Aust. J. Chem., 1984, **37**, 1659–76

Photosolvolysis of Bridgehead Quaternary Ammonium Salts. II* Synthesis of Some 2,5-Benzoxazonine Derivatives and Attempted Synthesis of the 1,2,4,5,6,7-Hexahydro-3,5-benzoxazonine System†

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Abstract

The medium-ring heterocyclic derivative 1,9,10-trimethoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine (6a) was obtained in fair yield from photosolvolysis of 8,9-dimethoxy-4-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinolinium iodide (5a) in methanol, together with minor amounts of 3,9,10-trimethoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine (8) and 2-[*N*-2-{2-(dimethoxymethyl)-4,5-dimethoxyphenyl}ethyl-*N*-methylamino]ethanol (7). Photosolvolysis products analogous to (6a) were obtained from other related 10b-substituted oxazolo[2,3-*a*]isoquinolinium iodides in high to low yields depending upon the nature of the angular substituent and the presence or absence of substituents in the fused aromatic ring. No methanolysis of the methiodide salts (5a–f) was observed in the absence of ultraviolet irradiation, whereas 1-(2-ethenyl-4,5-dimethoxyphenyl)ethanone (14) was formed on heating (5b) with methanolic potassium hydroxide. Attempted synthesis of 1,2,4,5,6,7-hexahydro-3,5-benzoxazonine derivatives by photosolvolysis of 8,9-dimethoxy-4-methyl-1,5,6,10b-tetrahydro-3*H*-oxazolo[4,3-*a*]isoquinolinium iodide (17) in methanol or water was unsuccessful, ring-opened products being obtained in low yield instead.

Introduction

Amongst the many possible approaches to medium-sized heterocyclic systems, those involving a ring-destruction strategy[2] offer considerable versatility and control (cf.[3]). Photosolvolysis of bridgehead quaternary ammonium salts is one way of achieving ring enlargement by this general strategy, and applications to the synthesis of some 3-benzazonine derivatives have been described.[1,4] We now wish to report, in full, results on the extension of this reaction to the synthesis of 2,5-benzoxazonine derivatives and the attempted synthesis of a reduced 3,5-benzoxazonine system. Of the 21 possible isomeric benzoxazonine ring skeletons, only five, the 1,4-, 2,3-, 2,5-, 2,6- and 4,1-systems, have so far been reported.[5,6] Apart from their general chemical

* Part I, *Aust. J. Chem.*, 1984, **37**, 1203.
† A preliminary report of some of these results has been published.[1]

[1] Bremner, J. B., and Winzenberg, K. N., *Chem. Ind. (London)*, 1980, 421.
[2] Stoodley, R. J., *Chem. Ind. (London)*, 1977, 377.
[3] Lednicer, D., *Adv. Org. Chem.*, 1972, **8**, 236.
[4] Bremner, J. B., and Winzenberg, K. N., *Aust. J. Chem.*, 1984, **37**, 1203.
[5] Bremner, J. B., Browne, E. J., and Gunawardana, I. W. K., *Heterocycles*, 1982, **19**, 709.
[6] Bremner, J. B., and Thirasasana, N., *Aust. J. Chem.*, 1982, **35**, 2307.

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interest, a number of these heterocyclic systems exhibit significant pharmacological activity. For example, some 2,6-benzoxazonine derivatives are claimed[7] to be useful as diuretics, skeletal muscle relaxants, and stimulants of the central nervous system, whereas some 4,1-benzoxazonine-2,7(1*H*,3*H*)-diones show[8] antihypertensive, bactericidal, and fungicidal activity. It was thus hoped to uncover further pharmacologically active benzoxazonine derivatives as a result of this work.

Results and Discussion

Preparation of the Hexahydro-2,5-benzoxazonines (6a–f)

(*a*) *Precursor Salts*

The 2,5-benzoxazonine precursor salts (5a–f) were prepared from the known 3,4-dihydroisoquinoline derivatives (2a–f), readily accessible, in turn, by Bischler–Napieralski cyclization of the amides (1a–f) (Scheme 1). Oxazolidine annelation was effected by reaction of the imine derivatives (2a–f) with 2-bromoethanol, followed by treatment of the resultant salts (3a–f) with aqueous potassium hydroxide, after the general method of Schneider and Kämmerer.[9] Quaternization of (4a–f) with iodomethane gave the requisite tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinolinium salts (5a–f). The quaternization of (2c), (2d), and (2f) proceeded with difficulty probably largely as a result of steric hindrance by the C 1 substituent. The extended reaction times or vigorous conditions necessary also resulted in increased imine hydrobromide salt formation from dehydrobromination[10] of the alkylating agent. Pure (3c) was readily obtained by fractional recrystallization. In the other cases, treatment with base afforded a mixture of the appropriate imine (2) and oxazoloisoquinoline derivative (4); the latter was then separated by fractional recrystallization.

(*b*) *Photosolvolysis*

Ultraviolet irradiation (Corex filter) of the salts (5a–f) in methanol gave the expected 2,5-benzoxazonine derivatives (6a–f) in yields ranging from 11 to 89% (Scheme 2 and Table 1) after basification of the photolysate and chromatography.

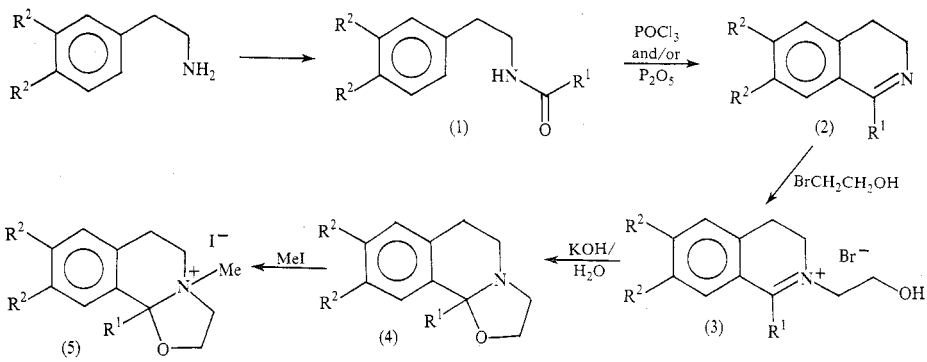
The assignment of structures (6a–f) was supported by analytical and spectroscopic data. By way of illustration, detailed accounts of the structural elucidation of (6a) and (6b) only are given. Carbon-13 n.m.r. spectra were not obtained for (6c–f).

The reduced 2,5-benzoxazonine (6a) was obtained as an oil, the molecular formula being confirmed by high-resolution mass spectroscopy and elemental analysis on the crystalline methiodide salt derivative.

In the 270-MHz ^{1}H n.m.r. spectrum of (6a), the two three-proton singlets at δ 3·54 and 2·29 were assigned, in turn, to the C 1 aliphatic methoxy group and the methylamino group. The one-proton singlet at δ 5·62 was assigned to the hydrogen atom at C 1. This proton experienced a downfield shift of 0·43 ppm compared to the corresponding C 10b proton of (4a), consistent with solvolysis at this position.

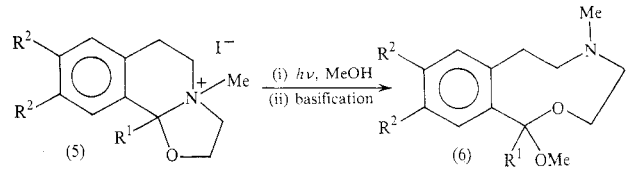
The two-proton multiplet at δ 3·68–3·56 was assigned to the hydrogen atoms at C 3. Irradiation of this multiplet resulted in the collapse of the two-proton multiplet

[7] Rexall Drug and Chemical Co., Neth. Appl. 6,606,390 (*Chem. Abstr.*, 1967, **66**, 55535w).
[8] Demerson, C. A., and Humber, L. G., U.S. Pat. 4,100,277 (*Chem. Abstr.*, 1979, **90**, 38974s).
[9] Schneider, W., and Kämmerer, E., *Arch. Pharm.* (*Weinheim, Ger.*), 1966, **299**, 817.
[10] Donetti, A., and Bellora, E., *Tetrahedron Lett.*, 1973, 3573.



	R^1	R^2		R^1	R^2
(a)	H	MeO	(d)	3,4-$(MeO)_2C_6H_3CH_2$	MeO
(b)	Me	MeO	(e)	Me	H
(c)	Ph	MeO	(f)	3,4-$(MeO)_2C_6H_3$	H

Scheme 1



Scheme 2

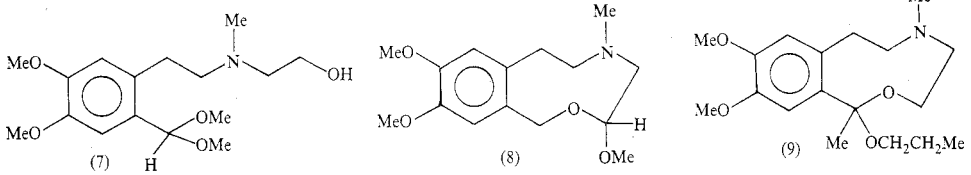


Table 1. Photolysis of tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinolinium salts (5a–f) in methanol (unless otherwise stated)

Salt	Amount (mmol)	Irradiation time (h)	2,5-Benzoxazonine derivatives[A]	Other compounds isolated
(5a)	0·854	1·0	(6a) 55%	(7) 12% (8) 8%
(5b)	3·836	7·0	(6b)[B] 89%	(5b) 7%
(5b)[C]	1·022	1·25	(9) 67%	
(5c)	0·882	0·5	(6c) 49%	(5c) 15%
(5d)	0·758	0·33	(6d) 72%	—
(5e)	0·755	2·0	(6e) 28%	(5e) 35%
(5e)	1·208	1·25[D]	(6e) 32%	(5e) 17%
(5f)	0·760	0·83	(6f) 11%	(5f) 11%

[A] Obtained after p.l.c. of the basified photolysate.
[B] (6b) could be crystallized directly from the basified photolysate.
[C] Photolysis in propan-1-ol (see Experimental).
[D] Vycor filter.

at δ 2·57–2·34 to an AB quartet centred at δ 2·51 and 2·38 (J 15 Hz), indicative of residual geminal coupling. This latter multiplet was thus assigned to the hydrogen atoms at C4. The remaining C6 and C7 methylene protons appeared as multiplets at δ 3·20–3·10 and 2·90–2·73.

The ^{13}C n.m.r. spectrum of (6a) was consistent with the proposed structure. The methylene carbon resonances were tentatively assigned by comparison of the experimental chemical shifts with the calculated[11,12] chemical shifts (in parentheses) as follows: C3, 64·4 (69·7); C4, 57·6 (55·7); C6, 59·7 (56·7); C7, 32·9 (34·7). The assignments of C3 and C4 were verified by selective proton decoupling experiments.

In the expanded proton-coupled spectrum the aliphatic methoxyl carbon appeared as a doublet of quartets ($^1J_{C-H}$ 141, $^3J_{C-O-C-H}$ 3 Hz), indicative of long-range coupling to the hydrogen atom at C1, while the aromatic methoxyl carbons appeared as a single simple quartet ($^1J_{C-H}$ 140 Hz). The signal for the methylamino carbon appeared as a broadened quartet ($^1J_{C-H}$ 132 Hz), which is apparently often characteristic[13] of such carbons. The assignment of the aliphatic methoxyl carbon was confirmed by selective proton decoupling.

The molecular composition, $C_{16}H_{25}NO_4$, of the 2,5-benzoxazonine derivative (6b) was established from high-resolution mass spectroscopy and this was reinforced by elemental analysis. The salient features of the ^1H n.m.r. spectrum of (6b) were three three-proton singlets at δ 1·53, 2·23 and 3·37, which were ascribed respectively to the C1 methyl, the aminomethyl and the C1 methoxy groups.

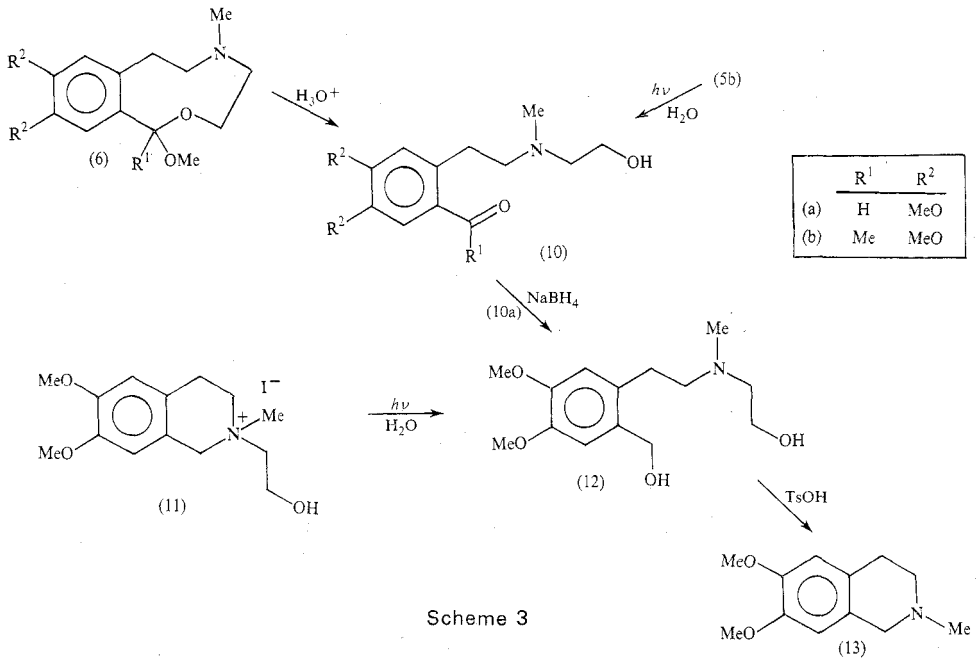
In the ^{13}C n.m.r. spectrum of (6b) the assignments of all carbon resonances, except those of the methylamino and aliphatic methoxy groups, were apparent from comparison with those of (6a). The latter two resonances were separated by only 0·1 ppm. On the basis of the magnitude of the $^1J_{C-H}$ coupling constants the carbon atoms of the methylamino group and the aliphatic methoxy group were assigned, in turn, to quartets centred at δ 47·9 ($^1J_{C-H}$ 128 Hz) and 48·0 ($^1J_{C-H}$ 138 Hz). Consistent with these assignments, an expansion of this region of the spectrum showed the former quartet to be broadened, as expected for a methylamino group, while the latter was sharp.

The structures of (6a) and (6b) were also supported by further chemical reactions. Acid hydrolysis of (6a) gave the aldehyde (10a), whereas (6b) afforded the ketone (10b) (Scheme 3). The infrared absorption spectra of these compounds displayed absorption bands centred at 3400 cm^{-1} attributed to the hydroxy group, while additional bands at 1675 and 1690 cm^{-1} for (10a) and at 1680 cm^{-1} for (10b) were assigned to the carbonyl group. Furthermore, the ^1H n.m.r. spectrum of (10a) exhibited a downfield one-proton singlet at δ 10·14 consistent with an aldehyde group, whereas that of (10b) showed a three-proton singlet at δ 2·58 for the acetyl group.

Reduction of (10a) with sodium tetrahydroborate afforded the amino diol (12), which had spectroscopic properties identical with those of an authentic sample

[11] Wehrli, F. W., and Wirthlin, T., 'Interpretation of Carbon-13 N.M.R. Spectra' p. 36 (Heyden: London 1978).
[12] Breitmaier, E., and Voelter, W., '^{13}C N.M.R. Spectroscopy' (Monographs in Modern Chemistry, Ed. H. F. Ebel) Vol. 5, p. 119 (Verlag Chemie: Weinheim 1974).
[13] Jones, A. J., personal communication.

prepared[14] from photosolvolysis of the tetrahydroisoquinolinium salt (11) (Scheme 3). [An attempt to recyclize the readily available amino diol (12) to 9,10-dimethoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine by acid-catalysed dehydration (cf.[7]) was unsuccessful, the tetrahydroisoquinoline (13) being the only identified product.]



Scheme 3

Finally, proof of the structures of (6a) and (6b) was obtained[15] by single-crystal X-ray diffraction studies on their methiodide salts, undertaken by Dr M. F. C. Ladd at the University of Surrey, England.

In order to further extend the usefulness of the photosolvolytic approach to the 2,5-benzazonine system, the photolysis of (5b) in some other hydroxylic solvents was investigated. Ultraviolet irradiation of (5b) in propan-1-ol afforded the corresponding 1-propoxy-2,5-benzoxazonine derivative (9) in good yield (see Table 1); this indicates that it may be possible to employ a range of alcohols in this photoinduced solvolysis reaction. On the other hand, only the amino ketone (10b) was obtained from the photolysis of (5b) in water (Scheme 3); it is probable that (10b) is derived from the initially formed cyclic hemiacetal.

(*c*) *Minor Products*

A number of minor products were detected in the methanol photolysates from (5c–f); however, due to the small amounts of material involved and difficulties of purification, none were identified. On the other hand, the acetal derivative (7) was isolated in 12% yield (Table 1) from the photolysate of (5a).

[14] Dragar, C., B.Sc. (Hons) Thesis, University of Tasmania, 1978.
[15] Ladd, M. F. C., unpublished data.

The assignment of structure (7) was supported by analytical and spectroscopic data. The salient features of the ^1H n.m.r. spectrum of this compound were the six-proton singlet at δ 3·36 and the downfield one-proton singlet at 5·46 ascribed in turn to the methoxyl and benzylidene protons of the acetal group. The exchangeable one-proton singlet at δ 3·15 was attributed to the hydroxy group; the presence of this group was confirmed from the infrared spectrum which displayed a broad absorption band at 3380 cm^{-1}. Acidic hydrolysis of (7) afforded the aldehyde (10a).

Yet another compound, tentatively identified as the 2,5-benzoxazonine derivative (8) on the basis of limited spectroscopic evidence, was isolated from the photolysate of (5a) (see Table 1).

The molecular composition of (8), $C_{15}H_{23}NO_4$, was established from high-resolution mass spectroscopy. In the ^1H n.m.r. spectrum of this compound the downfield one-proton triplet (J 5 Hz) at δ 4·26 and the two-proton singlet at 3·86 were assigned in turn to the hydrogen atoms at C3 and C1. The two three-proton singlets at δ 3·38 and 2·38 were ascribed to the aliphatic methoxy group and to the aminomethyl group respectively.

(d) Discussion

The photosolvolysis of the 5*H*-oxazolo[2,3-*a*]isoquinolinium salts (5a–f) provides a useful approach to the synthesis of 2,5-benzoxazonine derivatives.

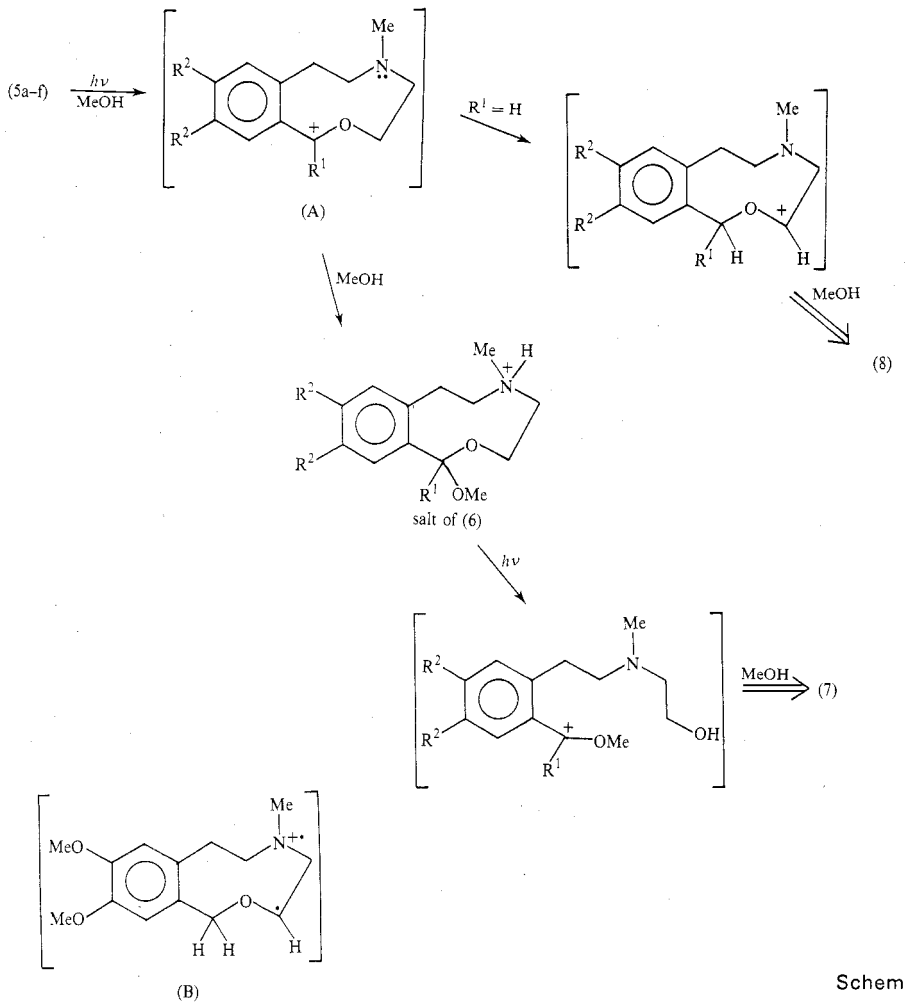
It is particularly significant that benzylic C–O bond fission products were not isolated from the photolyses of (5b–f) in methanol; such a product, the acetal (7), was obtained from the photolysis of (5a) in methanol, but is thought to be a secondary photochemical product. This is in contrast to the strong preference for this mode of cleavage in reported[9,16] reactions of 5*H*-oxazolo[2,3-*a*]isoquinoline bases. It is most probable that the C–O fission products from these reactions arise via iminium salt intermediates formed from reversible ring opening of the oxazolidine moiety of the tertiary amines. This ring opening is blocked by quaternization of the bridgehead amine, and thus photosolvolysis affords a methodology conducive to selective benzylic C–N bond cleavage of the 5*H*-oxazolo[2,3-*a*]isoquinoline system.

From the results summarized in Table 1, the efficacy of this reaction is, however, markedly influenced by the substituents at the C8 and C9, and C10b positions of the 5*H*-oxazolo[2,3-*a*]isoquinolinium salts.

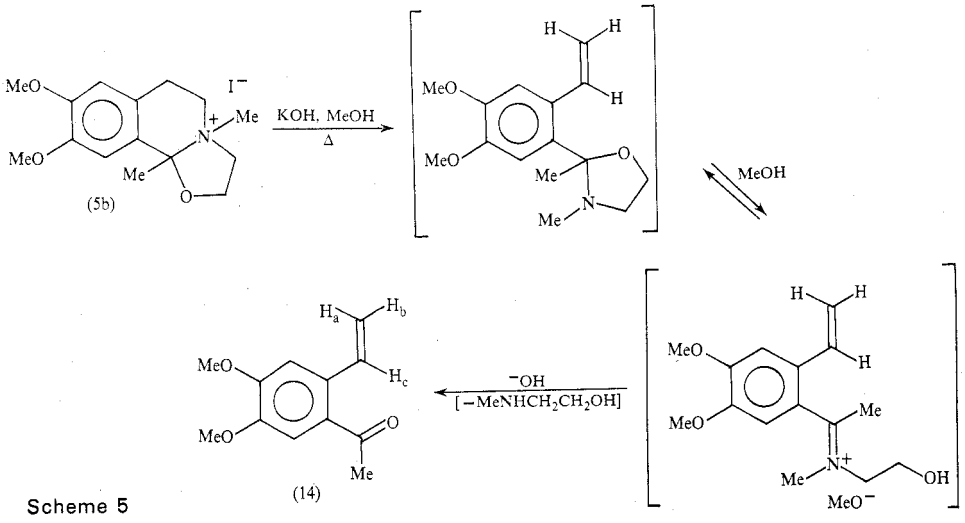
It appears that photosolvolysis is facilitated by methoxyl substitution at the C8 and C9 positions. Briscoe likewise observed[17] that photosolvolysis of simple tetrahydroisoquinolinium salts proceeded most efficiently when methoxyl substituents were present in the aromatic ring chromophore, and a similar effect has been reported by others.[18,19] It was thought that higher yields of (6e) might be obtained by a shorter irradiation time with lower-wavelength light. However, in the event, irradiation through a Vycor filter ($\lambda > 210$ nm) of (5e) in methanol gave no significant increase in yield (Table 1).

In the photolyses of (5a) and (5b), the low yield of (6a), compared with (6b), may be attributed, at least in part, to the competing reactions which afford (7) and

[16] Schneider, W., and Müller, B., *Arch. Pharm.* (*Weinheim, Ger.*), 1962, **295**, 571.
[17] Briscoe, J. R., B.Sc. (Hons) Thesis, University of Tasmania, 1977.
[18] Bremner, J. B., and Winzenberg, K. N., *Aust. J. Chem.*, 1978, **31**, 313.
[19] Jeffs, P. W., Hansen, J. F., and Brine, G. A., *J. Org. Chem.*, 1975, **40**, 2883.



Scheme 4



Scheme 5

(8). The acetal (7) is most probably a secondary product arising from a photoinduced heterolysis of the C 1–O bond of the initially formed 2,5-benzoxazonine salt derivative of (6a), followed by methanolysis at the oxa-stabilized C 1 carbonium ion (Scheme 4). The photoinduced heterolysis of the C–O bond of an acetal has precedent.[20] In support of this view, the ^{1}H n.m.r. spectrum of the crude photolysate obtained from the 3-h irradiation of the methiodide salt of (6a) in methanol was essentially the same as that of the methiodide salt of (7). It is curious that this secondary photochemical reaction was observed only with the C 10b unsubstituted 5*H*-oxazolo[2,3-*a*]-isoquinolinium salt (5a), especially since other salts, particularly (5b), were irradiated for longer periods of time. It is not known why the presence of an alkyl or phenyl substituent at the C 10b position should disfavour the reaction pathway leading to ring-opened acetal products.

The mechanism of formation of (8) is also not clear. It is possible, however, that (8) is derived from an initially formed (cf.[4]) oxa-stabilized carbonium ion intermediate (A) (Scheme 4) through a 1,3-hydride shift followed by methanol attack (Scheme 4). Although not common, carbonium ion rearrangement reactions involving 1,3-hydride shifts[21] have been reported.[22] It is also conceivable that (8) may arise from a diradical intermediate by a 1,3-hydrogen shift[23] to give (B) (see Scheme 4), followed by aziridinium salt formation and subsequent attack by methanol on this salt to give the hydriodide salt of (8).

Separate blank experiments showed that all the starting quaternary ammonium salts were stable in methanol under argon at room temperature in the absence of ultraviolet irradiation. Furthermore, no reactions were observed when methanolic solutions of these salts were refluxed in the absence of such irradiation. In one attempt to induce nucleophilic substitution,[24] the salt (5b) was subjected to prolonged refluxing in methanolic potassium hydroxide solution. However, none of the 2,5-benzoxazonine derivative (6b) was formed. Instead, the ketone (14) was isolated in 51% yield; (14) is possibly formed through Hofmann elimination and hydroxide-induced cleavage of an iminium salt intermediate (Scheme 5).

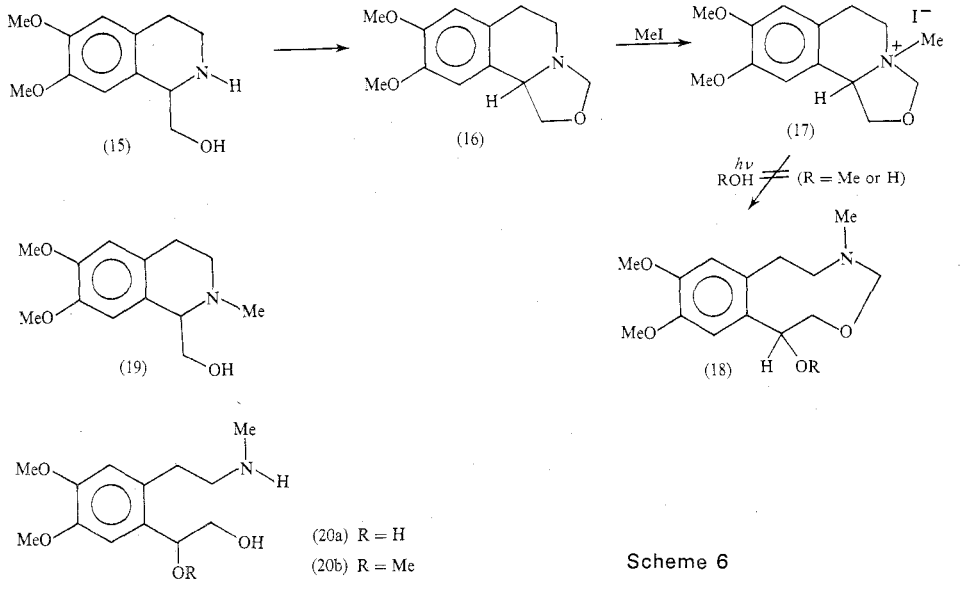
Attempted Synthesis of Some 3,5-Benzoxazonine Derivatives

The potential 3,5-benzoxazonine precursor (17) was obtained from the synthetically accessible[25–27] alkaloid (±)-calycotomine (15) by treatment[27] with paraformaldehyde to give (16), followed by reaction with iodomethane (Scheme 6).

In marked contrast to the successful photosolvolysis of the reduced 5*H*-oxazolo-[2,3-*a*]isoquinolinium salt (5a), the photolysis of the tetrahydro-3*H*-oxazolo[4,3-*a*]-isoquinolinium salt (17) either in methanol or in water, at pH 7 or buffered to pH 9·4, afforded none of the expected 3,5-benzoxazonine derivatives (18; R = H or Me)

[20] Westhuizen, J. H. van der, Ferreira, D., and Roux, D. G., *J. Chem. Soc., Perkin Trans. 1*, 1977, 1517.
[21] Färcasiu, D., and Horsley, J. A., *J. Am. Chem. Soc.*, 1980, **102**, 4906.
[22] Brouwer, D. M., and Hogeveen, H., *Progr. Phys. Org. Chem.*, 1972, **9**, 225.
[23] Freidlina, R. Kh., and Terent'ev, A. B., *Adv. Free Radical Chem.*, 1980, **6**, 2.
[24] Cope, A. C., and Trumbull, E. R., in 'Organic Reactions' (Ed. A. C. Cope) Vol. 11, Ch. 5, pp. 350–2 (John Wiley: New York 1960).
[25] Battersby, A. R., and Edwards, T. P., *J. Chem. Soc.*, 1959, 1909.
[26] Grüssner, A., Jaeger, E., Hellerbach, J., and Schnider, O., *Helv. Chim. Acta*, 1959, **42**, 2431.
[27] Schneider, W., and Schilken, K., *Arch. Pharm. (Weinheim, Ger.)*, 1963, **296**, 389.

(Scheme 6). A complex mixture of products resulted from each of the photolysates after the appropriate workup. Two products were isolated and identified. The photolysis of (17) in water at pH 7 afforded (±)-*N*-methylcalycotomine (19) in 8% yield, while the secondary-amino alcohol (20b) was obtained in 25% yield from the photolysis of (17) in methanol.



Scheme 6

The structure of (20b) was readily ascertained from spectroscopic data. The ^1H n.m.r. spectrum of (20b) exhibited a one-proton downfield multiplet at δ 4·67–4·49 and a three-proton singlet at 3·25 attributed, in turn, to the hydrogen atom and to the methoxy group at C 2. Furthermore, a broad exchangeable two-proton signal at δ 2·95–2·72, partly obscured by resonances from the aminoethyl side chain, was assigned to the secondary-amine and hydroxyl protons. The methylamino group appeared as a three-proton singlet at δ 2·42. The presence of the hydroxy group was confirmed from the infrared spectrum which displayed a broad absorption band centred at 3350 cm^{-1}. The base peak in the mass spectrum of (20b) appeared at *m/e* 44; this was attributed to the *N*-methylenemethanaminium ion, $H_2C{=}N^+(Me)H$, arising from cleavage of the aminoethyl side chain.

The secondary-amino alcohol (20b) was also obtainable from the methanol photosolvolysis of the hydrochloride salt of (±)-*N*-methylcalycotomine. This reaction proceeded slowly, and after 6 h of irradiation a 25% yield of (20b) was obtained together with a considerable amount of unchanged (±)-*N*-methylcalycotomine (39%) on workup. A number of minor products were detected.

It is somewhat surprising that (19), formed from the photolysis of (17) in water at pH 7, and presumably present as the hydriodide salt in solution, did not undergo further photosolvolysis to yield the secondary-amino diol (20a) analogous to the amino alcohol (20b). In subsequent experiments it was shown that the hydrochloride salt of (±)-*N*-methylcalycotomine likewise did not undergo photosolvolysis in water at either pH 7 or pH 1. In both cases, an essentially quantitative recovery of (±)-*N*-methylcalycotomine (19) was obtained on basification. It is possible, however, that

some (20a) may have been formed in these experiments, but underwent rapid recyclization to (19) during, or perhaps before, workup of the photolysate; facile reverse dehydration reactions of this type have been observed previously.[28,29] Although precise details of the mechanisms of formation of (20b) and (19) from (17) are not known, it should be noted that cleavage of the N–C–O linkage is characteristic[27,30] of the chemistry of reduced 3*H*-oxazolo[4,3-*a*]isoquinolines.

Further applications of the photosolvolysis of bridgehead quaternary ammonium salts to the synthesis of medium-sized heterocycles will be described in subsequent papers.

Experimental

General experimental notes with respect to this section are the same as those described in Part I.[4]

All methiodide salts were prepared by reaction of the tertiary bases with excess iodomethane (distilled off anhydrous potassium carbonate) in dry acetone at room temperature, unless otherwise stated.

For photolyses in methanol the usual workup involved concentration in vacuum to a volume of about 10 ml, basification to pH 9 with concentrated aqueous ammonia, dilution to a volume of about 20 ml with distilled water, and extraction with chloroform (3 × 30 ml).

All organic solvent extracts were dried with anhydrous sodium sulfate.

*8,9-Dimethoxy-4-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinolinium Iodide (5a)*

Reaction of 2-(3,4-dimethoxyphenyl)ethanamine with formic acid, by the method of Späth and Epstein,[31] gave, in quantitative yield, *N*-[2-(3,4-dimethoxyphenyl)ethyl]methanamide (1a) which was cyclized by using phosphorus oxychloride, after the method of Buck and Ide,[32] to afford 6,7-dimethoxy-3,4-dihydroisoquinoline (2a) in 90% yield. Reaction of (2a) with 2-bromoethanol, after the method of Schneider and Kämmerer,[9] afforded in 85% yield 2-(2-hydroxyethyl)-6,7-dimethoxy-3,4-dihydroisoquinolinium bromide (3a), m.p. 192–193° (lit.[9] 171°). Treatment of (3a) with 20% aqueous potassium hydroxide gave, in 87% yield, the 5*H*-oxazolo[2,3-*a*]isoquinoline derivative (4a), m.p. 89–91° (lit.[9] 97°).

To a solution of (4a) (2·50 g, 10·6 mmol) in dry acetone (20 ml) was added iodomethane (3 ml). The precipitate which formed, after this solution had been allowed to stand at room temperature for 2·5 h, was collected and recrystallized from methanol to afford yellow granules of the *methiodide salt* (5a) (3·50 g, 88%). On slow heating, (5a) melted at 173–176° then solidified to remelt at 208–210° (Found: C, 44·3; H, 5·3; N, 3·7. $C_{14}H_{20}INO_3$ requires C, 44·6; H, 5·4; N, 3·7%). ^{1}H n.m.r. δ ($CDCl_3$): 6·92, s, ArH; 6·80, s, ArH; 6·08, s, H10b; 4·95–2·90, m, 4 × CH_2; 3·94, 3·90, 2s, 2 × OCH_3; 3·64, s, NCH_3. λ_{max} (log ε) 221sh (4·33), 282 (3·60), 287sh (3·54); λ_{min} 257 nm (3·26).

*Photolysis of the 5*H*-Oxazolo[2,3-*a*]isoquinolinium Salt (5a) in Methanol*

A solution of (5a) (322 mg, 0·854 mmol) in methanol (200 ml) was irradiated for 1 h. P.l.c. (chloroform/6% methanol) of the photolysate, obtained from the usual workup, afforded the following fractions.

Fraction 1 (R_F 0·60) gave *3,9,10-trimethoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine* (8) (20 mg, 8%) as an oil. Mass spectrum: *m/e* 281 ($M^{+\cdot}$, accurate mass 281·1625; $C_{15}H_{23}NO_4$ requires 281·1627). ^{1}H n.m.r. δ ($CDCl_3$): 6·87, s, ArH; 6·65, s, ArH; 4·26, t, *J* 5 Hz, H3; 3·89, s, 2 × OCH_3; 3·86, s, (H1)$_2$; 3·38, s, 3-OCH_3; 3·10–2·43, m, 3 × CH_2; 2·38, s, NCH_3.

[28] Hootelé, C., *Tetrahedron Lett.*, 1969, 2713.
[29] Bremner, J. B., Browne, E. J., and Davies, P. E., *Aust. J. Chem.*, 1980, **33**, 1335.
[30] Schneider, W., and Schilken, K., *Arch. Pharm. (Weinheim, Ger.)*, 1966, **299**, 997.
[31] Späth, E., and Epstein, H., *Ber. Dtsch. Chem. Ges.*, 1926, **59**, 2791.
[32] Buck, J. S., and Ide, W. S., *J. Am. Chem. Soc.*, 1938, **60**, 2101.

Fraction 2 (R_F 0·55) gave *1,9,10-trimethoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxaxonine* (6a) (131 mg, 55%) as an oil. Mass spectrum: *m/e* 281 ($M^{+\cdot}$, accurate mass 281·1611; $C_{15}H_{23}NO_4$ requires 281·1627), 266, 250. ^{1}H n.m.r. (270 MHz) δ ($CDCl_3$): 7·11, s, H11; 6·64, s, H8; 5·62, s, H1; 3·87, s, 2×OCH_3; 3·68–3·56, m, $(H3)_2$; 3·54, s, 1-OCH_3; 3·20–3·10, m, 1H, H7; 2·90–2·73, m, 3H, H7 and $(H6)_2$; 2·57–2·34, m, $(H4)_2$; 2·29, s, NCH_3. ^{13}C n.m.r. δ ($CDCl_3$):* 148·9[A], C9; 147·0[A], C10; 132·6[B], C7a; 129·8[B], C11a; 112·9, C8; 110·4, C11; 102·3, C1; 64·4, C3; 59·7, C6; 57·6, C4; 55·9, 55·9, C9, 10-OCH_3; 55·3, 1-OCH_3; 47·2, NCH_3; 32·9, C7.

The *methiodide salt of* (*6a*) was obtained as colourless plates after recrystallization from methanol/diethyl ether, m.p. 223–224° (Found: C, 45·2; H, 6·0; N, 3·0. $C_{16}H_{26}INO_4$ requires C, 45·4; H, 6·2; N, 3·3%). ^{1}H n.m.r. δ ($CDCl_3/CD_3OD$): 7·15, s, H11; 6·87, s, H8; 5·86, s, H1; 4·44–2·90, m, 4×CH_2; 3·93, s, OCH_3; 3·90, s, OCH_3; 3·14, s, 1-OCH_3; 3·45, s, NCH_3; 3·29, s, NCH_3. λ_{max} (log ε) 233 (4·09), 282 (3·59), 286sh (3·57); λ_{min} 220 (3·85), 256 nm (2·95).

Fraction 3 (R_F 0·30) afforded the acetal *2-[N-2-{2-(dimethoxymethyl)-4,5-dimethoxyphenyl}-ethyl-N-methylamino]ethanol* (7) (31 mg, 12%) as an oil. Mass spectrum: *m/e* 313 (M), 88 [$H_2C{=}N^+(CH_3)CH_2CH_2OH$]. ^{1}H n.m.r. δ ($CDCl_3$): 7·12, s, H3; 6·70, s, H6; 5·46, s, $CH(OCH_3)_2$; 3·91, s, 2×OCH_3; 3·63, t, *J* 5 Hz, CH_2OH; 3·36, s, 6H, $CH(OCH_3)_2$; 3·15, br s, exchanged with D_2O, OH; 3·00–2·50, m, 3×CH_2; 2·39, s, NCH_3. ν_{max} (thin film): 3380m cm^{-1} (OH).

The *methiodide salt of* (*7*) was recrystallized from methanol/diethyl ether as colourless needles, m.p. 116–117° (Found: C, 44·9; H, 6·6; N, 3·1. $C_{17}H_{30}INO_5$ requires C, 44·8; H, 6·7; N, 3·1%).

Photolysis of the Methiodide Salt of the 2,5-Benzoxazonine (*6a*) *in Methanol*

A solution of the methiodide salt of (6a) (200 mg, 0·472 mmol) in methanol (200 ml) was irradiated for 3 h. The ^{1}H n.m.r. spectrum of the photolysate residue, obtained by the careful evaporation of the methanol, was essentially the same as that of the methiodide salt of the acetal (7).

Hydrolysis of the 2,5-Benzoxazonine (*6a*) *and of the Acetal* (*7*) *with Dilute Hydrochloric Acid*

The 2,5-benzoxazonine (6a) (75 mg, 0·267 mmol) was added to distilled water (10 ml) acidified by the addition of concentrated hydrochloric acid (1 ml). The solution was stirred at room temperature for 0·5 h, then basified to pH 9 with concentrated aqueous ammonia and extracted with chloroform (3×30 ml). P.l.c. (chloroform/10% methanol) of the residue from the dried chloroform extracts gave (R_F 0·50) the aldehyde (10a), *2-[2-{N-(2-hydroxyethyl)-N-methylamino}ethyl]-4,5-dimethoxybenzaldehyde* (65 mg, 91%), as an oil. Mass spectrum: *m/e* 267 (M), 88 [$H_2C{=}N^+(CH_3)$-CH_2CH_2OH]. ^{1}H n.m.r. δ ($CDCl_3$): 10·14, s, CHO; 7·34, s, H6; 6·74, s, H3; 3·98, s, OCH_3; 3·92, s, OCH_3; 3·60, t, *J* 5 Hz, CH_2OH; 3·30–3·05, m, $ArCH_2$; 3·0, br s, exchanged with D_2O, OH; 2·85–2·50, m, 2×CH_2; 2·38, s, NCH_3. ν_{max} (thin film): 3400s(br) (OH), 1675s and 1690s cm^{-1} (C=O).

The *methiodide salt of* (*10a*) crystallized from methanol as colourless needles, m.p. 150° (Found: C, 43·9; H, 5·6. $C_{15}H_{24}INO_4$ requires C, 44·0; H, 5·9%). λ_{max} (log ε) 232 (4·53), 281 (4·00), 308 (3·83); λ_{min} 251 (3·19), 297 nm (3·79).

The acetal (7) (91 mg, 0·290 mmol) was hydrolysed likewise to afford the amino hydroxy aldehyde (10a) (60 mg, 77%).

Reduction of the Aldehyde (*10a*) *with Sodium Tetrahydroborate*

To a stirred solution of the aldehyde (10a) (145 mg, 0·542 mmol) in methanol (10 ml) at room temperature was added sodium tetrahydroborate (200 mg). Stirring was continued for 3 h. The mixture was evaporated to dryness. Water (30 ml) was added and the emulsion extracted with chloroform (3×30 ml). The dried chloroform extracts were evaporated to afford the amino diol (12)[14] (135 mg, 93%) as a colourless oil. Mass spectrum: *m/e* 269 ($M^{+\cdot}$, accurate mass 269·1618;

* Each assigned resonance showed the expected multiplicities in the proton-coupled ^{13}C n.m.r. spectrum. Assignments of resonances indicated with the same superscript capital letter may be interchanged.

$C_{14}H_{23}NO_4$ requires 269·1627), 88 [$H_2C{=}N^+(CH_3)CH_2CH_2OH$]. ^{1}H n.m.r. δ ($CDCl_3$): 6·86, 6·71, 2s, 2×1H, 2ArH; 5·00–4·30, br s, 2H, exchanged with D_2O, 2×OH; 4·52, s, $ArCH_2OH$; 3·91, s, 2×OCH_3; 3·49, t, J 5 Hz, CH_2CH_2OH; 2·87–2·47, m, 3×CH_2; 2·27, s, NCH_3. ν_{max} (thin film): 3360s cm^{-1} (OH). Dragar[14] obtained (12), on freezing, as an amorphous solid, m.p. 66–69°.

Attempted Acid-Catalysed Dehydration of the Amino Diol (12)

To a solution of (12) (350 mg, 1·299 mmol) in refluxing xylene (40 ml) was added *p*-toluenesulfonic acid (400 mg). The mixture was refluxed for 1 h. After being allowed to cool, the mixture was extracted with 5% hydrochloric acid (3×30 ml). The aqueous extracts were basified with concentrated aqueous ammonia, and extracted with diethyl ether (3×30 ml). The residue from the dried diethyl ether extracts was subjected to p.l.c. (chloroform/6% methanol) to afford 6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (13) (156 mg, 58%) as a colourless solid. Recrystallization from light petroleum (b.p. 40–60°) afforded (13) as rosettes of colourless needles, m.p. 83° (lit.[33] 83–84°). ^{1}H n.m.r. δ ($CDCl_3$): 6·57, 6·48, 2s, 2×1H, H5 and H8; 2·81, s, 2×OCH_3; 3·47, s, (H1)$_2$; 2·90–2·50, m, (H3)$_2$ and (H4)$_2$; 2·41, s, NCH_3.

8,9-Dimethoxy-4,10b-dimethyl-2,3,6,10b-tetrahydro-5H-oxazolo[2,3-a]isoquinolinium Iodide (5b)

Reaction of (2b)[34,35] with 2-bromoethanol, after the method of Schneider and Kämmerer,[9] afforded in 70% yield 2-(2-hydroxyethyl)-6,7-dimethoxy-1-methyl-3,4-dihydroisoquinolinium bromide (3b), m.p. 177–178° (lit.[9] 178°). Treatment of (3b) with 20% aqueous potassium hydroxide gave,[9] in 95% yield, the 5*H*-oxazolo[2,3-*a*]isoquinoline derivative (4b) as an oil. Mass spectrum: *m/e* 249 ($M^{+\cdot}$, accurate mass 249·1357; $C_{14}H_{19}NO_3$ requires 249·1365), 234. ^{1}H n.m.r. δ ($CDCl_3$): 6·98, 6·96, 2s, 1H, H10; 6·58, s, H7; 3·89, s, OCH_3; 3·85, s, OCH_3; 4·00–3·30, m, (H2)$_2$; 3·25–2·50, m, 6H, 3×CH_2; 1·58, s, exchanged with D_2O, 3H, 10b-CH_3.

Reaction of (4b) with iodomethane gave the methiodide salt (5b), in 84% yield, m.p. 212–213° (lit.[9] 210–214°) (Found: C, 45·6; H, 5·7; N, 3·5. Calc. for $C_{15}H_{22}INO_3$: C, 46·0; H, 5·7; N, 3·6%). ^{1}H n.m.r. δ ($CDCl_3$/CD_3OD): 6·82, 6·72, 2s, 2×ArH; 4·5–3·1, m, 4×CH_2; 3·90, s, 2×OCH_3; 3·44, s, NCH_3; 2·0, s, 3H, 10b-CH_3. λ_{max} (log ε) 219 (4·30), 281 (3·51), 286sh (3·47); λ_{min} 217 (4·29), 254 nm (2·77).

Photolysis of the 5H-Oxazolo[2,3-a]isoquinolinium Salt (5b) in Methanol

A solution of (5b) (1·500 g, 3·836 mmol) in methanol (200 ml) was irradiated for 7 h. The solution was evaporated to dryness and concentrated aqueous ammonia (5 ml) was added followed by distilled water (10 ml). The mixture was extracted with diethyl ether (4×50 ml) and then with chloroform (4×50 ml). The dried ether extracts were evaporated to yield *1,9,10-trimethoxy-1,5-dimethyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine* (6b) (1·006 g, 89%) as an oil which crystallized on standing at 0°. Recrystallization from light petroleum (b.p. 60–80°) afforded colourless needles of (6b) (0·894 g, 79%), m.p. 80–81° (Found: C, 65·1; H, 8·3; N, 4·7. $C_{16}H_{25}NO_4$ requires C, 65·1; H, 8·6; N, 4·7%). Mass spectrum: *m/e* 295 ($M^{+\cdot}$, accurate mass 295·1790; $C_{16}H_{25}NO_4$ requires 295·1783), 280, 264. ^{1}H n.m.r. δ ($CDCl_3$): 7·18, s, H11; 6·66, s, H8; 3·87, s, 2×OCH_3; 3·8–3·4, m, 4H; 3·37, s, 1-OCH_3; 3·0–2·3, m, 4H; 2·23, s, NCH_3; 1·53, s, 1-CH_3. ^{13}C n.m.r. δ ($CDCl_3$): 148·4^A, C9; 146·7^A, C10; 134·8^B, C7a; 130·9^B, C11a; 112·9, C8; 111·0, C11; 102·0, C1; 63·4, C3; 60·3, C6; 57·6, C4; 55·8, 55·7, C9, 10-OCH_3; 48·0, 1-OCH_3; 47·9, NCH_3; 31·9, C7; 26·0, 1-CH_3. λ_{max} (log ε) 233 (3·98), 280 (3·49), 285sh (3·45); λ_{min} 221 (3·91), 256 nm (3·02).

The *methiodide salt of* (6b) was recrystallized from methanol to give colourless needles, m.p. 207–208° (Found: C, 46·8; H, 6·7. $C_{17}H_{28}INO_4$ requires C, 46·7; H, 6·5%). ^{1}H n.m.r. δ ($CDCl_3$): 7·20, s, H11; 6·89, s, H8; 4·3–2·7, m, 4×CH_2; 4·00, 3·92, 2s, 2×OCH_3; 3·70 and 3·27, 2s, $N(CH_3)_2$; 3·40, s, 1-OCH_3; 1·58, 1-CH_3.

The dried chloroform extracts from the initial photolysate were evaporated to give unchanged (5b) (110 mg, 7%).

[33] Pyman, F. L., *J. Chem. Soc.*, 1909, 1266.
[34] Whaley, W. M., and Govindachari, T. R., in 'Organic Reactions' (Ed. R. Adams) Vol. 6, p. 108 (John Wiley: New York 1951).
[35] Späth, E., *Ber. Dtsch. Chem. Ges.*, 1929, **62**, 1021.

Hydrolysis of the 2,5-Benzoxazonine (6b) with Dilute Hydrochloric Acid

The 2,5-benzoxazonine (6b) (133 mg, 0·450 mmol) was hydrolysed, in the same manner as for (6a), to afford (R_F 0·45) the ketone (10b), *1-[2-(2-{N-(2-hydroxyethyl)-N-methylamino}ethyl)-4,5-dimethoxyphenyl]ethanone* (101 mg, 80%), as an oil. Mass spectrum *m/e* 281 (M), 88 [$H_2C{=}N^+(CH_3)$-CH_2CH_2OH]. ^{1}H n.m.r. δ ($CDCl_3$): 7·26, s, H6; 6·76, s, H3; 3·95, 3·93, 2s, 2×OCH_3; 3·62, t, *J* 5 Hz, CH_2OH; 3·51, s, exchanged with D_2O, OH; 3·23–2·95, m, $ArCH_2$; 2·80–2·60, m, 2×CH_2; 2·58, s, $COCH_3$; 2·39, s, NCH_3. ν_{max} (thin film): 3400s(br) (OH), 1680s cm^{-1} (C=O).

The *methiodide salt of (10b)* was obtained as colourless granules (from methanol/diethyl ether), m.p. 154–156° after softening at 135–145° (Found: C, 45·4; H, 6·2. $C_{16}H_{26}INO_4$ requires C, 45·4; H, 6·2%).

Photolysis of the 5H-Oxazolo[2,3-a]isoquinolinium Salt (5b) in Propan-1-ol

A solution of (5b) (400 mg, 1·022 mmol) in propan-1-ol (200 ml) was irradiated for 1·25 h. P.l.c. (chloroform/5% methanol) of the photolysate residue, obtained from the usual workup, afforded (R_F 0·55) *9,10-dimethoxy-1,5-dimethyl-1-propoxy-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine* (9) (220 mg, 67%) as an oil which crystallized on prolonged standing at 0°. Recrystallization from light petroleum (b.p. 40–60°) gave (9) as colourless plates, m.p. 66–67° (Found: C, 67·0; H, 9·1; N, 4·1. $C_{18}H_{29}NO_4$ requires C, 66·8; H, 9·1; N, 4·3%). Mass spectrum: *m/e* 323 ($M^{+\cdot}$, accurate mass 323·2096; $C_{18}H_{29}NO_4$ requires 323·2096), 264. ^{1}H n.m.r. δ ($CDCl_3$): 7·28, s, H11; 6·66, s, H8; 4·02–3·30, m, 2×CH_2; 3·86, s, 2×OCH_3; 3·00–2·00, m, 3×CH_2; 2·22, s, NCH_3; 1·83–1·35, m, CH_2; 1·53, s, 1-CH_3; 1·01, t, *J* 7 Hz, CH_2CH_3). λ_{max} (log ε) 233 (3·98), 280 (3·49), 285sh (3·45); λ_{min} 221 (3·91), 256 nm (3·02).

Photolysis of the 5H-Oxazolo[2,3-a]isoquinolinium Salt (5b) in Water

A solution of (5b) (400 mg, 1·023 mmol) in distilled water (200 ml) was irradiated for 1 h. The solution was basified to pH 9 with concentrated aqueous ammonia, and extracted with chloroform (4×50 ml). P.l.c. (chloroform/10% methanol) of the residue from the dried chloroform extracts gave the ketone (10b) (150 mg, 52%). The aqueous solution was evaporated to dryness. Concentrated aqueous ammonia (*c.* 1 ml) was added and the solution extracted with chloroform (3×10 ml). The dried chloroform extracts were evaporated to afford unchanged (5b) (157 mg, 39%).

8,9-Dimethoxy-10b-phenyl-2,3,6,10b-tetrahydro-5H-oxazolo[2,3-a]isoquinoline (4c)

To a solution of the imine (2c)[36] (2·04 g, 7·63 mmol) in dry toluene (50 ml) was added 2-bromoethanol (2·62 g). The solution was kept at 90° under nitrogen for 32 h, and allowed to cool. The precipitate which had formed was collected and recrystallized from methanol/ethyl acetate to afford fine yellow needles of *2-(2-hydroxyethyl)-6,7-dimethoxy-1-phenyl-3,4-dihydroisoquinolinium bromide* (3c) (2·20 g, 73%), m.p. 185–186° (Found: C, 58·2; H, 5·7. $C_{19}H_{22}BrNO_3$ requires C, 58·2; H, 5·7%). ^{1}H n.m.r. δ ($CDCl_3$): 7·80–7·50, m, 5×ArH; 7·02, 6·30, 2s, 2×ArH; 5·35–5·15, br s, exchanged with D_2O, OH; 4·67–4·42, m, CH_2; 4·17–3·80, m, 2×CH_2; 4·02, s, OCH_3; 3·65–3·40, m, CH_2; 3·55, s, OCH_3. ν_{max} (Nujol): 3240m (OH), 1620m cm^{-1} (C=N).

To a solution of the salt (3c) (1·15 g, 2·93 mmol) in water was added 20% aqueous potassium hydroxide solution (20 ml). This solution was extracted with diethyl ether (3×30 ml). The dried ether extracts were evaporated to afford the *title compound (4c)* (0·861 g, 94%) as a gum, which crystallized as colourless granules from diethyl ether/light petroleum (b.p. 40–60°), m.p. 76–77° (Found: C, 73·2; H, 6·7; N, 4·2. $C_{19}H_{21}NO_3$ requires C, 73·3; H, 6·8; N, 4·5%). ^{1}H n.m.r. δ ($CDCl_3$): 7·6–7·0, m, 5×ArH; 6·44, s, H7 and H10; 4·05–3·50, m, $(H2)_2$; 3·65, 3·53, 2s, 2×OCH_3; 3·2–2·4, m, 3×CH_2. Mass spectrum: *m/e* 311 (M), 296, 234 (base peak).

8,9-Dimethoxy-4-methyl-10b-phenyl-2,3,6,10b-tetrahydro-5H-oxazolo[2,3-a]isoquinolinium Iodide (5c)

The *methiodide salt* (5c) of (4c) was obtained as a yellow glass which could not be induced to crystallize (Found: C, 52·0; H, 5·4. $C_{20}H_{24}INO_3.0{\cdot}5H_2O$ requires C, 51·9, H, 5·4%). ^{1}H n.m.r. δ ($CDCl_3$): 7·80–7·30, m, 5×ArH; 6·83, 6·46, 2s, H7 and H10; 4·90–2·90, m, 4×CH_2; 3·95, 3·70, 2s, 2×OCH_3; 3·02, s, NCH_3.

[36] Harwood, H. J., and Johnson, T. B., *J. Am. Chem. Soc.*, 1934, **56**, 468.

Photolysis of the 5H-Oxazolo[2,3-a]isoquinolinium Salt (5c) in Methanol

A solution of (5c) (400 mg, 0·882 mmol) in methanol (200 ml) was irradiated for 0·5 h. P.l.c. (chloroform/5% methanol) of the photolysate residue, obtained from the usual workup, afforded (R_F 0·60) *1,9,10-trimethoxy-5-methyl-1-phenyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine* (6c) (154 mg, 49%), m.p. 143–145° (colourless plates from diethyl ether) (Found: C, 70·9; H, 7·5. $C_{21}H_{27}NO_4$ requires C, 70·6; H, 7·6%). ^{1}H n.m.r. δ (CCl_4): 7·42, s, H 11; 7·5–7·0, m, 5 × ArH; 6·42, s, H 8; 3·88, 3·73, 2s, 2 × OCH_3; 3·80–1·80, m, 4 × CH_2; 2·95, s, 1-OCH_3; 2·15, s, NCH_3. Mass spectrum: *m/e* 357 (M), 342, 326.

A number of other fractions were also obtained: R_F 0·65 (10 mg), R_F 0·80 (22 mg) and R_F 1·00 (34 mg); ^{1}H n.m.r. analysis indicated that these fractions were mixtures, and they were not investigated further.

Some unchanged (5c) (R_F 0·15; 58 mg, 15%) was also recovered.

10b-(3,4-Dimethoxybenzyl)-8,9-dimethoxy-2,3,6,10b-tetrahydro-5H-oxazolo[2,3-a]isoquinoline (4d)

The amide (1d), prepared in quantitative yield by the method of Späth and Burger,[37] was treated with phosphorus oxychloride after the method of Onda[38] to afford, in 70% yield, the hydrochloride salt of 1-(3,4-dimethoxybenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (2d), m.p. 180–182° (lit.[38] 180–182°).

A solution of the hydrochloride salt of (2d) (2·05 g, 5·42 mmol) in water (30 ml) was basified to pH 9 with concentrated aqueous ammonia, and extracted with chloroform (3 × 30 ml). To the residue from the dried chloroform extracts was added dry toluene (30 ml) followed by 2-bromoethanol (1·64 g, 13·1 mmol). The solution was heated under nitrogen for 18 h at 80°, and then the solvents were evaporated. Water (30 ml) was added; the solution was washed with diethyl ether (2 × 30 ml), basified with 50% aqueous potassium hydroxide (20 ml), and extracted with diethyl ether (3 × 30 ml). These latter ether extracts were dried and evaporated to give impure (4d) as a pale yellow solid (1·34 g); t.l.c. analysis of this material indicated the presence of unchanged (2d). Fractional recrystallization (three times) from methanol/diethyl ether afforded the *5H-oxazolo[2,3-a]isoquinoline (4d)* (791 mg, 39%) as colourless prisms, m.p. 105–106° (Found: C, 68·3; H, 7·2. $C_{22}H_{27}NO_5$ requires C, 68·5; H, 7·1%). ^{1}H n.m.r. δ ($CDCl_3$): 6·92, s, 1 × ArH; 6·75–6·35, m, 4 × ArH; 4·10–2·00, m, 4 × CH_2; 3·84, 3·83, 3·81, 3·66, 4s, 4 × OCH_3; 3·01, s, 10b-CH_2. Mass spectrum: *m/e* 385 (M), 234 (base peak).

10b-(3,4-Dimethoxybenzyl)-8,9-dimethoxy-4-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[2,3-a]-isoquinolinium Iodide (5d)

The *methiodide salt (5d)* of (4d) was obtained as rosettes of small colourless prisms (from methanol), m.p. 181–182° [Found (after drying at 120° for 2 days): C, 52·1; H, 5·5; I, 24·1. $C_{23}H_{30}INO_5$ requires C, 52·4; H, 5·7; I, 24·1%]. ^{1}H n.m.r. δ [$(CD_3)_2SO$]: 7·26, d, *J* 9 Hz, ArH; 7·24, s, ArH; 6·96, d, *J* 9 Hz, ArH; 6·76, s, ArH; 6·38, s, ArH; 4·90–3·30, complex m, 25H, singlets present at 4·14, 4·10, 3·91, 3·78 and 3·68. λ_{max} (log ε) 227sh (4·35), 280 (3·72), 285sh (3·69); λ_{min} 256 nm (2·99).

Photolysis of the 5H-Oxazolo[2,3-a]isoquinolinium Salt (5d) in Methanol

A solution of (5d) (400 mg, 0·758 mmol) in methanol (200 ml) was irradiated for 20 min. P.l.c. (chloroform/5% methanol) of the residue obtained from the usual workup gave (R_F 0·65) *1-(3,4-dimethoxybenzyl)-1,9,10-trimethoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine (6d)* (237 mg, 72%) as a colourless solid. Recrystallization from diethyl ether gave (6d) as colourless prisms, m.p. 126–127° (Found: C, 66·9; H, 7·5; N, 3·2. $C_{24}H_{33}NO_6$ requires C, 66·8; H, 7·7; N, 3·3%). ^{1}H n.m.r. δ ($CDCl_3$):* 6·71, 6·67, 2s, H 8 and H 11; 6·58, sharp d, *J* 8 Hz, H 5′; 6·37, br d, *J* 8 Hz, H 6′; 6·96, br s, H 2′; 3·84, 3·78, 3·58, 3·55, 3·49, 5s, 5 × OCH_3; 3·90–2·10, m, 5 × CH_2; 2·23, s, NCH_3. Mass spectrum: *m/e* 431 (M), 416, 400.

* Primes denote protons on benzyl ring.

[37] Späth, E., and Burger, A., *Ber. Dtsch. Chem. Ges.*, 1927, **60**, 704.

[38] Onda, M., *Yakugaku Zasshi*, 1954, **74**, 915 (*Chem. Abstr.*, 1955, **49**, 10960f).

*10b-Methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinoline (4e)*

The amide (1e), m.p. 35–40° (lit.[39] 42–44°), prepared in 90% yield by the method of Bischler and Napieralski,[39] was treated with phosphorus pentoxide and phosphorus oxychloride after the method of Whaley and Hartung[40] to afford 1-methyl-3,4-dihydroisoquinoline (2e) in 70% yield.

A solution of (2e) (7·55 g, 0·052 mol) and 2-bromoethanol (10·65 g, 0·098 mol) in dry toluene (50 ml) was heated to 80° for 3 h. The crystalline material which had formed was collected and recrystallized twice from methanol/ethyl acetate to give *2-(2-hydroxyethyl)-1-methyl-3,4-dihydroisoquinolinium bromide* (3e) (7·40 g, 53%) as colourless prisms, m.p. 134–136° (Found: C, 53·6; H, 6·0. $C_{12}H_{16}BrNO$ requires C, 53·3; H, 6·0%). ^{1}H n.m.r. δ ($CDCl_3$): 8·05–7·85, m, ArH; 7·80–7·30, m, 3×ArH; 4·50–4·00, m, 3×CH_2; 4·00–3·50, br s, exchanged with D_2O, OH; 3·45–3·20, m, ArCH_2; 3·03, s, 1-CH_3. ν_{max} (Nujol): 3420m, 3370m and 3250s (OH), 1620s cm^{-1} (C=N$^+$).

A solution of (3e) (3·04 g, 0·011 mol) in water (25 ml) was basified with 50% potassium hydroxide (20 ml), and extracted with diethyl ether (3×30 ml). The dried (potassium carbonate) diethyl ether extracts were evaporated to afford the *title compound* (4e) (2·06 g, 100%) as a pale yellow oil. Mass spectrum: *m/e* 189 (M), 174 (base peak). ^{1}H n.m.r. δ ($CHCl_3$): 7·60–7·40, m, ArH; 7·35–6·95, m, 3×ArH; 3·95–3·75, m, $(H2)_2$; 3·65–3·30, m, 1H; 3·15–2·60, m, 5H; 1·55, s, 3H, exchanged with D_2O, 10b-CH_3.

*4,10b-Dimethyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinolinium Iodide (5e)*

The *methiodide salt* (5e) of (4e) was obtained as colourless plates on recrystallization from methanol/diethyl ether, m.p. 185–186° (Found: C, 47·4; H, 5·5. $C_{13}H_{18}INO$ requires C, 47·1; H, 5·5%). ^{1}H n.m.r. δ ($CDCl_3$): 7·50–7·10, m, 4×ArH; 4·80–4·20, m, 2×CH_2; 4·00–3·70, m, CH_2; 3·58, s, NCH_3; 3·55–3·25, m, $(H6)_2$; 2·04, s, 10b-CH_3. λ_{max} (log ε) 214 (4·23), 263 (2·50), 271 (2·45); λ_{min} 253 (2·36), 268 nm (2·26).

*Photolysis of the 5*H*-Oxazolo[2,3-*a*]isoquinolinium Salt (5e) in Methanol*

A solution of (5e) (250 mg, 0·755 mmol) in methanol (100 ml) was irradiated for 2 h through a Corex filter. The solution was evaporated to dryness and water (20 ml), basified to pH 9 with concentrated aqueous ammonia, was added. The mixture was extracted with diethyl ether (3×30 ml), and then with chloroform/10% methanol (3×30 ml). The residue (85 mg) from the dried ether extracts was subjected to p.l.c. (chloroform/3% methanol) to give (R_F 0·55) *1-methoxy-1,5-dimethyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine* (6e) (50 mg, 28%) as a colourless oil. Mass spectrum: *m/e* 235 (M), 220, 204. ^{1}H n.m.r. δ ($CDCl_3$): 7·75–7·60, m, ArH; 7·33–7·05, m, 3×ArH; 4·00–2·25, m, 4×CH_2; 3·40, s, OCH_3; 2·22, s, NCH_3; 1·56, s, 1-CH_3.

After crystallization from methanol/diethyl ether, the *methiodide salt of* (6e) was obtained as fine colourless needles, m.p. 210–211° (Found: C, 47·8; H, 6·4; I, 33·8. $C_{15}H_{24}INO_2$ requires C, 47·8; H, 6·4; I, 33·6%). ^{1}H n.m.r. δ ($CDCl_3$): 7·75–7·57, m, ArH; 7·50–7·10, m, 3×ArH; 4·50–2·70, m, 4×CH_2; 3·72, s, NCH_3; 3·38, s, OCH_3; 3·31, s, NCH_3; 1·57, s, 1-CH_3.

At least 10 other products could be detected from p.l.c. but, due to the small quantity of material involved, these were not further investigated.

Unchanged (5e) (87 mg, 35%) was recovered from the dried chloroform/methanol extracts.

In another experiment, (5e) (400 mg, 1·208 mmol) in methanol (100 ml) was irradiated through a Vycor filter for 1·25 h. After the usual workup, p.l.c., as described above, gave the 2,5-benzoxazonine (6e) (90 mg, 32%) together with unchanged (5e) (R_F 0·15) (66 mg, 17%). Many minor products were present.

*10b-(3,4-Dimethoxyphenyl)-4-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[2,3-*a*]isoquinolinium Iodide (5f)*

To a stirred solution of 3,4-dimethoxybenzoyl chloride (20 g, 0·100 mol), prepared after the method of Meyer,[41] in dry toluene (50 ml) was added dropwise a solution of 2-phenylethanamine (12·1 g, 0·100 mol) and pyridine (8 ml) in toluene (50 ml). After stirring for 1 h, chloroform (100 ml) was added and the solution washed in turn with 5% hydrochloric acid (100 ml), 5% sodium

[39] Bischler, A., and Napieralski, B., *Ber. Dtsch. Chem. Ges.*, 1893, **26**, 1903.
[40] Whaley, W. M., and Hartung, W. H., *J. Org. Chem.*, 1949, **14**, 650.
[41] Meyer, H., 'Beilsteins Handbuch der Organischen Chemie' Vol. 10, p. 397 (Springer: Berlin 1927).

carbonate (100 ml), and water (100 ml). Recrystallization from benzene of the residue obtained from the evaporation of solvents from the dried organic extract afforded 3,4-dimethoxy-*N*-(2-phenylethyl)benzamide (1f) (21·3 g, 76%), m.p. 120–121° (lit.[42] 120–121°).

To a solution of (1f) (14·0 g, 0·050 mol) in dry xylene (150 ml) was added phosphorus oxychloride (18 ml). The solution was refluxed for 1 h, phosphorus pentoxide (30 g) added, and the refluxing continued for a further 2 h. After cooling, ice (300 g) was added. The aqueous layer was removed, washed with diethyl ether (200 ml), basified with concentrated potassium hydroxide solution, and extracted with diethyl ether (3 × 200 ml). The residue from the dried diethyl ether extracts was crystallized from acetone/diethyl ether to afford colourless, hexagonal plates of 1-(3,4-dimethoxy)phenyl-3,4-dihydroisoquinoline (2f) (9·0 g, 67%), m.p. 110–111° (lit.[42] 87°). (Found: C, 76·6; H, 6·4; N, 4·8. Calc. for $C_{17}H_{17}NO_2$: C, 76·4; H, 6·4; N, 5·2%). ^{1}H n.m.r. δ ($CDCl_3$): 7·50–6·80, m, 7 × ArH; 3·95, s, 2 × OCH_3; 3·90–3·60, m, $(H3)_2$; 2·90–2·65, m, $(H4)_2$. Mass spectrum: *m/e* 267 (M). ν_{max} ($CHCl_3$): 1610s cm^{-1} (C=N).

A solution of (2f) (3·10 g, 11·6 mmol) in 2-bromoethanol (6·67 g, 53·4 mmol) was heated under nitrogen for 5 h at 75°, and then worked up, in the same manner as described for the synthesis of (4d), to give impure (4f) as a viscous oil (3·57 g); t.l.c. indicated the presence of unchanged (2f). Fractional crystallization from methanol/diethyl ether afforded the *5H-oxazolo[2,3-a]isoquinoline* (*4f*) (2·36 g, 65%) as colourless prisms, m.p. 143–144° (Found: C, 73·3; H, 6·8; N, 4·4. $C_{19}H_{21}NO_3$ requires C, 73·3; H, 6·8; N, 4·5%). ^{1}H n.m.r. δ ($CDCl_3$): 7·30–7·05, m, 6 × ArH; 6·90–6·75, m, ArH; 4·30–3·80, m, $(H2)_2$; 3·88, s, 2 × OCH_3; 3·40–2·70, m, 3 × CH_2. Mass spectrum: *m/e* 311 (M), 174 (base peak).

Treatment of (4f) (2·00 g, 6·42 mmol) with excess iodomethane, gave a viscous oil which was crystallized from methanol/benzene/diethyl ether to afford the *methiodide salt* (*5f*) (2·33 g, 74%) as fine colourless needles, m.p. 157·5–158·5° (Found: C, 56·0; H, 5·6; N, 2·8. $C_{20}H_{24}INO_3.0{\cdot}5C_6H_6$ requires C, 56·1; H, 5·5; N, 2·9%). ^{1}H n.m.r. δ ($CDCl_3$):* 7·45–6·75, m, 10H, H7, H8, H9, H10, H2′, H5′ and H6′, and 3H from solvent of crystallization; 5·00–3·30, m, 4 × CH_2; 3·86, s, 2 × OCH_3; 3·06, s, NCH_3. λ_{max} (log ε) 237sh (4·11), 280 (3·64), 284sh (3·62); λ_{min} 263 nm (3·37).

Photolysis of the 5H-Oxazolo[2,3-a]isoquinolinium Salt (5f) in Methanol

A solution of (5f) (374 mg, 0·760 mmol) in methanol (100 ml) was irradiated for 50 min. P.l.c. (chloroform/5% methanol) of the residue obtained from the usual workup afforded (R_F 0·45) *1-(3,4-dimethoxyphenyl)-1-methoxy-5-methyl-1,3,4,5,6,7-hexahydro-2,5-benzoxazonine* (6f) (30 mg, 11%) as a colourless gum. Mass spectrum: *m/e* 357 ($M^{+\cdot}$, accurate mass 357·1907; $C_{21}H_{27}NO_4$ requires 357·1940), 342, 326. ^{1}H n.m.r. δ ($CDCl_3$): 8·10–7·90, m, ArH; 7·40–6·50, m, 6 × ArH; 4·10–1·90, m, 4 × CH_2; 3·84, 3·82, 2s, 2 × OCH_3; 3·04, s, 1-OCH_3; 2·23, s, NCH_3.

A large number of minor products were detected by p.l.c., but none was further investigated. Some unchanged starting material (R_F 0·15; 40 mg, 11%) was also recovered.

In another experiment, a solution of (5f) (400 mg) in methanol (100 ml) was irradiated for 15 min to afford the 2,5-benzoxazonine (6f) (23 mg, 8%) together with unchanged starting material (184 mg, 46%). Many minor products were also present.

1-(2-Ethenyl-4,5-dimethoxyphenyl)ethanone (*14*)

A solution of (5b) (400 mg, 1·023 mmol) in 10% methanolic potassium hydroxide (15 ml) was refluxed for 15 h. The methanol was evaporated and water (10 ml) added to the residue. The emulsion which formed was extracted with chloroform (3 × 30 ml). P.l.c. (chloroform/2% methanol) of the residue from the dried chloroform extracts gave (R_F 0·70) the ketone (14) (108 mg, 51%) as a colourless solid. Recrystallization from diethyl ether afforded colourless needles of the ketone (14) (54 mg), m.p. 79–80° (lit.[43] 77–78°). Mass spectrum: *m/e* 206 (M), 205, 191, 163. ^{1}H n.m.r. δ ($CDCl_3$): 7·26, dd, J_1 18, J_2 11 Hz, H_c; 7·20, s, ArH; 7·03, s, ArH; 5·56, d, *J* 18 Hz, H_a; 5·31, d, *J* 11 Hz, H_b; 3·98, 3·94, 2s, 2 × OCH_3; 2·56, s, $COCH_3$. ν_{max} ($CHCl_3$): 1680s cm^{-1} (C=O). λ_{max} (log ε) 234 (4·52), 284 (4·07), 310sh (3·89); λ_{min} 254 nm (3·88).

* Primes denote protons on the dimethoxyphenyl ring.

[42] Nakajima, S., *Yakugaku Zasshi*, 1956, **76**, 1008 (*Chem. Abstr.*, 1957, **51**, 2788i).
[43] Gensler, W. J., Healy, E. M., Onshuus, I., and Bluhm, A. L., *J. Am. Chem. Soc.*, 1956, **78**, 1713.

Another fraction (R_F 0·45) gave a colourless solid (10 mg), the ^{1}H n.m.r. spectrum of which was different from that of the 2,5-benzoxazonine (6b). The low R_F values (less than 0·20) of a number of other minor components indicated that none could be the 2,5-benzoxazonine (6b), and these, together with the above mentioned fraction, were not further investigated.

*8,9-Dimethoxy-4-methyl-1,5,6,10b-tetrahydro-3*H*-oxazolo[4,3-*a*]isoquinolinium Iodide (17)*

Reaction of 2-(3,4-dimethoxyphenyl)ethanamine with diethyl oxalate after the method of Grüssner *et al.*[26] afforded ethyl *N*-[2-(3,4-dimethoxyphenyl)ethyl]oxamate in 91% yield, m.p. 72–74° (lit.[26] 73–74°). Treatment of this amide with phosphorus oxychloride gave[26] the crude ester ethyl 6,7-dimethoxy-3,4-dihydroisoquinoline-1-carboxylate, which was recrystallized[27] twice from diethyl ether to afford pure ester in 60% yield as pale yellow needles, m.p. 78–80° (lit.[25] 79–80°).

To a stirred refluxing mixture of lithium tetrahydroaluminate (2·05 g) in dry, peroxide-free, tetrahydrofuran (100 ml) was added dropwise under nitrogen a solution of the above ester (4·55 g, 17·3 mmol) in tetrahydrofuran (100 ml). The mixture was refluxed for 1 h and then allowed to cool. Water (10 ml) was added followed by chloroform (100 ml). The mixture was centrifuged to remove inorganic salts, and the residue from the dried organic extracts recrystallized from benzene to afford (±)-calycotomine, 1-(hydroxymethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (15) (2·60 g, 67%), m.p. 134–135° (lit.[25] 133–134°).

Reaction of (15) with paraformaldehyde after the method of Schneider and Schilken[27] gave the oxazoloisoquinoline (16) in 83% yield, m.p. 129–130° (lit.[27] 129–130°). ^{1}H n.m.r. δ ($CDCl_3$): 6·67, s, ArH; 6·53, s, ArH; 4·63, s, (H 3)$_2$; 4·45–3·90, m, (H 1)$_2$; 3·86, s, 2 × OCH_3; 3·48, dd, J_1 9, J_2 7 Hz, H 10b; 3·10–2·50, m, CH_2CH_2.

A solution of (16) (1·60 g, 6·80 mmol) in dry toluene (20 ml) and iodomethane (5 ml) was heated to 80° for 6 h. The precipitate which had formed was collected and recrystallized from methanol to afford the *isoquinolinium salt* (17) (2·45 g, 96%) as colourless granules, m.p. 166–167° (Found: C, 44·2; H, 5·6. $C_{14}H_{20}INO_3$ requires C, 44·6; H, 5·4%). ^{1}H n.m.r. δ [$(CD_3)_2SO$]: 7·38, 7·31, 2s, 2 × ArH; 5·70, 5·56, AB q, *J* 5 Hz, (H 3)$_2$; 5·36, dd, J_1 10, J_2 7·5 Hz, H 10b; 4·60–3·35, m, 3 × CH_2; 4·19, 4·16, 2 × OCH_3; 3·69, s, NCH_3. λ_{max} (log ε) 220sh (4·27), 283 (3·55), 286sh (3·52); λ_{min} 255 nm (2·64).

1-(Hydroxymethyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline [(±)-N-Methylcalycotomine] (19)

A solution of ethyl 6,7-dimethoxy-3,4-dihydroisoquinoline-1-carboxylate (7·16 g, 27·4 mmol) in benzene (100 ml) and iodomethane (5 ml) was allowed to stand for 7 days at room temperature. The precipitate which had formed was collected and recrystallized from methanol/acetone to afford the methiodide salt of this ester (10·72 g, 97%), m.p. 140–142° (lit.[44] 142°).

To a solution of the above salt (10·0 g, 24·7 mmol) in tetrahydrofuran (75 ml) was added portionwise lithium tetrahydroaluminate (1·4 g). The mixture was refluxed for 0·5 h and then worked up, as described for the preparation of (15), to afford the title compound (19) (5·38 g, 92%) as an oil. ^{1}H n.m.r. δ ($CDCl_3$): 6·56, 6·53, 2s, 2 × ArH; 3·95–3·45, m, 3H, $CHCH_2OH$; 3·83, s, 2 × OCH_3; 3·65, br s, exchanged with D_2O, OH; 3·25–2·55, m, CH_2CH_2; 2·50, s, NCH_3. ν_{max} (thin film): 3380s cm^{-1} (OH).

To a solution of (19) (5·38 g) in methanol (30 ml) was added concentrated hydrochloric acid (3 ml). The solution was evaporated to dryness and the residue recrystallized from ethanol to afford the hydrochloride salt of (19) (4·80 g, 77%), m.p. 220–223° (lit.[44] 223°). ^{1}H n.m.r. δ [$(CD_3)_2SO$]: 10·79, br s, exchanged with D_2O, OH; 7·23, 7·19, 2s, 2 × ArH; 4·85–4·60, m, H 1; 4·50–3·05, m, (H 3)$_2$, (H 4)$_2$ and CH_2OH; 4·10, s, 2 × OCH_3; 3·75, br s, exchanged with D_2O, NH; 3·21, s, NCH_3. λ_{max} (log ε) 230 (3·89), 283 (3·53), 287sh (3·49); λ_{min} 218 (3·84), 253 nm (2·69).

*Photolysis of the 3*H*-Oxazolo[4,3-*a*]isoquinolinium Salt (17) in Methanol*

A solution of (17) (400 mg, 1·060 mmol) in methanol (200 ml) was irradiated for 1 h. Analytical t.l.c. of the photolysate residue, obtained after the usual workup, showed it to be a complex mixture. P.l.c. (chloroform/8% methanol) afforded (R_F 0·25) the secondary-amino alcohol *2-[4,5-dimethoxy-2-{2-(methylamino)ethyl}phenyl]-2-methoxyethanol* (20b) (72 mg, 25%). Recrystallization from diethyl ether/light petroleum (b.p. 40–60°) gave (20b) as tan-coloured granules, m.p. 92–93° (Found:

[44] Matsuo, I., Takahashi, T., and Ohki, S., *Yakugaku Zasshi*, 1964, **84**, 711.

C, 62·8; H, 8·8; N, 5·4. $C_{14}H_{23}NO_4$ requires C, 62·4; H, 8·6; N, 5·2%). Mass spectrum: *m/e* 269 (M), 251, 44 [base peak, $H_2C{=}N^+(CH_3)H$]. ^{1}H n.m.r. δ ($CDCl_3$): 6·91, s, ArH; 6·69, s, ArH; 4·67–4·49, m, H2; 3·87, s, 2×OCH_3; 3·75–3·55, m, CH_2OH; 3·25, s, 2-OCH_3; 2·95–2·72, m, 6H, 2H exchanged with D_2O, NH, OH and CH_2CH_2; 2·42, s, NCH_3. ν_{max} ($CHCl_3$): 3350m(br) (OH), 3310m cm^{-1} (NH).

Photolysis of the Hydrochloride Salt of (19) in Methanol

A solution of the hydrochloride salt of (19) (400 mg, 1·461 mmol) in methanol (200 ml) was irradiated for 1·5 h. After the usual workup, p.l.c. (chloroform/8% methanol) gave the secondary-amino alcohol (20b) (42 mg, 11%), together with (R_F 0·50) unchanged (19) (250 mg, 72%).

In another experiment, a solution of the hydrochloride salt of (19) (400 mg, 1·461 mmol) in methanol (200 ml) was irradiated for 6 h to afford (20b) (100 mg, 25%), together with unchanged (19) (136 mg, 39%), after basification of the photolysate. A number of minor products were isolated but these were not further investigated.

Photolysis of the 3H-Oxazolo[4,3-a]isoquinolinium Salt (17) in Water

A solution of (17) (400 mg, 1·060 mmol) in distilled water (150 ml) was irradiated for 1·5 h. The solution was basified to pH 9 with concentrated aqueous ammonia, and extracted with chloroform (4×50 ml). Analytical t.l.c. of the residue (250 mg) from the chloroform extracts indicated the presence of a complex mixture of products. P.l.c. (chloroform/10% methanol) afforded (R_F 0·60) (±)-*N*-methyl calycotomine (19) (20 mg, 8%) as the only identifiable product. The aqueous solution was evaporated to dryness and the residue was extracted with boiling chloroform (2×30 ml). ^{1}H n.m.r. spectroscopic analysis of the residue (83 mg) from these latter chloroform extracts indicated that it consisted of a complex mixture of products. The residue was not investigated further.

In another experiment, a solution of (17) (400 mg) in water (150 ml), buffered at pH 9·4,[45] was irradiated for 1·5 h. P.l.c. of the residue (180 mg) from the chloroform extracts, obtained as described above, gave a complex mixture of products which was not investigated further.

Photolysis of the Hydrochloride Salt of (19) in Water

A solution of the hydrochloride salt of (19) (400 mg, 1·461 mmol) in distilled water (150 ml) was irradiated for 1·5 h. The solution was basified to pH 9 with concentrated aqueous ammonia, and extracted with chloroform (4×50 ml). Unchanged (19) (341 mg, 98%) was recovered from the dried and evaporated chloroform extracts. Similarly, no reaction was observed when a solution of the hydrochloride salt of (19) (400 mg) in water (150 ml) acidified to pH 1–2, by the addition of concentrated sulfuric acid, was irradiated for 1·5 h.

Acknowledgments

The award of a Commonwealth Postgraduate Research Award (to K.N.W.) is gratefully acknowledged, together with a grant in support of this work from the Australian Research Grants Committee. We thank the Upjohn Company (Kalamazoo, Michigan, U.S.A.) for their support of this work, Mr J. C. Bignall and Mr M. Power (Central Science Laboratory of this University), and Drs C. P. Whittle and M. J. Lacey (Division of Entomology, CSIRO, Canberra) for the determination of the mass spectra, and Dr A. J. Jones (of the former National N.M.R. Centre, Canberra) for the measurement of ^{1}H and ^{13}C n.m.r. spectra. We also thank Professor L. N. Mander for providing facilities (to J.B.B.) at the Research School of Chemistry, Australian National University, where this paper was initially prepared.

Manuscript received 21 March 1984

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