosulphate, which was extracted with chloroform (2 × 50 ml). Concentration of the combined extracts gave solids or gums which were analysed by n.m.r., and purified by crystallisation or separation on preparative thin-layer plates (silica gel).

(a) *4′-methoxybiphenyl-2-carboxamide* (1b). This gave 3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (68%), identical (n.m.r., i.r., t.l.c., m.p.) with an authentic specimen,[4] and a minor amount of impure solid which contained a δ-lactam [$\nu_{max.}$ ($CHCl_3$) 1 670 cm^{-1}].

(b) *N-methyl-4′-methoxybiphenyl-2-carboxamide* (1a). This gave after chromatography *N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (65%), m.p. 218—219 °C (lit.,[4] m.p. 218—219 °C), and the less polar 3-methoxy-*N*-methylphenanthridone (17%) (similar spectroscopically to that reported by Hey *et al.*[16]), M^+ 239; δ($CDCl_3$) 3.78 (3 H, s), 3.95 (3 H, s), 6.82—7.1 (1 H, d, and 1 H, dd), 7.27—8.0 (2 H, m,) 8.24 (2 H, d), and 8.58 (1 H, d); $\nu_{max.}$ ($CHCl_3$) 1 615 and 1 650 cm^{-1} (doublet, carbonyl).*

(c) *4′-Iodo-N-methylbiphenyl-2-carboxamide* (1c). This afforded *N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (70%) and *3-iodo-N-methylphenanthridone* (17%) which crystallised from benzene–ether as needles, m.p. 149—152 °C, M^+ 335; δ($CDCl_3$) (3 H, s), 7.2—8.58 (7 H, m); $\nu_{max.}$ ($CHCl_3$) 1 600, 1 612, and 1 650 cm^{-1} (Found: C, 50.4; H, 3.0; N, 3.9. $C_{14}H_{10}INO$ requires C, 50.15; H, 3.0; N, 4.2%).

(d) *4′-Chloro-N-methylbiphenyl-2-carboxamide* (1d). This gave *N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (40%, n.m.r.), 3-chloro-*N*-methylphenanthridone (17%; n.m.r.), m.p. 129—130 °C [ether–light petroleum (b.p. 40—60 °C)], M^+ 243; δ($CDCl_3$) 3.76 (3 H, s), 7.18—7.97 (4 H, m), 8.18 (2 H, d), and 8.57 (1 H, dd); $\nu_{max.}$ ($CHCl_3$) 1 608 and 1 650 cm^{-1} (doublet, carbonyl); and a minor quantity of spiro-components [$\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1}].

(e) *4′,N-Dimethylbiphenyl-2-carboxamide* (1e). This afforded a complex mixture which was separated into *3,N-dimethylphenanthridone* (15%) (needles from benzene), m.p. 110—112.5 °C, M^+ 223; δ($CDCl_3$) 2.39 (3 H, s), 3.64 (3 H, s), 7.05 (2 H, overlapping s and d), 7.25—8.2 (4 H, m), and 8.51 (1 H, dd); $\nu_{max.}$ ($CHCl_3$) 1 614 and 1 650 cm^{-1} (doublet, carbonyl) (Found: C, 79.8; H, 5.6; N, 6.2. $C_{15}H_{13}NO$ requires C, 80.7; H, 5.8; N, 6.25%).

(f) *4′-Cyano-N-methylbiphenyl-2-carboxamide* (1f). This was recovered unchanged from the reaction mixture.

(g) *Identification of 4′-iodo-4′-methoxy-N-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dienes* (4a). 4′-Methoxy-*N*-methylbiphenyl-2-carboxamide was treated as in the

* Doublet carbonyls are diagnostic of *N*-alkyl-3-substituted phenanthridones (*cf.* ref. 16).

[13] H. Gilman and A. H. Blatt, *Org. Synth.*, Coll. Vol. I, 1964, p. 162.

[14] O. G. Backeberg and B. Staskun, *J. Chem. Soc.*, 1962, 3961.

[15] G. W. Kenner, M. A. Murray, and C. M. B. Taylor, *Tetrahedron*, 1957, **1**, 259.

[16] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 105, 1150.

general procedure. A sample worked up after 1 h was analysed by i.r. [$\nu_{max.}$ ($CHCl_3$) 1 695vs (γ-lactam) and 1 685 cm^{-1} (shoulder, dienone)] and n.m.r. which, from integration of *N*-methyl resonances, showed it to contain starting amide [δ 2.7 (d), 13%], spirodienone (δ 3.01, 17%), 3-methoxy-*N*-methylphenanthridone (δ 3.76 and 3.95, 14.3%), and isomeric 4′-iodo-4′-methoxy-*N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-diene (4a) [δ 2.95 (3 H, s), 3.47 and 3.42 (3 H, 2 × s), 5.56 (2 H, m), and 6.32 (2 H, m) 56%]. The mixture, in methanol (5 ml) was treated with methanolic silver nitrate, diluted (30 ml) and extracted with dichloromethane (2 × 10 ml). Concentration afforded a mixture (n.m.r.) of spirodienone (3a) (δ 3.01, 73%) and 3-methoxy-*N*-methylphenanthridone (δ 3.75, 14%).

The reaction mixture upon work-up gave a straw-coloured gum (0.63 g) which was divided into three portions. (*i*) Addition of iodine to an n.m.r. sample in $CDCl_3$ effected rapid conversion of spirodienyl iodides (55%) into dienone (3a) (73%). (*ii*) The mixture (0.5 g) in dry benzene (70 ml) in a quartz flask was irradiated for 2 h with a medium-pressure mercury lamp. Analysis (n.m.r.) of the product showed formation of dienone (3a) (73%). (*iii*) A portion of the mixture left (12 h) in benzene contained (n.m.r. after work-up) one of the isomeric spirodienyl iodides (4a) [δ 2.95 (3 H, s), 3.47 (3 H, s), 5.56 (2 H, d, *J* 10 Hz), and 6.32 (2 H, d, *J* 10 Hz), 42%], dienone (δ 3.01, 31%), and 3-methoxy-*N*-methylphenanthridone (δ 3.76, 14%).

(h) *Rate studies.* 4′-Methoxy-4′-iodo- and 4′-chloro-*N*-methylbiphenyl-2-carboxamides (1a, c, and d) and *N*-methylbiphenyl-2-carboxamide (1j) were treated at 26 °C. The reaction was monitored as before.[5] The overall first-order rate constants [*k*(overall)] were obtained from plots of ln[amide] *vs.* time while $k(Ar_1\text{-}5)$ and $k(Ar_2\text{-}6)$ were found from the plots of total spiro-products concentration and phenanthridone concentration *vs.* [1 − exp(− *kt*)] [5] (Table 2).

(i) 3-*Methoxy*-N-*methylphenanthridone* (1g). This afforded, after irradiation (2.5 h) and chromatographic separation, 2-methoxy-*N*-methylphenanthridone, m.p. 157—159 °C (lit.,[17] 161 °C), $\nu_{max.}$ ($CHCl_3$) 1 642 cm^{-1}, and 4-methoxy-*N*-methylphenanthridone, m.p. 121—123 °C (lit.,[17] 125 °C), $\nu_{max.}$ ($CHCl_3$) 1 643 cm^{-1}, in 23 and 17% yield, respectively.

(j) (*i*) 2′-*Methoxybiphenyl*-2-*carboxamide* (1i). This was converted quantitatively (2.5 h) into 2′-methoxy-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (3d), m.p. 246—248 °C, M^+ 241; δ($CDCl_3$) 3.58 (3 H, s), 5.73 (1 H, d, *J* 0.5 Hz), 6.36 (2 H, overlapping s and d, *J* 0.5 Hz), and 7.09—7.95 (4 H, m); $\nu_{max.}$ ($CHCl_3$), 1 600, 1 669, 1 719, and 3 462 cm^{-1} (Found: C, 69.4; H, 4.6; N, 5.8. $C_{14}H_{11}NO_3$ requires C, 69.7; H, 4.6; N, 5.8%). (*ii*) The amide (1i) (0.4 g), t-butyl hypoiodite [from potassium t-butoxide (0.68 g), iodine chloride (0.85 g), and iodine (2.55 g)] in carbon tetrachloride (40 ml) was irradiated. Work-up after 2.5 h afforded unchanged amide. (*iii*) The experiment [as in (*ii*)] repeated with t-butyl alcohol as solvent gave the dienone (3d) quantitatively. (*iv*) The amide (1i) (0.4 g) was added to an equimolar amount of t-butyl hypoiodite [from potassium t-butoxide (0.202 g) and iodine chloride (0.284 g)] and excess of iodine in t-butyl alcohol (50 ml). Irradiation for 2.5 h at room temperature gave 2′-methoxy-dienone (3d) (26%) and starting material (74%). (*v*) The experiment [as in (*iv*)] was repeated, except that iodine was omitted, and gave 2′-methoxy-dienone (3d), (22%) and starting material (78%).

(k) 2′-*Methoxy*-N-*methylbiphenyl*-2-*carboxamide* (1h). This gave 2′-methoxy-*N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (96%), m.p. 230—231 °C (lit.,[6a] 232—236 °C), M^+ 255; δ($CDCl_3$) 2.9 (3 H, s), 3.6 (3 H, s), 5.82 [1 H, d, *J*(XA) 1.5 Hz], 6.21 [1 H, d, *J*(BA) 9.5 Hz], and 6.47 [1 H, dd, *J*(AB) 9.5, *J*(AX) 1.5 Hz]; $\nu_{max.}$ ($CHCl_3$) 1 602, 1 669, and 1 700 cm^{-1} (Found: C, 70.5; H, 5.0; N, 5.7. $C_{15}H_{13}NO_3$ requires C, 70.6; H, 5.15; N, 5.5%).

Synthesis of 4′-*Iodo*-4′-*methoxy*-N-*methyl*-3-*oxoisoindoline*-1-*spiro*-1′-*cyclohexa*-2′,5′-*dienes* (4a).—A mixture of 4′-methoxy-*N*-methylbiphenyl-2-carboxamide (1a) (13%), 3-methoxy-*N*-methylphenanthridone (2a) (14%), and *N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dien-4′-one (3a) (73%) (0.60 g) in absolute ethanol (25 ml) was treated with $NaBH_4$ (0.2 g) in ethanol (10 ml). After 20 min the mixture was diluted (5% acetic acid solution, 20 ml), and extracted with $CHCl_3$ (2 × 20 ml). The extract was dried (Na_2SO_4) and concentrated to a gum (0.56 g) which was a mixture (n.m.r.) of amide (13%), phenanthridone (14%), and isomeric 4′-hydroxy-*N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dienes (4b) (73%) identical (n.m.r., t.l.c.) with an authentic mixture.[3] The mixture in methanolic sulphuric acid (2 ml acid in 25 ml alcohol) was refluxed for 6 min, diluted, and extracted with CH_2Cl_2 (2 × 20 ml) which gave a gum (0.42 h). Analysis (n.m.r.) of the mixture showed amide (12%), 3-methoxy-phenanthridone (22%), and isomeric 4′-methoxy-*N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dienes (4c) (66%) [6b] [δ($CDCl_3$) 2.84 and 2.93 (3 H, 2 × NMe s), 3.42 and 3.46 (3 H, 2 × methoxy s), 4.53 (1 H, m), and 5.47 and 6.33 (4 H, 2 × overlapping dd)]. The mixture (0.2 g) in t-butyl alcohol (5 ml) was added to a solution of t-butyl hypoiodite [from iodine (2.05 g, 0.0081 mol), t-butyl hypochlorite (0.291 g; 0.002 7 mol], and potassium t-butoxide (0.302 g, 0.002 7 mol) in t-butyl alcohol (10 ml) and the product was irradiated for 0.75 h at 26 °C. Analysis (n.m.r.) of the mixture after work-up showed amide (1a) [δ 2.7 (d); 7%], 3-methoxy-*N*-methylphenanthridone (2a) [δ 3.76 (s); 21%], methoxy-dienes (4c) [δ 2.84 (s); 10%], spirodienone (3a) (δ 3.01; 28%), and 4′-iodo-4′-methoxy-dienes (4a) [δ 2.95 (s), 5.58 and 6.33 (2 × d, *J* 10 Hz); 32%]. Treatment with methanolic silver nitrate as above gave (n.m.r.) amide (1a) (7%), phenanthridone (2a) (22%), methoxydienes (4c) (11%), and spirodienone (3a) (60%).

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