Oxidative Coupling of Phenols and Phenolic Ethers. Part 4.[1] Synthesis of Dibenz[*d,f*]azonines and a Dibenz[*d,f*]azecine, *via* Direct Coupling

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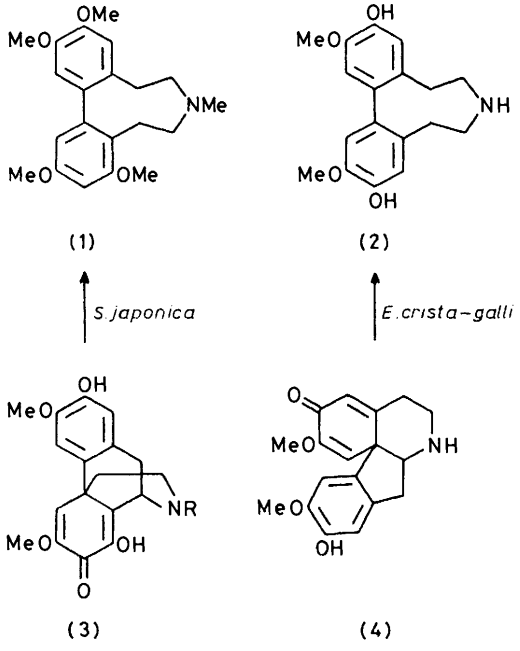
Two series of amides, the *N*-phenethylphenylacetamides (9) and the bisphenethylamides (11), including diphenolic, monophenolic, and non-phenolic types, were treated with a range of one-electron oxidants. With the tetramethoxy-derivative (11e) intramolecular coupling yielded a dibenzazonine (16) in 36% yield. Similar oxidation of the homologue (18) gave a dibenzazecine (19) in 60% yield.

PROTOSTEPHANINE (1), a minor alkaloid from *Stephania japonica*, was the first naturally-occurring dibenz[*d,f*]-azonine to be discovered.[2] Several additional examples have now been isolated [3] and erybidine (2) has been

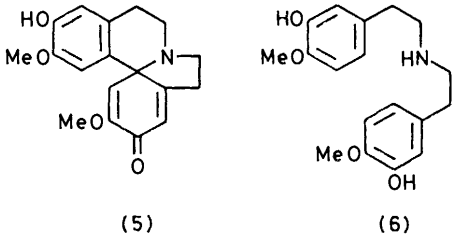


identified [4] as a key intermediate in the biosynthesis of the *Erythrina* alkaloids. Despite their close structural similarity, protostephanine (1) and erybidine (2) are synthesised in nature from their 1-benzylisoquinoline parents by quite different pathways: protostephanine (1) *via* fragmentation of a morphinandienone,[5] *e.g.* (3); and erybidine (2) *via* fragmentation of the proerythrinadienone (4). *In vitro* analogies for both processes have been worked out.[6,7]

In addition to these biomimetic syntheses, dibenz[*d,f*]-azonines have been synthesised (*a*) from a biphenyl 2,2-dicarboxylic acid by homologation and cyclisation reactions; [8] and (*b*) by reductive fragmentation [9] of erysodienone (5) which can be obtained in >30% yield by $K_3Fe(CN)_6$ oxidation [10] of the simple bisphenethylamine (6). We now report studies on the oxidation of a variety of bisphenethylamine derivatives, resulting in a new *direct* route to the dibenzazonine (and dibenzazecine) skeleton by oxidative coupling.

The substrates for our oxidation studies were prepared by the general route outlined in the Scheme, all phenolic OH groups being protected throughout as *O*-benzyl ethers and released, prior to oxidation, by hydrogenolysis. The ^1H n.m.r. spectra of the trifluoroacetamides (11) were found to be complicated because of restricted rotation about the amide bond. Oxidations were attempted on the amides (9) and (11), but not generally on the amines (10) since we hoped to avoid oxidative cyclisation of primary dibenzazonine products [*e.g.* (2) ⟶ (5)] by reducing the reactivity of the nitrogen atom.

Diphenolic Oxidation.—The first amide which we studied was (9a), a 'masked' version of the amine (6). Oxidation by K_3FeCN_6 under similar conditions to those [10] which converted the amine (6) to erysodienone



(5) resulted in the slow conversion of (9a), to material of R_F 0, presumably a polymer.† Oxidation of the corresponding trifluoroacetamide (11a) by $VOCl_3$, VOF_3, and $Tl(OCOCF_3)_3$ (TTFA) in a variety of solvents similarly failed to produce any significant amount of isolable monomeric product.

It seems likely that the problem with the substrates (9a) and (11a) is over-oxidation. The initial products should have low redox potentials and may be further oxidised to the extended quinone [as (12)]. This reactive intermediate is trapped in the case of (6) but may lead to unidentified products when the nitrogen atom is not nucleophilic.

To overcome this problem we studied the oxidation of amides (9b) and (11b) which should give a more stable type of primary oxidation product (13): subsequent

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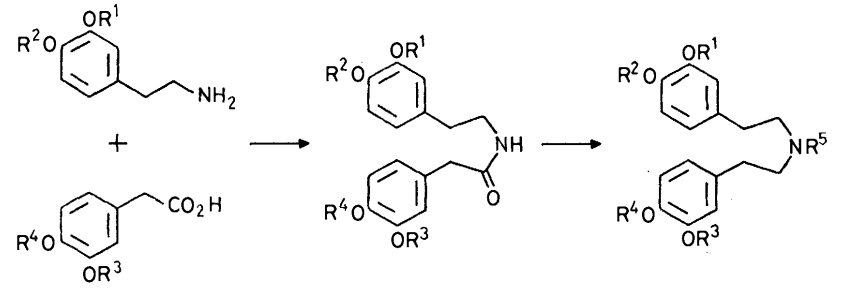
† Barton and Widdowson have recently reported [11] that $K_3Fe(CN)_6$ oxidation of (9a) in the presence of a phase-transfer catalyst gave 8% of the intramolecularly coupled product.

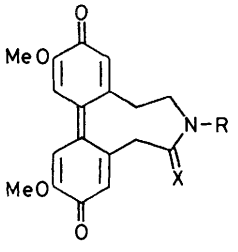
dienone–phenol rearrangement would then afford the required dibenzazonines. However, despite an intensive study of the oxidation of (9b), (11b), and the free base (10b) with $K_3Fe(CN)_6$, $VOCl_3$, and VOF_3 under a wide variety of conditions no dienone product was obtained. We conclude that the activation energy for cyclisation to an 8-membered ring is so high that the reactive intermediates generated by oxidation undergo *inter-* rather than *intra*-molecular reaction.*



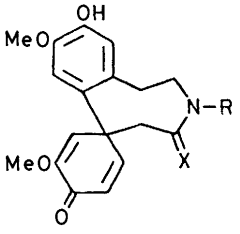
(9) (10) R^5= H; (11) R^5= $COCF_3$

a; R^1=R^3=H, R^2=R^4=Me
b; R^1=R^4=H, R^2=R^3=Me
c; R^1=R^2=R^4=Me, R^3=H
d; R^1=R^2=R^3=Me, R^4=H
e; R^1=R^2=R^3=R^4=Me

SCHEME

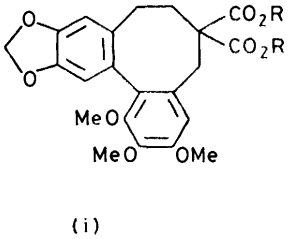


(12)

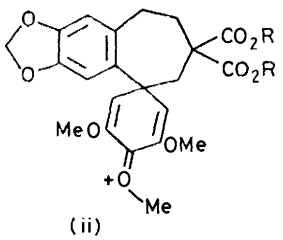


(13)

Monophenolic Oxidation.---Excellent yields have been reported in certain monophenolic oxidations [13,14] and we therefore investigated the reaction of the amides (9c) and (11c) with $VOCl_3$, VOF_3, and TTFA. Cleaner reactions were observed with (11c) which with all oxidants gave, amongst others, the same yellow spot by t.l.c. This product (14% yield from TTFA) was identified by its spectra as the quinone (14), and it could be produced in better yield by oxidation of (11c) with $Tl(NO_3)_3$ in methanol.[15] With VOF_3–CH_2Cl_2–TFA the quinone (14) was obtained in 9% yield but the required dibenzazonine (15) was also produced in 11% yield.



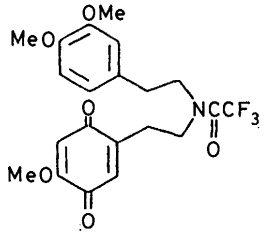
(i)



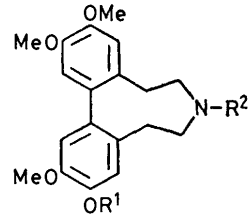
(ii)

* Kende's synthesis of steganone [12] includes oxidative formation of the 8-membered ring of (i), but this might arise *via* rearrangement of the 7-membered intermediate (ii).

Oxidation of the isomeric monophenolic trifluoroacetamide (11d) gave no sign of intramolecular coupling under the conditions used for (11c), and so it seems that, in this series as elsewhere,[16] cyclisation to a 9-membered ring is easier than that to an 8-membered ring.



(14)

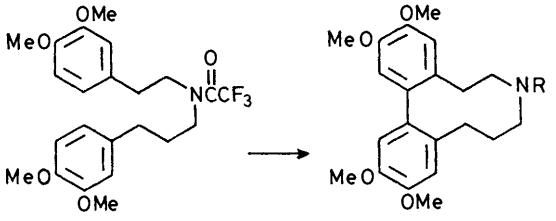


(15) R^1=H, R^2=$COCF_3$
(16) R^1=Me, R^2=$COCF_3$
(17) R^1=Me, R^2=H

Non-phenolic Oxidations.—Oxidation of phenolic ethers by vanadium(v) and thallium(iii) reagents is a useful new method [17] for oxidative coupling which proved itself superior in this study. Thus oxidation of the tetramethoxytrifluoroacetamide (11e) by TTFA in TFA at 25 °C gave the dibenzazonine (16) in 36% yield. The reaction could not be followed by t.l.c. because we were unable to find a system capable of distinguishing between (11e) and (16), but ^{1}H n.m.r. and mass spectroscopy proved that intramolecular coupling had occurred.

The trifluoroacetyl group was readily removed by alkaline hydrolysis and the aromatic protons of the free base (17) appeared as singlets proving that coupling had been *para–para* (with respect to the 3-MeO group of each aromatic ring).

Having now a satisfactory method for producing the 9-membered azonine system directly by oxidative coupling we turned to the analogous 10-membered azecine system. The homologous trifluoroacetamide (18) was prepared by the route outlined above, and oxidation by TTFA–TFA at −15 °C gave the dibenzazecine (19) in 60% yield. Hydrolysis of (19) afforded the free base (20) and *para–para* coupling was again proven by the appearance of the aromatic protons as singlets.



(18) (19) R = $COCF_3$ (20) R = H

Conclusions.—Oxidative coupling of phenols and phenolic ethers proceeds *via* reactive intermediates (radicals, radical cations, diradicals) which are susceptible to numerous side-reactions in addition to the required intramolecular cyclisation. Here the ease of cyclisation depended on the size of the newly formed ring and followed the order 10 > 9 > 8. Monophenolic substrates gave better results than diphenols, but non-phenolic substrates were oxidised to intramolecular coupled products in highest yield, affording a useful synthetic entry to the dibenzazonine and dibenzazecine [18] systems.

EXPERIMENTAL

For general directions see Part 1.[18b]

N-(3,4-Dimethoxyphenethyl)-2-(3,4-dimethoxyphenyl)-acetamide (9e).—A solution of dicylohexylcarbodi-imide (DCC, 2.4 g) in dry CH_2Cl_2 (35 ml) was added to a solution of 3,4-dimethoxyphenethylamine (1.92 g) and 3,4-dimethoxyphenylacetic acid (2.49 g) at 0 °C under N_2, and the reaction was stirred at 0 °C for 30 min and at 25 °C for 16 h. Crystals of dicyclohexylurea were removed by filtration through Celite and the filtrate was washed with aqueous K_2CO_3 and water, and evaporated to give the amide (9e), m.p. 124—125° (from EtOAc) (lit.,[19] 124—126°).

Similarly prepared were the dibenzyl ether of (9a), m.p. 112—113.5° (from benzene–hexane) (lit.,[20] 112—113°); the dibenzyl ether of (9b), m.p. 127—128° (from ethanol–ether) (lit.,[21] 128°); the benzyl ether of (9c), m.p. 109—111° (from EtOH) (lit.,[22] 111.5—112.5°); the benzyl ether of (9d), m.p. 114—116° (from benzene–hexane) (lit.,[22] 114—116°); and *N*-(3,4-dimethoxyphenethyl)-3,4-dimethoxyphenylpropionamide, m.p. 99—100° (from benzene–hexane) (lit.,[23] 99—100°).

Bis-N-[2-(3,4-dimethoxyphenyl)ethyl]amine Hydrochloride (10e).—BF_3–Et_2O (3.78 ml) was added dropwise to a stirred suspension of sodium borohydride (0.76 g) and the foregoing amide (9e) (1.79 g) in dry THF (120 ml) at 0 °C under N_2.[24] The mixture was stirred at 0 °C for 1 h and then heated under reflux for 16 h. After cooling, 3N-NaOH was added carefully until effervescence ceased and the mixture was refluxed for 30 min, then partially evaporated *in vacuo*. After dilution with water and extraction with CH_2Cl_2 the extract was washed and evaporated. The residue in EtOH was treated with ethanolic HCl to give the bisphenethylamine hydrochloride (10e) (1.54 g; 81%), m.p. 202—205° (from EtOH) (lit.,[25] 195—196°) (Found: C, 62.85; H, 7.55; N, 3.75; Cl, 9.1. Calc. for $C_{20}H_{28}ClNO_4$: C, 63.0; H, 7.3; N, 3.75; Cl, 9.3%).

By the same method were prepared the hydrochlorides of the dibenzyl ether of (10a), m.p. 172—174° (from MeOH) (lit.,[26] 173—174°); the dibenzyl ether of (10b), m.p. 160—162° (from MeOH) (lit.,[24] 162.5—163.5°); the benzyl ether of (10c), m.p. 167—169° (from EtOH); and the benzyl ether of (10d), m.p. 185—187° (from MeOH); and *N-(3,4-dimethoxyphenethyl)-N-(3,4-dimethoxyphenylpropyl)amine hydrochloride*, m.p. 194—195° (from EtOH) (Found: C, 63.05; H, 7.7; N, 3.55; Cl, 8.75. $C_{21}H_{30}ClNO_4$ requires C, 63.7; H, 7.6; N, 3.5; Cl, 8.95%).

Bis-N-[2-(3,4-dimethoxyphenyl)ethyl]trifluoroacetamide (11e).—Trifluoroacetic anhydride (0.42 ml; redistilled) was added to a solution of the amine (0.65 g) liberated from the foregoing hydrochloride (10d) in dry pyridine (17 ml) at 25 °C under N_2. After stirring for 3 h the solution was evaporated (Rotovap) and the residue partitioned between CH_2Cl_2 and 3N-H_2SO_4. The organic layer was washed, dried, and evaporated to give the title *trifluoroacetamide* (11e), m.p. 103—104° (from benzene–hexane) (Found: C, 60.05; H, 6.0; N, 2.9. $C_{22}H_{26}F_3NO_5$ requires C, 59.9; H, 5.9; N, 3.15%), M^+ 441, $\nu_{max.}$ (Nujol) 1 680 cm^{-1}, $\lambda_{max.}$ 273 nm, δ 2.74* and 2.84* (each 2H, t, *J* 8 Hz, $ArCH_2$), 3.38* and 3.58* (each 2 H, t, *J* 8 Hz, CH_2N), 3.84 (12 H, s, 4 × OMe), and 6.56—6.90 (6 H, m, ArH).

Similarly were prepared *bis-N-[2-(3-benzyloxy-4-methoxyphenyl)ethyl]trifluoroacetamide* [the dibenzyl ether of (11a)] as a gum† (Found *m/e*, 593.2366. $C_{34}H_{34}F_3NO_5$ requires *M*, 593.2387), $\nu_{max.}$ (film) 1 685 cm^{-1}, $\lambda_{max.}$ 279 nm, δ 2.64 and 2.75 (each 2 H, t, *J* 7.5 Hz, $ArCH_2$), 3.28 and 3.48 (each 2 H, t, *J* 7.5 H2, CH_2N), 3.82 (6 H, s, 2 × OMe), 5.09 (4 H, s, 2 × CH_2Ph), 6.58—6.88 (6 H, m, ArH), 7.2—7.5 (10 H, m, Ph); *N-(3-benzyloxy-4-methoxyphenethyl)-N-(4-benzyloxy-3-methoxyphenethyl)trifluoroacetamide* [the dibenzyl ether of (11b)] as a gum† (Found: *m/e*, 593.2390. $C_{34}H_{34}F_3NO_5$ requires *M*, 593.2387), $\nu_{max.}$ 1 685 cm^{-1}, $\lambda_{max.}$ 279 nm, δ 2.6—2.9 (4 H, m, 2 × $ArCH_2$), 3.2—3.6 (4 H, m, 2 × CH_2N), 3.86 (6 H, s, 2 × OMe) 5.12 (4 H, s, 2 × CH_2Ph), 6.5—6.9 (6 H, m, ArH), and 7.2—7.5 (10 H, m, Ph); *N-(3-benzyloxy-4-methoxyphenethyl)-N-(3,4-dimethoxyphenethyl)trifluoroacetamide* [the benzyl ether of (11c)] as a gum† (Found: *m/e*, 517.2044. $C_{28}H_{30}F_3NO_5$ requires *M*, 517.2075), $\nu_{max.}$ 1 685 cm^{-1}, $\lambda_{max.}$ 279 nm, δ 2.6—2.9 (4 H, m, 2 × CH_2Ar), 3.2—3.6 (4 H, m, 2 × CH_2N), 3.85 (9 H, s, 3 × OMe), 5.11 (2 H, s, CH_2Ph), 6.56—6.9 (6 H, m, ArH), and 7.2—7.5 (5 H, m, Ph); *N-(4-benzyloxy-3-methoxyphenethyl)-N-(3,4-dimethoxyphenethyl)-*

* *N.B.* The non-equivalence of these signals is due to restricted rotation of the amide.

†All non-crystalline compounds were homogenous by t.l.c. in at least two different solvent systems before analytical and spectral data were determined.

trifluoroacetamide [the benzyl ether of (11d)] as a gum * (Found: *m/e*, 517.2061. $C_{28}H_{30}F_3NO_5$ requires *M*, 517.2075), $\nu_{max.}$ 1 685 cm^{-1}, $\lambda_{max.}$ 278 nm, δ 3.37 and 3.57 (each 2 H, t, *J* 8 Hz, CH_2Ar), 3.74 and 3.83 (each 2 H, t, *J* 8 Hz, CH_2N), 3.84, 3.85 (9 H, OMe), 5.10 (2 H, s, CH_2Ph), 6.5—6.9 (6 H, m, ArH), and 7.2—7.5 (5 H, m, Ph); and N-(3,4-*dimethoxyphenethyl*)-N-(3,4-*dimethoxyphenylpropyl*)*trifluoroacetamide* (18) as a gum * (Found: *m/e*, 455.1934. $C_{23}H_{28}F_3NO_5$ requires *M*, 455.1920), $\nu_{max.}$ 1 680 cm^{-1}, $\lambda_{max.}$ 227 and 279 nm, δ 1.7—2.1 (2 H, m, $ArCH_2CH_2CH_2N$), 2.56 (2 H, t, *J* 8 Hz, $ArCH_2CH_2N$), 2.7—3.0 (2 H, m, $ArCH_2[CH_2]_2N$), 3.1—3.4 (2 H, m, $Ar[CH_2]_2CH_2N$), 3.56 (2 H, t, *J* 8 Hz, $ArCH_2CH_2N$), 3.88 (12 H, s, 4 × OMe), and 6.6—6.9 (6 H, m, ArH).

N-(3,4-*Dimethoxyphenethyl*)-2-(3-*hydroxy*-4-*methoxyphenyl*)*acetamide* (9c).—A solution of the corresponding benzyl ether (200 mg) in 3 : 1 v/v MeOH–$CHCl_3$ containing 0.2 ml methanolic HCl was hydrogenated over 10% Pd–C (40 mg). The catalyst was filtered off (Celite) and the filtrate evaporated to give the title *phenolic amide* (9c), m.p. 125—127° (from ethanol) (Found: C, 66.0; H, 6.9; N, 3.9. $C_{15}H_{23}NO_5$ requires C, 66.1; H, 6.7; N, 4.1%), M^+ 345, $\nu_{max.}$ 3 540, 3 420, and 1 655 cm^{-1}, $\lambda_{max.}$ 282 nm, $\lambda_{max.}$ (OH^-) 279 and 291 nm, δ 2.67 (2 H, t, *J* 7 Hz, $ArCH_2CH_2$), 3.46 (2 H, q, *J* 7 Hz, $ArCH_2CH_2NH$), 3.42 (2 H, s, $ArCH_2CO$), 3.80, 3.84, and 3.86 (each 3 H, s, 3 × OMe), 5.6 (2 *H*, br, exch. D_2O, OH and NH), and 6.5—6.9 (6 H, m, ArH).

Similarly were prepared the diphenolic amide (9a), m.p. 116—117° (from CH_2Cl_2–Et_2O) (lit.,[24] 117°); the diphenolic amide (9b) as a gum [24] (Found : *m/e*, 331.1412. $C_{18}H_{21}NO_5$ requires *M*, 331.1418); the diphenolic amine hydrochloride (10b), m.p. 188—191° (from EtOH), $\nu_{max.}$ (Nujol) 3 500 and 2 460 cm^{-1}, $\lambda_{max.}$ 227 and 281 nm, $\lambda_{max.}$ (OH^-) 243 and 293 nm, δ ([$^2H_6$]DMSO) 2.7—3.4 (10 H, m; 2 H exch. D_2O, 4 × CH_2, 2 × OH), 3.76 and 3.78 (each 3 H, s, 2 × OMe), 6.6—6.9 (6 H, m, ArH), and 9.7—10.0 (2 H, br, exchanged with D_2O, 2 × NH), *m/e* 317; the diphenolic trifluoroacetamide (11a) as a gum, *m/e* 413, $\nu_{max.}$ 3 540 and 1 683 cm^{-1} $\lambda_{max.}$ 211 and 285 nm, $\lambda_{max.}$ (OH^-) 245 and 299 nm (OH), δ 2.6—2.9 (4 H, m, 2 × $ArCH_2$), 3.3—3.7 (4 H, m, 2 × CH_2N), 3.88 (6 H, s, 2 × OMe), 6.54—6.86 (6 H, m, ArH), and 5.2—5.8 (2 H, b, exchange with D_2O, 2 × OH); N-(3-*hydroxy*-4-*methoxyphenethyl*)-N-(4-*hydroxy*-3-*methoxyphenethyl*)*trifluoroacetamide* (11b) as a gum * (Found: *m/e*, 413.1473. $C_{20}H_{22}F_3NO_5$ requires M^+, 413.1448), $\nu_{max.}$ 3 540 and 1 690 cm^{-1}, $\lambda_{max.}$ 227 and 281 nm, $\lambda_{max.}$ (OH^-) 287 and 298 nm, δ 2.74 and 2.82 (each 2 H, t, *J* 8 Hz, 2 × CH_2Ar), 3.38 and 3.57 (each 2 H, t, *J* 8 Hz, 2 × CH_2N), 3.86 (6 H, s, 2 × OMe), 5.2—5.6 (2 H, br, exch. D_2O, 2 × OH), and 6.5—6.9 (6 H, m, ArH); N-(3,4-*dimethoxyphenethyl*)-N-(3-*hydroxy*-4-*methoxyphenethyl*)*trifluoroacetamide* (11c) as a gum * (Found: *m/e*, 427.1612. $C_{21}H_{24}F_3NO_5$ requires *M*, 427.1604), $\nu_{max.}$ 3 540 and 1 680 cm^{-1} $\lambda_{max.}$ 227 and 280 nm, $\lambda_{max.}$ (OH^-) 284 and 290 nm, δ 2.6—2.9 (4 H, m, 2 × CH_2Ar), 3.35 and 3.55 (each 2 H, t, *J* 7 Hz, 2 × CH_2N), 3.82 (9 H, s, 3 × OMe), 5.60 (1 H, br, exch. D_2O, OH), and 6.45—6.85 (6 H, m, ArH); and N-(3,4-*dimethoxyphenethyl*)-N-(3-*hydroxy*-4-*methoxyphenethyl*)*trifluoroacetamide* (11d) as a gum * (Found: *m/e*, 427.1594. $C_{21}H_{24}F_3NO_5$ requires *M*, 427.1604), $\nu_{max.}$ 3 200—3 700br and 1 680 cm^{-1}, $\lambda_{max.}$ 230 and 280 nm, $\lambda_{max.}$ (OH^-) 284 and 300 nm, δ 2.77 and 2.84 (each 2 H, t, *J* 8 Hz, 2 × CH_2Ar), 3.40 and 3.58 (each 2 H, t, *J* 8 Hz, 2 × CH_2N), 3.55 (9 H, s, 3 × OMe), 5.3—5.5 (1 H, br, exch. D_2O, OH), and 6.5—6.9 (m, 6 H, ArH).

Oxidation of the Monophenol (11c) *to the Quinone* (14).—A solution of the trifluoroacetamide (11c) (100 mg) in dry CH_2Cl_2 (20 ml) was added to a slurry of TTFA (178 mg) in dry CH_2Cl_2 (60 ml) under N_2 at 0 °C and the mixture stirred at this temperature for 1½ h. It was then diluted with $CHCl_3$ (10 ml) and filtered through a column of silica (5 g) using $CHCl_3$ as eluant to give an oil (109 mg). Preparative t.l.c. (SiO_2; $CHCl_3$–MeOH, 19 : 1 v/v) gave N-(3,4-*dimethoxyphenyl*)-N-[2-(5-*methoxy*-1,4-*benzoquinon*-2-*yl*)-*ethyl*]*trifluoroacetamide* (14) as a yellow oil (14 mg, 14%) (Found: *m/e*, 441.1389. $C_{21}H_{22}F_3NO_6$ requires *M*, 441.1398), $\nu_{max.}$ (film) 1 610, 1 650, and 1 685 cm^{-1}, $\lambda_{max.}$ 229 and 262 nm, δ 2.6—3.7 (8 H, m, CH_2), 3.83, 3.87, and 3.90 (each 3 H, s, OMe), 5.93 (1 H, d, *J* 1.5 Hz, MeO–C:C*H*–CO), 6.50 (1 H, m, OC–CH:C), and 6.68—6.90 (3 H, m, ArH).

The mass spectrum also showed a peak at *m/e* 443 which could be due to a trace of the corresponding hydroquinone but none of the other spectra showed evidence for this.

Oxidation of the Monophenol (11c) *to the Dibenzazonine* (15).—A solution of VOF_3 (264 mg) in TFA (15 ml) was added to a solution of the amide (11c) (420 mg) in CH_2Cl_2 (54 ml) and TFA (2 ml) at −23 °C for 1 h and then poured into H_2O and extracted (× 3) with CH_2Cl_2. The combined organic extracts were washed (×5) with H_2O until the aqueous layer had *ca.* pH 7, then with brine, dried (Na_2SO_4), and filtered through a column of SiO_2 (8 g, $CHCl_3$ as eluant); the filtrate was evaporated leaving a gum (0.26 g) which was purified by preparative t.l.c. (SiO_2; Et_2O–MeOH, 49 : 1 v/v). Two fractions were taken and were plated again (SiO_2; CH_2Cl_2–MeOH, 49 : 1 v/v) to give two products, one of which was 5,6,8,9-*tetrahydro*-3-*hydroxy*-2,11,12-*trimethoxy*-N-*trifluoroacetyl*-7H-*dibenz*[d,f]*azonine* (15) (45 mg, 11%), m.p. 183—184 °C (from $CHCl_3$–Et_2O) (Found: C, 59.05; H, 5.3; N, 3.4%; *m/e*, 425.1431. $C_{21}H_{22}F_3NO_5$ requires C, 59.3; H, 5.2; N, 3.3%; *M*, 425.1448), $\nu_{max.}$ (Nujol) 3 400 br and 1 680 cm^{-1}, $\lambda_{max.}$ 227 and 284 nm, $\lambda_{max.}$ (OH^-) 286 and 300 nm, δ 2.4—3.8 (8 H, m, CH_2), 3.84—3.94 (9 H, m, OMe), 6.6—6.82 (4 H, m, ArH), and 5.4—5.8 (1 H, br, exch. D_2O, OH). The other product (39 mg, 9%) was the quinone (14).

5,6,8,9-*Tetrahydro*-2,3,11,12-*tetramethoxy*-N-*trifluoroacetyl*-7H-*dibenz*[d,f]*azonine* (16).—A solution of the amide (11e) (110 mg) in TFA (2.5 ml) was added to a stirred solution of TTFA (340 mg) in TFA (2.5 ml) at 20 °C under N_2 and the mixture was stirred at this temperature for 18 h. It was then poured into H_2O and extracted with CH_2Cl_2. The combined organic extracts were washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The residue was purified by preparative t.l.c. (SiO_2; Et_2O–MeOH, 49 : 1 v/v) to give the *dibenzazonine* (16) (40 mg, 37%) as a gum (Found: *m/e*, 439.1609. $C_{22}H_{24}F_3NO_5$ requires *M*, 439.1609), $\nu_{max.}$ 1 675 cm^{-1}, $\lambda_{max.}$ 211, 229, and 279 nm, δ 2.30—3.70 (8 H, m, CH_2), 3.82, 3.84, 3.86, and 3.88 (each 3 H, s, OMe), and 6.5—6.8 (4 H, m, ArH).

The oxidation was also attempted with $VOCl_3$ and VOF_3 in CH_2Cl_2 and TFA, but TTFA gave the cleanest reaction.

The product had the same R_F value as starting material and the long reaction time and excess of TTFA ensured complete conversion to the product and hence facilitated isolation although it also probably led to lower yields.

5,6,8,9-*Tetrahydro*-2,3,11,12-*tetramethoxy*-7H-*dibenz*[d,f]-*azonine* (17).—A solution of the dibenzazonine (16) (75 mg)

* All non-crystalline compounds were homogenous by t.l.c. in at least two different solvent systems before analytical and spectral data were determined.

in MeOH (10 ml) and aqueous 3N-NaOH (5 ml) was stirred under N_2 for 1 h. It was then poured into brine and extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with H_2O and brine, dried (Na_2SO_4), and evaporated to leave the amine (17) (55 mg, 94%), $\nu_{max.}$ 3 360 br cm^{-1}, $\lambda_{max.}$ 214, 226, and 284 nm, δ 2.14—3.30 (9 H, m, goes to 8 H with D_2O, CH_2 and NH), 3.86 (6 H, s, OMe), 3.92 (6 H, s, OMe), 6.68 (2 H, s, ArH), and 6.70 (2 H, s, ArH), *m/e* 343 (M^+), 328 (M^+ — OMe), 301 (M^+ — MeOH), and 286. The oxalate salt had m.p. 185—188 °C (from propan-2-ol).

5,6,7,8,9,10-*Hexahydro*-2,3,12,13-*tetramethoxy*-N-*trifluoroacetyldibenz*[d,f]*azecine* (19).—A solution of the amide (18) (228 mg) in TFA (5 ml) and CH_2Cl_2 (2.2 ml) at −18 °C was added to a stirred solution of TTFA (400 mg, 0.75 mmol, 1.5 mol. equiv.) in TFA (7 ml) at −18 °C under N_2. After 30 min the mixture was poured into water and extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The residue was filtered through a column of SiO_2 with CH_2Cl_2 as eluant to give a starting material (18) (47 mg) and then with $CHCl_3$ to give the crude product which was purified by preparative t.l.c. (SiO_2; Et_2O) to give the *dibenzazecine* (19) (107 mg, 60% based on recovered starting material) as a gum (Found: *m/e*, 453.1753. $C_{23}H_{26}F_3NO_5$ requires *M*, 453.1763), $\nu_{max.}$ ($CHCl_3$) 1 680, 1 603, and 1 590 cm^{-1}, $\lambda_{max.}$ 210, 227, and 280 nm, δ 1.52—1.95 (2 H, m, $ArCH_2CH_2CH_2N$), 2.10—2.90 (4 H, m, $ArCH_2$), 2.90—3.60 (4 H, m, CH_2N), 3.80—3.90 (12 H, m, OMe), and 6.54—6.88 (4 H, m, ArH).

5,6,7,8,9,10-*Hexahydro*-2,3,12,13-*tetramethoxydibenz*[d,f]*azecine* (20).—A solution of the foregoing trifluoroacetamide (19) (50 mg) in MeOH (8 ml) and aqueous 3N-NaOH was stirred at 20 °C under N_2 for 1 h. It was then poured into brine and extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with H_2O and brine, dried (K_2CO_3), and evaporated to leave the crude amine (20) which was purified by column chromatography (Al_2O_3; Et_2O, $CHCl_3$, $CHCl_3$–MeOH) to give the *azecine* (29 mg, 76%) as a gum, $\nu_{max.}$ 3 400 cm^{-1}, $\lambda_{max.}$ 215, 227, and 280 nm, δ 1.4—1.8 (2 H, m, $ArCH_2CH_2CH_2$), 2.2—2.9 (9 H, m, goes to 8 H with D_2O, $ArCH_2$, CH_2N, and NH), 3.80 (3 H, s, OMe), 3.84 (6 H, s, OMe), 3.90 (3 H, s, OMe), and 6.56—6.90 (4 H, m, ArH). The oxalate salt had m.p. 193—195 °C (from propan-2-ol).

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