Nitrogen Heterocycles. Part 10.[1] Rearrangement of *N*-Methylisoindolo[1,2-*b*][3]benzazepinium to *N*-Methyldibenzo[*a*,*g*]quinolizinium (*N*-Methylberbinium) Ions, and a Convenient New Route to Some Alkaloid Analogues of the Isoquinoline Series

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3-(3,4-Dimethoxybenzylidene)phthalide gives, by reaction with glycine, a mixture of (*E*)- and (*Z*)-3-(3,4-dimethoxybenzylidene)phthalimidin-2-ylacetic acids (1), which upon hydrogenation afford 3-(3,4-dimethoxybenzyl)phthalimidin-2-ylacetic acid (2). This compound is cyclised by polyphosphoric acid to 13,13a-dihydro-10,11-dimethoxyisoindolo[1,2-*b*][3]benzazepine-5,8(7*H*)-dione (3). The ethylene acetal of (3) [(4)] gives, on reduction with lithium aluminium hydride followed by treatment with methyl iodide, 7,8,13,13a-tetrahydro-10,11-dimethoxy-6-methyl-8-oxo-5*H*-isoindolo[1,2-*b*][3]benzazepinium iodide ethylene acetal (6). This compound, by the action of alkali, is converted into a mixture of (*Z*)-5,6-dihydro-10,11-dimethoxy-6-methyldibenz[*c*,*g*]-azecin-8(7*H*)-one ethylene acetal (7), and 5,6,13,13a-tetrahydro-2,3-dimethoxy-7-methyl-5-oxo-8*H*-dibenzo-[*a*,*g*]quinolizinium iodide ethylene acetal (9). When either (6) or (9) are refluxed with sodium deuterioxide in deuterium oxide the methiodide (9) (formed or recovered) appears to be deuteriated at positions 6, 8, 13, and 13a. The methiodide (9) gives, by Hofmann elimination, (*E*)-5,6-dihydro-10,11-dimethoxy-6-methyldibenz[*c*,*g*]-azecin-8(7*H*)-one ethylene acetal (11), which may be transformed into 5,6,13,13a-tetrahydro-13a-hydroxy-2,3-dimethoxy-7-methyl-5-oxo-8*H*-dibenzo[*a*,*g*]quinolizinium chloride (14), and its ethylene acetal (13). The ketones derived from (6) and (9) [(8) and (10)] give, by treatment with alkali, the same relatively stable ylide (15) which rearranges on heating to 6,7,12,13-tetrahydro-6,13-imino-2,3-dimethoxy-14-methyldibenzo[*a*,*e*]-cyclononen-5-one (16).

THE total synthesis of alkaloids, alkaloid analogues (particularly ' unnatural ' alkaloids),[2] and related compounds[3] may play an important role in medicinal chemistry. In our preceding paper[1] a convenient synthesis of isoindolo[1,2-*b*][3]benzazepine derivatives † related to Schöpf-Schweickert's base VI[4] was reported, and the opinion was formulated that such compounds, bearing the appropriate oxygenated substituents in the benzene rings, could be converted, by suitable reactions, into alkaloids and alkaloid analogues of the protopine, protoberberine, and possibly rhoeadine series.

In continuation of these studies we now report some recent results which appear to be in striking agreement with our previous hypothesis.

RESULTS AND DISCUSSION

3-(3,4-Dimethoxybenzylidene)phthalimidin-2-ylacetic acid (1) was obtained as a mixture of the (*E*)- and (*Z*)-isomers from 3-(3,4-dimethoxybenzylidene)phthalide[5] by the method described previously for the parent compound.[1] Cyclisation of the dihydro-acid (2) with polyphosphoric acid at 70 °C proceeded smoothly and in good yield to give the isoindolobenzazepinedione (3). This compound was converted into the ethylene acetal (4), which was reduced with lithium aluminium hydride in tetrahydrofuran, and the unstable product (5) thus formed was rapidly quaternised with methyl iodide. The resulting quaternary salt (6), which was obtained as a single isomer, was therefore chosen as an attractive starting product mainly for two reasons: (i) only an azecine and not also a styrene, as it occurs with compounds having a methylene at C-8,[6] could be formed by Hofmann elimination, and (ii) a carbonyl group in products derived from (6) could obviously be susceptible of further chemical elaboration.

Indeed, when (6) was treated with 33% aqueous potassium hydroxide at reflux, a 15—30% yield of the (*Z*)-olefin (7) (J_{cis} 12.5 Hz) was obtained. The stereochemistry of the elimination was therefore the same as that observed for a similar compound.[6] However, the major product (>60%) of this reaction was a new methiodide, whose elemental analysis and spectral data pointed to an isomer of (6).

In order to obtain less complex (and therefore more easily comparable) n.m.r. spectra, both (6) and the new methiodide were hydrolysed to the corresponding ketones by treatment either with hydriodic acid in tetrahydrofuran or with toluene-*p*-sulphonic acid in aqueous methanol. Structure (10) [and consequently structure (9) for the new methiodide] was thus deduced for the unknown ketone mainly on the basis of ^{13}C n.m.r. spectroscopy. In fact, whereas C-12 in the ^{13}C-undecoupled spectrum of ketone (8) gives rise to two triplets ($W_{\frac{1}{2}}$ *ca.* 9.5, $^3J_{CH}$ *ca.* 4.5 Hz), C-1 in the spectrum of (10) appears as two relatively narrow signals ($W_{\frac{1}{2}}$ *ca.* 4.5 Hz).

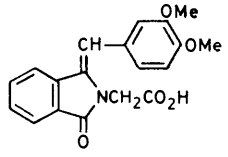
When the rearrangement (6) ⟶ (9) ‡ was performed with sodium deuterioxide in deuterium oxide the resulting reaction product appeared to be completely deuteriated at C-6, C-8, C-13, and C-13a. Unexpectedly, the same deuteriated product was obtained also from a similar treatment of (9). This result seems to show either that (6) and (9) are in equilibrium in basic solution, or more probably, that carbanions at C-13 in (6) and (9)

† In that paper, the compounds described were erroneously named isoindolo[2,3-*a*][3]benzazepines.

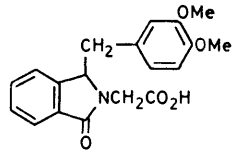
‡ Work in progress seems to indicate that base-catalysed rearrangements of this kind occur, although with lower speed and yield, also with compounds similar to (6) but lacking the oxygenated function at C-8.

are relevant intermediates both for the rearrangement and for the exchange. The other positions may undergo exchange *via* ylides, as generally observed for quaternary compounds.[7]

The assignments of the aliphatic proton resonances in



(1)



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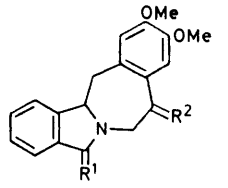
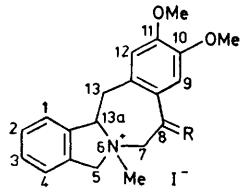
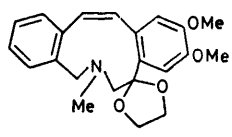


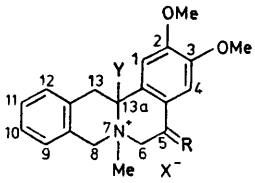
(3) $R^1 = R^2 = O$
(4) $R^1 = O$, $R^2 = [CH_2O]_2$
(5) $R^1 = H_2$, $R^2 = [CH_2O]_2$



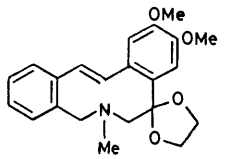
(6) $R = [CH_2O]_2$
(8) $R = O$



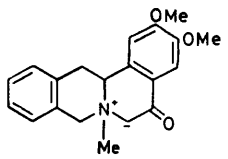
(7)



(9) $R = [CH_2O]_2$, $X = I$, $Y = H$
(10) $R = O$, $X = I$ (a) or Ts (b), $Y = H$
(12) $R = [CH_2O]_2$, $X = (O_2N)_3C_6H_2O$, $Y = H$
(13) $R = O$, $X = Cl$, $Y = OH$
(14) $R = [CH_2O]_2$, $X = Cl$, $Y = OH$



(11)



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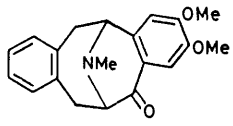

(16)

(6), (8), (9), and (10) (see Experimental section) were made as follows. The ethylene acetal (4) was reduced with lithium aluminium deuteride and quaternised with methyl iodide to obtain (6) deuteriated at C-5: thus, the signals arising from the hydrogens at C-7, C-13, and C-13a could be located. Polydeuteriated (9) was deacetalised to (10) containing (because of acid-catalysed D→H exchange) protons (aliphatic) only at C-6, whose resonance could be singled out.

The stereochemistry of the methyl group and the adjacent hydrogen at the tertiary carbon atom in compounds (9) and (10) appears to be *trans*, as deduced by the analysis of their n.m.r. spectra, and comparison with literature data.[8] A similar analysis does not permit, at present, to deduce with reasonable certainty the stereochemistry of (6) and (8), owing also to scarcity of data in the literature on similar compounds; however, we tentatively propose a *cis* stereochemistry, on the basis of arguments similar to those reported in ref. 6.

A further proof of the structure of (9) was obtained by passing an aqueous solution of the product through an ion-exchange resin pretreated with sodium hydroxide.[9] The aqueous eluate containing the quaternary hydroxide was degraded as described by Pyman [10] to give the (*E*)-olefin (11) (J_{trans} 16.5 Hz) in almost quantitative yield. The same olefin was formed also by a similar treatment of (6), thus indicating that in these conditions rearrangement to (9) precedes elimination.

The olefin (11) undergoes transannular cyclisation to give quaternary salts very readily. For instance, on being stood at room temperature for a few days, it gave a carbonate from which the methiodide (9) could be obtained by treatment with hydriodic acid. Moreover, an attempt to prepare the picrate resulted in the formation of the picrate salt (12). The ease with which (11) reverts to the quaternary cation has been already observed for similar compounds.[9,10]

Reaction of (11) with *m*-chloroperbenzoic acid and subsequent treatment of the crude *N*-oxide thus formed with hydrochloric acid in acetic acid gave, depending on the reaction time, the allocryptopine analogues (13) and (14).

Finally, when a solution of the ketone (10) in aqueous potassium hydroxide was heated at *ca.* 100 °C and then cooled, a crystalline product precipitated, whose i.r. spectrum shows no absorption in the carbonyl region, but presents two strong bands at 1 535 and 1 570 cm^{-1} and a broad absorption in the hydroxy-region. These data showed that this substance is the hydrated form of the ammonium ylide (15), as also indicated by the elemental analysis and its rearrangement. This ylide must be stabilised by the adjacent carbonyl group, as it has been observed for other carbonyl-stabilised ammonium ylides.[11-13]

Attempts to isolate an analogous ylide from the ketone (8) failed; however, more vigorous reaction conditions resulted in the formation of (15) owing obviously to rearrangement of (8) to (10) before precipitation.

The ylide (15) was smoothly transformed, on heating above 130 °C, into a Stevens rearrangement product. Of the two possibilities, *i.e.* either involvement of C-13a or of C-8 in the 1,2-migration, the spectral data appear to indicate the second as the most probable. We therefore propose structure (16) for the rearrangement product, which may be considered as an example of a derivative belonging to the 'homopavine' series of unnatural alkaloids.

CONCLUSION

Since the pioneer works of Haworth and Perkin [14] and Pyman [15] were first reported, several methods have been devised for the synthesis of alkaloids and alkaloid analogues of the berberine, protopine, and rhoeadine

series.[16] However, many of these alkaloids have been prepared only by transformation of naturally occurring compounds. For instance, to take into consideration an example [6] connected with the present work, α-allocryptopine has been obtained in poor yield from an isoindolobenzazepine derivative prepared from β-hydrastine, a commercial but quite expensive natural product.

The scheme of total synthesis described in this paper seems to have wide applicability and to be capable of extension.* The quaternary nitrogen and the oxygenated function should not constitute severe drawbacks for further elaboration of the structures. In fact, the former can be, if necessary, demethylated by reduction,[20] and the latter should constitute, on the contrary, an advantage. Incidentally, it may be recalled that the naturally occurring berberastine and thalidrastine are 5-hydroxyberbine derivatives.[21]

Work is in progress in order to extend the reactions described in this paper to the synthesis of alkaloids and especially of alkaloid analogues to be tested for biological activity.

EXPERIMENTAL

M.p.s were determined with a Kofler apparatus; i.r. spectra were recorded for Nujol mulls with a Perkin-Elmer 197 spectrophotometer, and the most intense and/or representative absorption bands are given; n.m.r. spectra were recorded with a Varian CFT-20 instrument, and most significant signals are quoted in p.p.m. from $SiMe_4$ as internal standard; evaporation of solvents was made with a rotary evaporator under diminished pressure; usual work-up means drying (when necessary) over magnesium sulphate, filtration, and evaporation.

(E)- *and* (Z)-3-(3,4-*Dimethoxybenzylidene*)*phthalimidin*-2-*ylacetic Acids* (1).—A mixture of 3-(3,4-dimethoxybenzylidene)phthalide [5,18] (50 g), glycine (16 g), 10M-sodium hydroxide (17.5 ml), and ethanol (300 ml) was refluxed for 1 h, then evaporated. To the deep red residue 3M-hydrochloric acid (200 ml) was added and the mixture was heated on a steam bath until an oil separated, which solidified on scratching (*ca.* 30 min). This material (50 g) was shown (n.m.r.) to contain the two isomers in the ratio *ca.* 3 : 1. Repeated fractional crystallisation from ether and from methanol gave (*Z*)-(1) as the less soluble, and (*E*)-(1) as the more soluble product. The (*Z*)-*isomer* (needles) had m.p. 202—204 °C (Found: C, 67.4; H, 5.0; N, 4.3. $C_{19}H_{17}NO_5$ requires C, 67.25; H, 5.05; N, 4.1%); $\nu_{max.}$ 1 620, 1 650, and 1 720 cm^{-1}; δ($CDCl_3$) 3.85 (3 H, s, OCH_3), 3.94 (3 H, s, OCH_3), 4.71 (2 H, s, CH_2), and 6.39 (1 H, s, olefinic H). The (E)-*isomer* (prisms) had m.p. 179—181 °C (Found: C, 67.4; H, 5.0; N, 4.1. $C_{19}H_{17}NO_5$ requires C, 67.25; H, 5.05; N, 4.1%); $\nu_{max.}$ 1 640 and 1 720 cm^{-1}; δ($CDCl_3$) 3.84 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 4.40 (2 H, s, CH_2), and 6.80 (1 H, s, olefinic H, partially overlapped by aromatic signals). The stereochemistry of the two products has been attributed on the basis of previous considerations.[1]

* It may be remembered at this point that the synthesis of some alkoxy-substituted phthalic anhydrides, whose preparation by classical methods was lengthy and inefficient, has been recently simplified and made very efficient;[17] 3-(3,4-methylenedioxybenzylidene)-6,7-methylenedioxyphthalide has been described;[18] and an azecine similar to (11) has been photochemically converted into an alkaloid of the rhoeadine series.[19]

3-(3,4-*Dimethoxybenzyl*)*phthalimidin*-2-*ylacetic Acid* (2).—The mixture of (*E*)- and (*Z*)-(1) (20 g) was hydrogenated at room temperature and pressure in ethanol (300 ml) in the presence of Pd–C (10%; 0.4 g). The usual work-up gave (2) (18 g), which crystallised from ethanol–water as *prisms*, m.p. 101—103 °C (Found: C, 67.0; H, 5.4; N, 4.2. $C_{19}H_{19}NO_5$ requires C, 66.85; H, 5.6; N, 4.1%); $\nu_{max.}$ 1 655 and 1 695 cm^{-1}; δ($CDCl_3$) 2.74, 2.83, 2.92, 3.01, 3.11, 3.18, 3.29, and 3.36 (2 H, C–CH_2), 3.71 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 3.83, 4.06, 4.57, and 4.80 (2 H, ABq, N–CH_2), and 4.90, 4.98, and 5.06 (1 H, CH).

13,13a-*Dihydro*-10,11-*dimethoxyisoindolo*[1,2-b][3]*benzazepine*-5,8(7H)-*dione* (3).—The acid (2) (15 g), finely ground, was stirred at 70 °C with polyphosphoric acid (Merck) (450 g) for 8 h. Dilution with water (2 l) caused separation of a solid which was dissolved in chloroform and the solution washed with 2M-sodium hydroxide. Usual work-up and crystallisation from chloroform–ether gave (3) (10 g) as *prisms*, m.p. 215—217 °C (Found: C, 70.7; H, 5.5; N, 4.3. $C_{19}H_{17}NO_4$ requires C, 70.6; H, 5.3; N, 4.3%); $\nu_{max.}$ 1 570 and 1 660 cm^{-1}; δ($CDCl_3$) 3.14, 3.16, 3.33, and 3.35 (1 H, one H-13; the other is overlapped by OCH_3 signals), 3.65 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 5.01 (1 H, m, H-13a), and 3.97, 4.20, 4.96, and 5.19 (2 H, ABq, H-7).

Ethylene Acetal (4).—A mixture of (3) (12 g), ethylene glycol (50 ml), toluene (150 ml), and toluene-*p*-sulphonic acid (0.3 g) was refluxed for 5 h with continuous removal of water. The solvent was then evaporated off and the residue crystallised from tetrahydrofuran–ether to give the acetal (4) (11 g) as *prisms*, m.p. 200—203 °C (Found: C, 68.9; H, 6.0; N, 3.6. $C_{21}H_{21}NO_5$ requires C, 68.65; H, 5.8; N, 3.8%); $\nu_{max.}$ 1 580 and 1 665 cm^{-1}; δ($CDCl_3$) 3.00—3.84 (2 H, m, H-13), 3.92 (6 H, s, OCH_3), 4.08—4.29 [4 H, m, $(CH_2O)_2$], 4.45, 4.49, 4.58, and 4.62 (1 H, H-13a), and 3.16, 3.34, 4.67, and 4.85 (2 H, ABq, H-7).

7,8,13,13a-*Tetrahydro*-10,11-*dimethoxy*-6-*methyl*-8-*oxo*-5H-*isoindolo*[1,2-b][3]*benzazepinium Iodide Ethylene Acetal* (6).—A mixture of (4) (7 g), and lithium aluminium hydride (3 g) in anhydrous tetrahydrofuran (200 ml) was refluxed for 5 h. The excess of hydride was destroyed by adding successively ethyl acetate and water, the precipitated aluminium hydroxide was filtered off, and the solution was evaporated. The residue [crude (5)] was dissolved in acetone (150 ml) and the solution was treated with methyl iodide (5 ml) at 0 °C. The mixture was kept in a refrigerator for 10 h and the precipitate was collected and crystallised from methanol to give (6) (6 g) as *blades*, m.p. 209—213 °C (decomp.) (Found: C, 53.5; H, 5.4; N, 2.6. $C_{22}H_{26}INO_4$ requires C, 53.3; H, 5.3; N, 2.8%); $\nu_{max.}$ 1 250, 1 530, 1 440, 1 498, and 1 585 cm^{-1}; δ($CDCl_3$) 3.52 (3 H, s, NCH_3), 3.72 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 4.25 (8 H, m, $[CH_2O]_2$, H-7, and H-13), 4.83, 5.01, 5.12, and 5.30 (2 H, ABq, H-5), and 5.31 (1 H, m, H-13a). 5,5-Dideuteriated-(6) was obtained as described above using as reducing agent lithium aluminium deuteride. The signals originated by H-5 were not present in the ^1H n.m.r. spectrum of the compound.

7,8,13,13a-*Tetrahydro*-10,11-*dimethoxy*-6-*methyl*-8-*oxo*-5H-*isoindolo*[1,2-b][3]*benzazepinium Iodide* (8).—Compound (6) (0.8 g) was refluxed for 2 h with a 1 : 2 : 3 mixture of 1M-hydriodic acid, acetic acid, and tetrahydrofuran (20 ml). Addition of ether to the solution caused separation of (8) (0.5 g) as *prisms*, m.p. 217—222 °C (decomp.) (Found: C, 53.0; H, 5.1; N, 3.0. $C_{20}H_{22}INO_3$ requires C, 53.2;

H, 4.9; N, 3.1%); $\nu_{max.}$ 1 260, 1 440, 1 500, 1 575, and 1 635 cm^{-1}; δ[$(CD_3)_2SO$] 3.47 (3 H, s, NCH_3), 3.75 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 4.00, 4.06 (2 H, H-13), 4.86 (2 H, s, H-7), 5.12 (2 H, s, H-5), and 5.55, 5.61, and 5.67 (1 H, H-13a); δ_C[$(CD_3)_2SO$] 34.6 (C-13), 53.8 (NCH_3), 68.0 (C-7), 70.4 (C-5), 80.7 (C-13a), 110.1 (C-9), 114.4 (C-12), and 188.5 (C-8). 5,5-Dideuteriated (8) was obtained by deacetalisation of 5,5-dideuteriated (6) as described above. The signal originated by H-5 was not present in the ^1H n.m.r. spectrum of the compound.

(Z)-5,6-*Dihydro*-10,11-*dimethoxy*-6-*methyldibenz*[c,g]*azecin*-8(7H)-*one Ethylene Acetal* (7), *and* 5,6,13,13a-*Tetrahydro*-2,3-*dimethoxy*-7-*methyl*-5-*oxo*-8H-*dibenzo*[a,g]*quinolizinium Iodide Ethylene Acetal* (9).—A suspension of (6) (1.5 g) in 33% aqueous potassium hydroxide (15 ml) was refluxed for 3.5 h, cooled, extracted with ether, and the insoluble material collected. The organic layer was separated from the aqueous solution and usual work-up afforded a residue which crystallised from ether–hexane to give (7) (0.15—0.30 g) as *needles*, m.p. 123—125 °C (Found: C, 72.0; H, 6.9; N, 3.7. $C_{22}H_{25}NO_4$ requires C, 71.9; H, 6.9; N, 3.8%); $\nu_{max.}$ 1 035, 1 430, 1 480, 1 550, and 1 575 cm^{-1}; δ($CDCl_3$) 2.07 (3 H, s, NCH_3), 2.88 (4 H, m, two overlapped AB systems, H-5 and H-7), 3.58 (3 H, s, OCH_3), 3.86 (3 H, s, OCH_3), 4.00 (4 H, m, $[CH_2O]_2$), and 6.60, 6.76, 6.88, and 7.04 (2 H, ABq, olefinic protons).

The insoluble material (0.9 g) crystallised from methanol to give (9) as *blades*, m.p. 247—250 °C (decomp.) (Found: C, 53.4; H, 5.5; N, 2.5. $C_{22}H_{26}INO_4$ requires C, 53.3; H, 5.3; N, 2.8%); $\nu_{max.}$ 1 270, 1 440, 1 500, 1 590, and 1 640 cm^{-1}; δ[$(CD_3)_2SO$] 2.91 (3 H, s, NCH_3), 3.82 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 4.20 (8 H, m, $[CH_2O]_2$, H-6, and H-13), 4.64, 4.84, 4.96, and 5.16 (2 H, ABq, H-8), and 5.25 (1 H, m, H-13a).

When compound (6) (0.5 g) was refluxed for 5 h with 15% sodium deuterioxide in deuterium oxide (7.5 ml), the ^1H n.m.r. spectrum of the dibenzoquinolizinium iodide (9) thus obtained showed aliphatic signals only for $[CH_2O]_2$, NCH_3, and OCH_3. The same polydeuteriated compound was obtained by submitting non-deuteriated (9) to the same reaction conditions.

5,6,13,13a-*Tetrahydro*-2,3-*dimethoxy*-7-*methyl*-5-*oxo*-8H-*dibenzo*[a,g]*quinolizinium Iodide* (10a) *and Toluene*-p-*sulphonate* (10b).—The acetal (9) (0.5 g) was hydrolysed as described above for (5). The product (10a) (0.3 g), *prisms*, had m.p. 235—240 °C (decomp.) (Found: C, 53.4; H, 5.0; N, 3.1. $C_{20}H_{22}INO_3$ requires C, 53.2; H, 5.0; N, 3.1%); $\nu_{max.}$ 1 040, 1 200, 1 275, 1 570, and 1 650 cm^{-1}; δ[$(CD_3)_2SO$] 2.99 (3 H, s, NCH_3), 3.58 (2 H, m, H-13), 3.89 (3 H, s, OCH_3), 4.04 (3 H, s, OCH_3), 4.45, 4.58, 4.76, and 4.89 (2 H, ABq, H-6), 4.82, 4.97, 5.12, and 5.27 (2 H, ABq, H-8), 5.61 (1 H, m, H-13a); δ_C[$(CD_3)_2SO$] 28.2 (C-13), 41.5 (NCH_3), 64.2 (C-13a), 64.7 (C-8), 67.7 (C-6), 107.7 (C-4), 109.6 (C-1), and 184.5 (C-5). This compound crystallised from water as *prisms*, m.p. 234—237 °C (decomp.) containing water of crystallisation; $\nu_{max.}$ 1 040, 1 200, 1 275, 1 570, 1 650, 3 375, and 3 425 cm^{-1}; ^1H and ^{13}C n.m.r. spectra identical with those of the anhydrous compound. The water was lost after heating *in vacuo* at 130 °C for 10 h.

The ^1H n.m.r. spectrum of the ketone obtained by deacetalisation of polydeuteriated (9) showed aliphatic signals attributable to the N- and O-methyls, and to the C-6 methylene only.

By refluxing (9) (1.8 g) with methanol (50 ml), water (0.5 ml), and toluene-*p*-sulphonic acid (1.8 g) for 2 h, usual work-up and crystallisation from methanol–tetrahydrofuran gave (10b) (1.5 g) as *blades*, m.p. 255—257 °C (decomp.) (Found: C, 65.1; H, 5.8; N, 2.5. $C_{27}H_{29}NO_6S$ requires C, 65.4; H, 5.9; N, 2.8%); $\nu_{max.}$ 1 170, 1 210, 1 280, 1 575, and 1 660 cm^{-1}; δ[$(CD_3)_2SO$] 2.30 (3 H, s, CCH_3), 3.02 (3 H, s, NCH_3), 3.20 (2 H, m, H-13), 3.96 (3 H, s, OCH_3), 4.07 (3 H, s, OCH_3), 4.56, 4.76, 4.90, and 5.10 (2 H, ABq, H-6), 4.81, 5.00, 5.18, and 5.37 (2 H, ABq, H-8), and 5.76 (1 H, m, H-13a).

(E)-5,6-*Dihydro*-10,11-*dimethoxy*-6-*methyldibenz*[c,g]*azecin*-8(7H)-*one Ethylene Acetal* (11).—A solution of (9) (0.6 g) in water (100 ml) was run through a column of IRA-400 activated resin [6] (10 g), washing with water (50 ml). The combined eluates were evaporated *in vacuo* at 100 °C and the residue was taken up in ether. Evaporation of the ethereal solution gave (11) as an *oil*, which was freely soluble in hexane. The product was analysed without further purification (Found: C, 71.5; H, 7.1; N, 3.4; $C_{22}H_{25}NO_4$ requires C, 71.9; H, 6.9; N, 3.8%); $\nu_{max.}$ 1 310, 1 440, 1 480, 1 548, and 1 580 cm^{-1}; δ($CDCl_3$) 2.85 (3 H, s, NCH_3), 3.75 (3 H, s, OCH_3), 3.78 (8 H, m, $[CH_2O]_2$, H-5 and H-7), 3.81 (3 H, m, OCH_3), and 6.20, 6.41, 7.60, and 7.81 (2 H, ABq, olefinic H).

The same results were obtained from the methiodide (6).

When this amine was kept at room temperature in an open vessel for 5 days a solid (probably a carbonate) was formed. Treatment of this solid with methanol containing hydriodic acid and addition of ether caused separation of (9). An attempt to prepare the picrate [by heating (11) with picric acid in ethanol] gave the salt (12) as *yellow prisms*, m.p. 218—221 °C (Found: C, 56.0; H, 4.9; N, 9.0. $C_{28}H_{28}N_4O_{11}$ requires C, 56.4; H, 4.7; N, 9.4%); $\nu_{max.}$ 1 260, 1 440, 1 530, 1 590, and 1 610 cm^{-1}.

5,5,13,13a-*Tetrahydro*-13a-*hydroxy*-2,3-*dimethoxy*-7-*methyl*-5-*oxo*-8H-*dibenzo*[a,g]*quinolizinium Chloride* (14) *and Ethylene Acetal* (13).—A solution of (11) (0.35 g) in chloroform (3 ml) was added to a solution of *m*-chloroperbenzoic acid (0.2 g) in ether (15 ml) while the temperature was maintained below 4 °C by immersion in an ice-bath. The mixture was left for 2 days in a refrigerator, and then treated with stirring with 2M-sodium hydroxide (4 ml); after 2 h acetic acid (1 ml) was added, and stirring was continued for 15 min. The oily precipitate was freed from the supernatant liquid by decantation and dissolved in methanol (2 ml) and acetic acid (0.5 ml) containing few drops of concentrated hydrochloric acid. After 2 h of reflux, addition of ether caused separation of (14) (0.3 g) which crystallised from water as *prisms*, m.p. 250—255 °C (decomp.) (Found: C, 64.1; H, 6.2; N, 3.6. $C_{20}H_{22}ClNO_4$ requires C, 63.9; H, 5.9; N, 3.7%); $\nu_{max.}$ 1 200, 1 290, 1 570, 1 650, and 3 180 cm^{-1}; δ(D_2O, internal reference DDS *) 3.02 (3 H, s, NCH_3), 3.05 (2 H, m, H-13), 3.96 (3 H, s, OCH_3), 4.09 (3 H s, OCH_3), 4.68, 4.87, 5.15, and 5.34, (2 H, ABq, H-6), and 5.25, 5.36, 5.56, and 5.67 (2 H, ABq, H-8).

When the methanol–acetic acid–hydrochloric acid solution was refluxed for 0.5 h, addition of ether caused separation of the acetal (13) [0.3 g from 0.35 g of (11)] as *needles*, m.p. 255—260 °C (decomp. and sintering at 225 °C) (Found: C, 62.6; H, 6.2; N, 3.3. $C_{22}H_{26}ClNO_5$ requires C, 62.9; H, 6.2; N, 3.3%); $\nu_{max.}$ 1 140, 1 440, 1 490, 1 590, and 3 070 cm^{-1}; δ(D_2O, int. ref. DDS) 2.92 (3 H, s, NCH_3), 3.91 (3 H, s, OCH_3), 3.94 (3 H, s, OCH_3), 4.10 (2 H, m, H-13),

* Sodium 3-(trimethylsilyl)propanesulphonate (Merck).

4.34 (4 H, m, $[CH_2O]_2$), 4.55, 4.72, 4.96, and 5.13 (2 H, ABq, H-6), and 4.84, 4.96, 5.33, and 5.45 (2 H, ABq, H-8).

Ylide (15).—(a) *From* (10b).—Toluene-*p*-sulphonate (10b) (2 g) was dissolved in the minimum amount of hot water (steam-bath) and potassium hydroxide (0.4 g) was added to the solution, which was then left overnight in a refrigerator. Compound (15) (0.8 g) precipitated as *needles*, m.p. 130—140 °C (decomp.) (Found: C, 63.4; H, 6.8; N, 3.4. $C_{20}H_{21}NO_3 \cdot 3H_2O$ requires C, 63.6; H, 7.2; N, 3.7%); $\nu_{max.}$ 1 010, 1 360, 1 535, 1 570, and 3 050—3 500 cm^{-1}. The compound was quantitatively converted into the starting toluene-*p*-sulphonate by treatment with an aqueous solution of toluene-*p*-sulphonic acid.

(b) *From* (8).—The methiodide (8) was treated as described above but the basic solution was refluxed for 15 min. A precipitate (15) was formed on cooling.

6,7,12,13-*Tetrahydro*-6,13-*imino*-2,3-*dimethoxy*-14-*methyldibenzo*[a,e]*cyclononen*-5-*one* (16).—The ylide (15) (0.6 g) was heated at 180 °C under nitrogen for 20 min. The product was taken up in hot ether, and the solution evaporated to give an oil which solidified on trituration with hexane. Recrystallisation from ether–hexane gave (16) (0.4 g) as *blades*, m.p. 145—148 °C (Found: C, 74.1; H, 6.5; N, 4.1. $C_{20}H_{21}NO_3$ requires C, 74.3; H, 6.55; N, 4.3%); $\nu_{max.}$ 1 580 and 1 635 cm^{-1}; $\delta(CDCl_3)$ 2.66 (3 H, s, NCH_3), 3.76 (3 H, s, OCH_3), 3.92 (3 H, s, OCH_3), and 2.68—4.20 (6 H, m, two overlapped ABX systems, H-6, -7, -12, and -13); δ_C ($CDCl_3$) 38.9 (C-7 or -12), 42.3 (C-12 or -7), 43.6 (NCH_3), 59.5 (C-6 or -13), 65.4 (C-13 or -6), 106.8 (C-4), 107.7 (C-1), and 196.3 (C-5). The NCH_3 quartet in the ^{13}C undecoupled spectrum is formed by triplets with $^3J_{CH}$ *ca.* 2.5 Hz.

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