A Photochemical Route to the Protoberberine Skeleton

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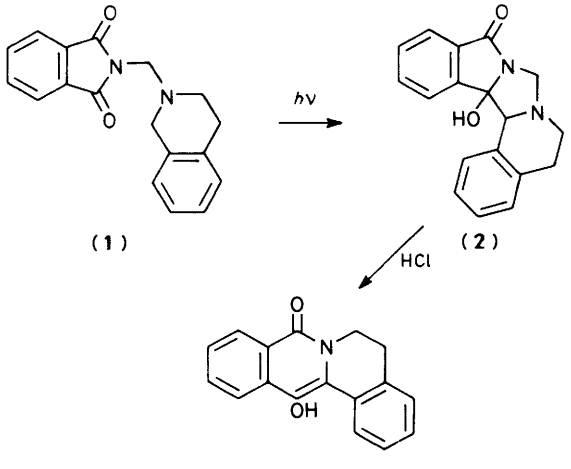
Irradiation of Mannich bases obtained from phthalimides, formaldehyde, and 1,2,3,4-tetrahydroisoquinolines and carrying methoxy or methylenedioxy substituents gave, in moderate yield, pentacyclic photoproducts. These underwent acid-promoted reaction leading to 13-hydroxydibenzo-[*a,g*]quinolizin-8-ones, one of which was 13-hydroxy-8-oxoxylopinine. Reduction to remove the 8,13 oxygenated functions was not achieved. Unsymmetrical substrates derived from 3,4-dimethoxyphthalimide gave a mixture of regio- and stereo-isomers in the photocyclisation, with no strong preference for one orientation of reaction.

Alkaloid synthesis has long been a testing ground for new synthetic procedures, and certain photochemical processes have been successfully employed in routes to a variety of alkaloid skeletons. The photocyclisation of *N*-chloroacetyl phenylethylamines and related systems enables a lactam ring to be built onto an existing aromatic unit, and this has proved useful in constructing the framework of many indole alkaloids.[1] Recently, a photo-induced 1,3-acyl shift in *N*-acylindoles has been used to provide an efficient route to medium-ring lactams for the synthesis of a variety of alkaloids of the strychnos, aspidosperma, schizozygane, or eburnamine families.[2] However, one of the most intensively studied photochemical cyclisations for the formation of nitrogen six-membered heterocycles involves enamides, either *N*-arylamides of α,β-unsaturated carboxylic acids or *N*-aroylenamines, which undergo six-electron ring-closure followed by a hydrogen shift and (often) oxidation. Such reactions have been used in routes to aporphine, protoberberine, yohimbane, and other alkaloid systems.[3,4]

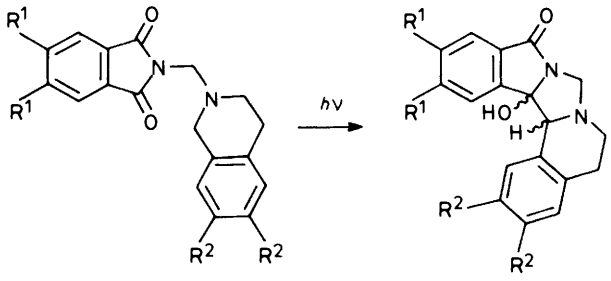
We have demonstrated[5] that irradiation of Mannich bases derived from phthalimide gives polycyclic compounds in which the ring formed in the cyclisation is an imidazolidine. Treatment with mineral acid converts the pentacyclic product (**2**), obtained from the 1,2,3,4-tetrahydroisoquinoline Mannich base (**1**), into 13-hydroxy-5,6-dihydro-8*H*-dibenzo[*a,g*]quinolizin-8-one (**3**), which has the ring system of the protoberberine alkaloids.[6] We now report the results of our efforts to extend this reaction to a synthesis of alkaloids.[7]



(1) (2) (3)

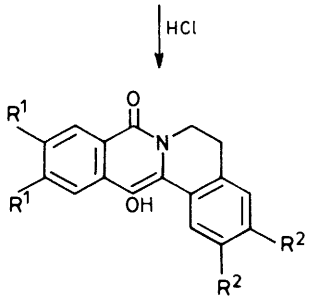
Results and Discussion

The overall yield of compound (**3**), obtained in three stages from phthalimide and 1,2,3,4-tetrahydroisoquinoline, is 67%, so that an efficient route is available from simple starting materials to this hydroxydibenzoquinolizinone. Since the aromatic rings in isoquinoline alkaloids generally carry oxygen functional groups, we prepared and irradiated four symmetrically substituted substrates (**4a—d**). T.l.c. indicated that one major photoproduct was formed in each case, which was isolated and identified as the corresponding substituted pentacyclic compound (**5**). The relative stereochemistry is probably that with OH and H *trans* at the bridgehead positions (by analogy with



(4) (5)

a; R^1 = OMe, R^2 = H 28%
b; R^1 = H, R^2 = OMe 25%
c; R^1 = R^2 = OMe 76%
d; R^1 = OMe, R^2R^2 = OCH_2O 60%



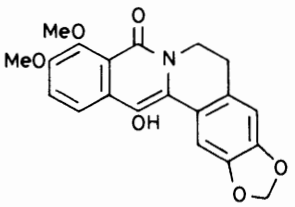
(6) **a**; 40%
b; 28%
c; 59%
d; 57%

related compounds[8]), but we cannot be certain of this in the absence of spectral data for the other diastereoisomer.

The i.r. spectra of compounds (**5**) showed bands for O–H (*ca.* 3 300 cm^{-1}) and C=O (1 710 cm^{-1}); the ^{13}C n.m.r. spectra contained signals for amide carbonyl (174 p.p.m.), quaternary (O)C(N) (97 p.p.m.), a methine carbon (67 p.p.m.), two methylene carbons, twelve aromatic carbons, and methoxy or methylenedioxy carbons as appropriate; the ^1H n.m.r. spectra showed a two-proton AB pattern for cyclic (N)CH_2(N) (δ_H 4.4 and 4.7), and signals for a methine proton (δ_H 4.5), four coupled protons in CH_2CH_2, and aromatic and substituent protons as appropriate. These spectral data are in accord with those determined for related compounds, including one whose structure has been confirmed by *X*-ray crystallographic analysis.[8]

Treatment of the photoproducts (**5**) with 2M-aqueous hydrochloric acid under reflux gave substituted dibenzo[*a*,*g*]quinolizin-8-ones (**6**), whose structures were assigned on the basis of microanalysis and mass spectral results, together with data from i.r. (O–H at 3 100 cm^{-1}, C=O at 1 610—1 645 cm^{-1}), ^1H n.m.r. (only four, coupled, aliphatic protons, apart from the aromatic ring substituents), and ^{13}C n.m.r. (only two methylene carbons, apart from substituents) spectra. The hydroxydibenzoquinolizinones readily formed acetates on treatment with acetic anhydride. The enol structure in solution was suggested by the n.m.r. spectra and supported by the u.v. absorption data, despite the previous contention[9] that 4-hydroxyisoquinolones exist as diones in neutral solution.

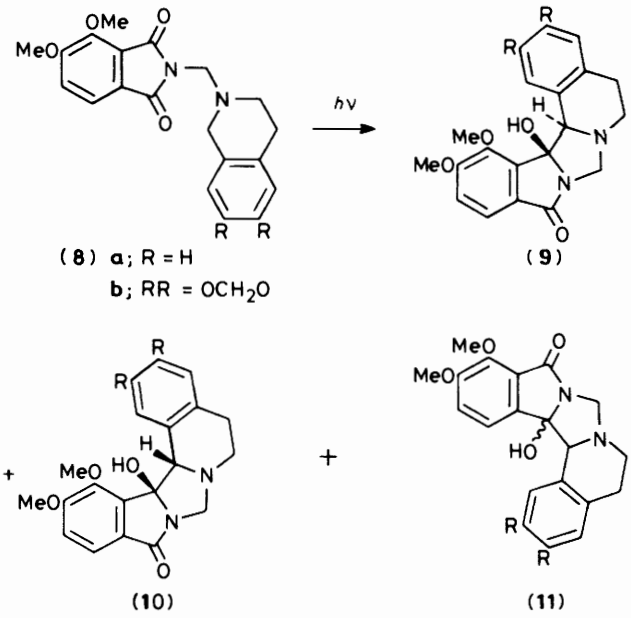
Compound (**6c**) is 13-hydroxy-8-oxoxylopinine; the related 13-hydroxyoxoberberine (**7**) has been reported previously,[10]



(**7**)

but this particular 8,13-dioxygenated pattern is not found in natural products. We therefore attempted to reduce the parent compound (**3**), and its acetate and benzoate, by catalytic hydrogenation (over palladium or over platinum oxide, using acetic acid, methanol, propan-2-ol, or methanol with added triethylamine as solvent), by using $LiAlH_4$ in tetrahydrofuran, or by using phosphoryl trichloride followed by sodium borohydride. Although reaction took place in most instances, mixtures of products were formed from which no one compound could be isolated in reasonable yield.

Many of the protoberberine alkaloids have substituents at C-9 and C-10 rather than at C-10 and C-11 as in xylopinine. We therefore studied two unsymmetrically substituted Mannich bases (**8**) to determine the orientation of ring-closure. From studies of the photoaddition of alkenes to ring-substituted phthalimides[11] it appears that substituents can exert a significant directing effect, although our own experience[8] with intramolecular cyclisations indicated that for these reactions the effect might be considerably less pronounced. Irradiation of the imide (**8a**) gave four products, as judged by t.l.c., and three of these could be isolated, in 51, 8, and 26% yield respectively. The first two products were assigned structures (**9a**) and (**10a**), and the third structure (**11a**), an assignment of orientation based largely on n.m.r. data. Compounds (**9a**) and (**10a**) gave rise to doublets (*J* 8 Hz) in their ^1H n.m.r. spectra at δ_H 6.9 and



7.25, and 7.05 and 7.5, respectively, corresponding to two aromatic protons of which one is *ortho* to carbonyl and *para* to methoxy; the isomer (**11a**) gave an AB pattern centred at δ_H 6.7, which is consistent with neither proton being *ortho* to carbonyl but with both being *ortho* or *para* to methoxy. In the ^{13}C n.m.r. spectra, the signal for one quaternary aromatic carbon is at 157 p.p.m. for isomers (**9a**) and (**10a**) but at 153 p.p.m. for (**11a**), in keeping with this carbon being *para* to the carbonyl group in (**9a**) and (**10a**) but *ortho* or *meta* to it in (**11a**); the hydrastines[12] and related compounds provide models for the chemical-shift values for the methoxy-bearing carbons in the isomer (**11a**). The relative stereochemistry in compounds (**9a**) and (**10a**) was suggested by the signals in the ^1H and ^{13}C n.m.r. spectra derived from the imidazolidine ring; the arguments have been developed for the parent phthalimide compounds.[8] Because the fourth product could not be isolated in a sufficiently pure state to enable us to record its spectral characteristics, the relative stereochemistry in compound (**11a**) could not be assigned with any certainty.

The major orientation of reaction has the more hindered arrangement of substituent groups, and it is the wrong one for making protoberberine alkaloids. Use of different solvents (acetonitrile, methanol, 2-methylpropan-2-ol) did not lead to significantly higher yields of compound (**11**), despite the possibility that the polar substituents might be made more bulky by solvation with the alcohol molecules.

Irradiation of (**8b**) in 2-methylpropan-2-ol gave a more complex mixture of products; despite careful separation by silica-gel column chromatography no product could be isolated in a pure state, although the n.m.r. spectra of the fractions indicated that the expected photocyclised compounds might be among the products.

In conclusion, the basic reaction offers an efficient route to certain substituted dibenzo[*a*,*g*]quinolizines, and in particular to 13-hydroxy-8-oxo derivatives. However, the difficulties in reducing these products and the lack of regioselectivity for unsymmetrically substituted substrates makes the process less attractive for the synthesis of naturally occurring protoberberine alkaloids than we had originally hoped.

Experimental

4,5-Dimethoxyphthalic acid,[13] 3,4-dimethoxyphthalic acid,[14] 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline,[15] and 6,7-

methylenedioxy-1,2,3,4-tetrahydroisoquinoline[16] were prepared accordingly to literature procedures. Mannich bases were prepared as described previously.[5] Other experimental details are given in our recent paper.[8]

4,5-*Dimethoxy*-N-(1,2,3,4-*tetrahydroisoquinolin*-2-*ylmethyl*)-*phthalimide* (**4a**) was obtained (55%) from the specific Mannich reaction in chloroform, and recrystallisation of the crude product from chloroform (heating in ethanol caused decomposition) gave the product, m.p. 199—201 °C (Found: C, 68.1; H, 5.7; N, 7.9. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.95%); $\nu_{max.}$(Nujol) 1 760 and 1 695 cm^{-1}; $\delta_H(CDCl_3)$ 2.8—3.05 (4 H, m), 3.80 (2 H, s), 4.00 (6 H, s), 7.05 (4 H, s), and 7.30 (2 H, s); $\delta_C(CDCl_3)$ 29.3, 48.7, 52.7, 56.5, 59.2, 105.4, 125.5, 126.0, 126.5, 128.6, 133.8, 134.6, 154.1, and 169.3 p.p.m.; *m/z* 220, 207, 146, 145, 144, and 132 (100%).

N-(6,7-*Dimethoxy*-1,2,3,4-*tetrahydroisoquinolin*-2-*ylmethyl*)-*phthalimide* (**4b**) was obtained in 81% yield, m.p. 185—186 °C (Found: C, 68.1; H, 5.4; N, 8.0. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.95%); $\nu_{max.}$(Nujol) 1 765 and 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 2.65—3.1 (4 H, m), 3.75 (2 H, s), 3.80 (6 H, s), 4.80 (2 H, s), 6.55 (2 H, s), and 7.6—7.95 (4 H, m); $\delta_C(CDCl_3)$ 28.9, 48.8, 52.4, 56.0, 59.3, 109.7, 111.8, 123.3, 125.7, 126.4, 132.0, 134.0, 147.4, 147.6, and 169.2 p.p.m.; *m/z* 352 (M^+), 206, 205, 192 (100%), 164, and 160.

N-(6,7-*Dimethoxy*-1,2,3,4-*tetrahydroisoquinolin*-2-*ylmethyl*)-4,5-*dimethoxyphthalimide* (**4c**) was obtained (76%) after recrystallisation from chloroform, m.p. 200—202 °C (Found: C, 64.1; H, 5.9; N, 6.7. $C_{22}H_{24}N_2O_6$ requires C, 64.1; H, 5.8; N, 6.8%); $\nu_{max.}$(Nujol) 1 770 and 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 2.75—3.0 (4 H, m), 3.76 (2 H, s), 3.81 (3 H, s), 3.82 (3 H, s), 4.00 (6 H, s), 4.77 (2 H, s), 6.53 (1 H, s), 6.56 (1 H, s), and 7.32 (2 H, s); $\delta_C(CDCl_3)$ 29.0, 48.8, 52.4, 56.0, 56.6, 59.3, 105.5, 109.9, 111.8, 125.5, 125.8, 126.6, 147.5, 147.7, 154.2, and 169.4 p.p.m.; *m/z* 220, 206, 192 (100%), and 166.

4,5-*Dimethoxy*-N-(6,7-*methylenedioxy*-1,2,3,4-*tetrahydroisoquinolin*-2-*ylmethyl*)*phthalimide* (**4d**) was obtained in 91% yield, m.p. 228—230 °C (Found: C, 63.6; H, 5.2; N, 7.05. $C_{21}H_{20}N_2O_6$ requires C, 63.6; H, 5.1; N, 7.1%); $\nu_{max.}$(Nujol) 1 760 and 1 705 cm^{-1}; $\delta_H(CDCl_3)$ 2.65—3.05 (4 H, m), 3.73 (2 H, s), 4.00 (6 H, s), 4.75 (2 H, s), 5.86 (2 H, s), 6.51 (1 H, s), 6.53 (1 H, s), and 7.32 (2 H, s).

3,4-*Dimethoxy*-N-(1,2,3,4-*tetrahydroisoquinolin*-2-*ylmethyl*)-*phthalimide* (**8a**) was obtained in 65% yield, m.p. 109—110 °C (Found: C, 68.0; H, 5.55; N, 7.9. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.95%); $\nu_{max.}$(Nujol) 1 770 and 1 715 cm^{-1}; $\delta_H(CDCl_3)$ 2.94 (4 H, s), 3.84 (2 H, s), 3.94 (3 H, s), 4.14 (3 H, s), 4.66 (2 H, s), 7.0—7.2 (5 H, m), and 7.58 (1 H, d, *J* 6 Hz); $\delta_C(CDCl_3)$ 29.4, 48.8, 52.7, 56.6, 59.2, 62.4, 116.2, 119.5, 124.5, 125.2, 126.0, 126.6, 128.6, 133.7, 134.5, 157.9, 167.3, and 168.5 p.p.m.

3,4-*Dimethoxy*-N-(6,7-*methylenedioxy*-1,2,3,4-*tetrahydroisoquinolin*-2-*ylmethyl*)*phthalimide* (**8b**) was obtained in 47% yield, m.p. 163—165 °C (Found: C, 63.6; H, 5.0; N, 7.0. $C_{21}H_{20}N_2O_6$ requires C, 63.6; H, 5.1; N, 7.1%); $\nu_{max.}$(Nujol) 1 760 and 1 715 cm^{-1}; $\delta_H(CDCl_3)$ 2.75—2.95 (4 H, m), 3.73 (2 H, s), 3.96 (3 H, s), 4.15 (3 H, s), 4.76 (2 H, s), 5.86 (2 H, s), 6.51 (2 H, s), 7.13 (1 H, d, *J* 8 Hz), and 7.57 (1 H, d, *J* 8 Hz).

Irradiations.—These were carried out under nitrogen in a reactor vessel of 350 cm^3 capacity; the light source was a 400- or 450-W medium-pressure mercury arc (Applied Photophysics or Hanovia) with a Pyrex water-cooling jacket.

2-*Hydroxy*-5,6-*dimethoxy*-10,12-*diazapentacyclo*-[10.8.0.0$^{2.10}$.0$^{3.8}$.0$^{15.20}$]*icosa*-3(8),4,6,15(20),16,18-*hexaen*-9-*one* (**5a**). After irradiation of compound (**4a**) (0.006 mol) in benzene for 2.5 h, the solution was reduced to 30 cm^3 and filtered; the solid was recrystallised from acetone to give the *title compound* (**5a**) as crystals (28%), m.p. 208—210 °C (Found: C, 68.0; H, 5.8; N, 7.8. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.95%); $\nu_{max.}$(Nujol) 3 350 and 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 2.05—2.95 (4 H, m), 3.55 (3 H, s), 3.80 (3 H, s), 4.2 (1 H, s, reduced in D_2O), 4.40 (1 H, d, *J* 11 Hz), 4.55 (1 H, s), 4.70 (1 H, d, *J* 11 Hz), 6.40 (1 H, s), 6.95 (1 H, s), 7.0—7.4 (3 H, m), and 7.55—7.7 (1 H, m); $\delta_C(CDCl_3)$ 28.6, 45.3, 56.0, 67.9, 97.3, 105.9, 106.8, 123.1, 125.4, 127.2, 127.9, 128.9, 131.2, 133.9, 142.6, 150.6, 153.1, and 174.7 p.p.m.; *m/z* 220, 207, 145 (100%), and 132 (100).

2-*Hydroxy*-17,18-*dimethoxy*-10,12-*diazapentacyclo*-[10.8.0.0$^{2.10}$.0$^{3.8}$.0$^{15.20}$]*icosa*-3(8),4,6,15(20),16,18-*hexaen*-9-*one* (**5b**). After irradiation of the Mannich base (**4b**) (0.006 mol) in benzene for 8 h, crystals of compound (**5b**) were filtered off, and a further sample was obtained by subjecting the residual reaction mixture (after removal of solvent) to silica-gel chromatography with chloroform–methanol as eluant. Recrystallisation of the combined material from ethanol gave the *title compound* (**5b**) as crystals (25%), m.p. 183—185 °C (Found: C, 67.85; H, 5.8; N, 7.9. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.9%); $\nu_{max.}$(Nujol) 3 450 and 1 720 cm^{-1}; $\delta_H(CDCl_3)$ 2.1—3.1 (4 H, m), 3.80 (3 H, s), 4.00 (3 H, s), 4.50 (1 H, d, *J* 9 Hz), 4.60 (1 H, s), 4.80 (1 H, d, *J* 9 Hz), and 7.0—7.75 (6 H, m); $\delta_C(CDCl_3)$ 28.0, 45.0, 55.8, 56.4, 67.5, 68.2, 97.9, 111.1, 111.3, 122.5, 124.1, 124.7, 126.2, 129.8, 131.4, 133.0, 147.5, 148.3, 148.5, and 173.8 p.p.m.; *m/z* 352 (M^+), 205, 192 (100%), and 190.

2-*Hydroxy*-5,6,17,18-*tetramethoxy*-10,12-*diazapentacyclo*-[10.8.0.0$^{2.10}$.0$^{3.8}$.0$^{15.20}$]*icosa*-3(8),4,6,15(20),16,18-*hexaen*-9-*one* (**5c**). After irradiation of compound (**4c**) (0.005 mol) in benzene for 3 h, the solution was reduced to 30 cm^3 and filtered; recrystallisation of the solid from benzene gave the *title compound* (**5c**) as crystals (76%), m.p. 176—179 °C (Found: C, 64.2; H, 5.85; N, 6.55. $C_{22}H_{24}N_2O_6$ requires C, 64.1; H, 5.8; N, 6.8%); $\nu_{max.}$(Nujol) 3 350 and 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 1.7 (1H, br), 2.05—2.95 (4 H, m), 3.60 (3 H, s), 3.80 (3 H, s), 3.81 (3 H, s), 3.98 (3 H, s), 4.40 (1 H, d, *J* 11 Hz), 4.46 (1 H, s), 4.71 (1 H, d, *J* 11 Hz), 6.45 (1 H, s), 6.52 (1 H, s), 6.98 (1 H, s), and 7.10 (1 H, s); $\delta_C(CDCl_3)$ 27.9, 45.2, 55.8, 55.9, 56.2, 67.5, 97.2, 105.7, 106.4, 110.9, 111.5, 122.7, 123.0, 126.1, 142.7, 147.4, 148.3, 150.5, 153.0, and 174.7 p.p.m.

2-*Hydroxy*-5,6-*dimethoxy*-17,18-*methylenedioxy*-10,12-*diazapentacyclo*[10.8.0.0$^{2.10}$.0$^{3.8}$.0$^{15.20}$]*icosa*-3(8),4,6,15(20),16,18-*hexaen*-9-*one* (**5d**). After irradiation of compound (**4d**) (0.0018 mol) in benzene for 20 min, the solvent was removed and the residue was subjected to silica-gel chromatography with chloroform–methanol as eluant. The *title compound* (**5d**) was obtained as a pale yellow solid (60%), m.p. 211—216 °C (decomp.) (Found: C, 62.4; H, 6.0; N, 6.3. $C_{23}H_{26}N_2O_7$ requires C, 62.4; H, 5.9; N, 6.3%); $\nu_{max.}$(Nujol) 3 300 and 1 715 cm^{-1}; $\delta_H(CDCl_3)$ 1.7 (1 H, br), 2.0—2.8 (4 H, m), 3.70 (3 H, s), 3.84 (3 H, s), 4.41 (1 H, d, *J* 11 Hz), 4.47 (1 H, s), 4.74 (1 H, d, *J* 11 Hz), 5.92 (2 H, m), 6.45 (1 H, s), 6.58 (1 H, s), 7.03 (1 H, s), and 7.12 (1 H, s).

2-*Hydroxy*-4,5(*and* 6,7)-*dimethoxy*-10,12-*diazapentacyclo*-[10.8.0.0$^{2.10}$.0$^{3.8}$.0$^{15.20}$]*icosa*-3(8),4,6,15(20),16,18-*hexaen*-9-*one* (**9a**), (**10a**), *and* (**11a**). After irradiation of the Mannich base (**8a**) (0.006 mol) in acetonitrile for 5 h, the solvent was removed and the residue was subjected to silica-gel chromatography with chloroform–methanol as eluant. The *title compound* (**9a**) was obtained as crystals (51%), and was recrystallised from ethanol, m.p. 154—155 °C (Found: C, 67.9; H, 5.7; N, 8.0. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.95%); $\nu_{max.}$(Nujol) 2 740br and 1 715 cm^{-1}; $\delta_H(CDCl_3)$ 2.3—3.0 (4 H, m), 3.82 (6 H, s), 4.33 (1 H, d, *J* 8.5 Hz), 4.65 (1 H, d, *J* 8.5 Hz), 4.70 (1 H, s), and 6.75—7.5 (6 H, m, including doublets at 6.88 and 7.25, *J* 8 Hz); $\delta_C(CDCl_3)$ 25.7, 45.2, 56.2, 60.9, 63.4, 69.0, 98.3, 114.1, 120.2, 125.4, 126.8, 128.2, 129.7, 130.4, 134.3, 138.6, 144.9, 157.1, and 170.6 p.p.m.

The *epimeric compound* (**10a**) was obtained as crystals (8%), and was recrystallised from ethanol, m.p. 78—80 °C; $\nu_{max.}$(thin film) 3 360 and 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 2.6—3.7 (5 H, m), 3.81 (3 H, s), 3.96 (3 H, s), 4.15 (1 H, s), 4.20 (1 H, d, *J* 7.5 Hz), 4.80 (1 H,

d, *J* 7.5 Hz), and 6.9—7.7 (6 H, m, including doublets at 7.05 and 7.25, *J* 8 Hz); $\delta_C(CDCl_3)$ 27.7, 47.4, 56.4, 61.1, 64.5, 67.7, 96.3, 114.3, 120.1, 125.7, 127.5, 128.4, 130.3, 137.2, 144.8, 157.1, and 171.0 p.p.m.

The *isomeric compound* (**11a**) was obtained as crystals (26%), and was recrystallised from ethanol, m.p. 179—181 °C (Found: C, 67.9; H, 5.8; N, 7.8. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.95%); $\nu_{max.}$(Nujol) 2 750br and 1 705 cm^{-1}; $\delta_H(CDCl_3)$ 1.9—3.0 (4 H, m), 3.72 (3 H, s), 3.95 (3 H, s), 4.37 (1 H, d, *J* 11 Hz), 4.58 (1 H, s), 4.75 (1 H, d, *J* 11 Hz), 6.67 (2 H, AB pattern), and 6.9—7.7 (6 H, m); $\delta_C(CDCl_3)$ 28.5, 45.3, 56.2, 62.2, 67.6, 68.4, 96.4, 116.8, 119.5, 126.0, 127.1, 128.0, 128.6, 130.9, 133.6, 140.9, 153.3, and 171.8 p.p.m.

Reaction of the Photoproducts with Acid.—The photoproduct (0.5—1.0 g) was finely ground, dissolved in boiling ethanol (20—40 cm^3), and heated under reflux with 2M-HCl (20—40 cm^3) for 1—3 h until t.l.c. analysis indicated that the starting material had been consumed. The solution was concentrated to half volume, and the product was obtained as yellow crystals by filtration.

13-*Hydroxy*-10,11-*dimethoxy*-5,6-*dihydro*-8H-*dibenzo*[a,g]-*quinolizin*-8-*one* (**6a**) was obtained in 40% yield, m.p. 195—210 °C (decomp.); $\nu_{max.}$(Nujol) 2 725, 1 620, and 1 610 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 2.8—3.0 (2 H, m), 3.90 (3 H, s), 3.95 (3 H, s), 4.0—4.5 (2 H, m), 7.2—7.7 (4 H, m), and 8.3—8.8 (2 H, m); $\delta_C[(CD_3)_2SO]$ 28.8, 40.2, 55.6, 102.7, 107.6, 118.4, 121.6, 123.9, 125.2, 125.5, 126.0, 127.0, 127.2, 128.6, 128.9, 129.3, 132.5, 136.1, 149.0, and 157.6 p.p.m.; *m/z* 323 (M^+), 322 (100%), and 320 (Found: M^+, 323.1149. $C_{19}H_{17}NO_4$ requires *M*, 323.1157).

The *acetate* was obtained as pale lemon crystals (48%), m.p. 204—207 °C (Found: C, 69.0; H, 5.4; N, 3.8. $C_{21}H_{19}NO_5$ requires C, 69.0; H, 5.2; N, 3.8%); $\nu_{max.}$(Nujol) 1 770 and 1 640 cm^{-1}; $\delta_H(CDCl_3)$ 2.35 (3 H, s), 2.8—3.1 (2 H, m), 3.5—5.0 (2 H, v br), 4.00 (3 H, s), 4.05 (3 H, s), 6.85 (1 H, s), 7.2—7.4 (3 H, m), 7.85 (1 H, s), and 7.9—8.15 (1 H, m).

13-*Hydroxy*-2,3-*dimethoxy*-5,6-*dihydro*-8H-*dibenzo*[a,g]-*quinolizin*-8-*one* (**6b**) was obtained in 28% yield after recrystallisation from ethanol, m.p. 163—174 °C (decomp.) (Found: C, 70.3; H, 5.4; N, 4.3. $C_{19}H_{17}NO_4$ requires C, 70.6; H, 5.3; N, 4.3%); $\nu_{max.}$(Nujol) 3 200, 1 630, and 1 610 cm^{-1}; $\delta_H(CDCl_3)$ 2.90 (2 H, t, *J* 6 Hz), 3.7—3.9 (2 H, m), 3.95 (6 H, s), 5.8 (1 H, br), 6.70 (1 H, s), 7.3—8.1 (4 H, m), and 7.60 (1 H, s).

13-*Hydroxy*-2,3,10,11-*tetramethoxy*-5,6-*dihydro*-8H-*dibenzo*-[a,g]*quinolizin*-8-*one* (**6c**) was obtained in 59% yield after recrystallisation from ethanol, m.p. 188—194 °C (decomp.); $\nu_{max.}$(Nujol) 3 000, 1 630, and 1 610 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 2.3—2.7 (2 H, m), 3.89 (3 H, s), 3.93 (3 H, s), 3.97 (6 H, s), 4.0—4.3 (2 H, m), 6.95 (1 H, s), 7.45 (1 H, s), 7.63 (1 H, s), and 8.06 (1 H, s); *m/z* 383 (M^+), 382, 381, and 380 (100%) (Found: M^+, 383.1346. $C_{21}H_{21}NO_6$ requires *M*, 383.1368).

The *acetate* was obtained as pale lemon crystals (77%), m.p. 188—192 °C (Found: C, 64.7; H, 5.4; N, 3.5. $C_{23}H_{23}NO_7$ requires C, 64.9; H, 5.4; N, 3.3%); $\nu_{max.}$(Nujol) 1 770 and 1 645 cm^{-1}; $\delta_H(CDCl_3)$ 2.40 (3 H, s), 2.8—3.05 (2 H, m), 3.85—4.1 (14 H, m), 6.75 (1 H, s), 6.80 (1 H, s), 7.60 (1 H, s), and 7.85 (1 H, s).

13-*Hydroxy*-10,11-*dimethoxy*-2,3-*methylenedioxy*-5,6-*dihydro*-8H-*dibenzo*[a,g]*quinolizin*-8-*one* (**6d**) was obtained as yellow crystals (57%), m.p. 142—146 °C (decomp.); $\nu_{max.}$(Nujol) 3 100, 1 635, and 1 615 cm^{-1}; cm^{-1}; $\delta_H[(CD_3)_2SO]$ 2.65—2.95 (2 H, m), 3.88 (3 H, s), 3.93 (3 H, s), 4.0—4.25 (2 H, m), 6.06 (2 H, s), 6.94 (1 H, s), 7.42 (1 H, s), 7.62 (1 H, s), and 7.90 (1 H, s); *m/z* 367 (M^+, 100%), 352, and 164 (Found: M^+, 367.1056. $C_{20}H_{17}NO_6$ requires *M*, 367.1056).

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