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The Action of Vanadium Oxytrifluoride on *N*-Arylbenzylamines—a Route to Some Phenanthridines

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The action of four equivalents of vanadium oxytrifluoride upon electron-rich *N*-arylbenzylamines provides a convenient synthesis of phenanthridines. Excess of oxidant can lead to selective hydroxylation of a methyl substituent. Benzylamines with a phosphonate substituent on the methylene group lead to 6-substituted phenanthridines.

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Introduction

Following the introduction of vanadium oxytrifluoride as a reagent for coupling monophenolic[1] and non-phenolic[2] electron-rich aromatic nuclei, it has found utility in the synthesis of several natural products[3,4] as well as in the conversion of substituted stilbenes[5,6] into phenanthrenes.

The phenanthridine ring system[7] represents an aza-analogue of the phenanthrenes, and we envisaged a synthesis based upon an oxidative coupling process starting from readily available imines (Schiff's bases) in place of stilbenes.

Results and Discussion

Addition of vanadium oxytrifluoride as a solution in a mixture of trifluoroacetic acid, dichloromethane, and ethyl acetate* to a solution of the Schiff's base **1a** (Scheme 1), obtained from piperonaldehyde and 2,4-dimethylaniline, resulted merely in a moderate darkening of the original yellowish† solution. Little further change was noted until dilution with water, which caused formation of deeply coloured mixtures.

When the reaction was quenched, piperonaldehyde was recovered accompanied by a complex mixture of coloured oxidation products. Evidently, little reaction had transpired until the mixture was diluted with water, whereupon the Schiff's base hydrolyzed to the precursor aldehyde (inert under these conditions) together with the (susceptible) aniline. The aniline then reacted further to produce a cascade of oxidation products, presumably through the action of vanadium pentoxide or related hydrolyzed V^V species.

In order to dissipate the potentially deactivating effect of the azomethine linkage, **1a** was reduced with dimethylamine borane[8] to the benzylamine **2a**. Reaction with four equivalents of vanadium oxytrifluoride readily effected cyclization with concomitant dehydrogenation to generate the phenanthridine **3a** in 41% yield. In addition, a trace of a more polar phenanthridine was isolated. Although the latter was obtained only in small quantity, the ^{1}H NMR spectrum of this product suggested a phenanthridine in which one of the methyl groups had been selectively converted into a hydroxymethyl group. An attempt was made to convert a purified sample of the phenanthridine **3a** into this putative hydroxymethyl product by further treatment with additional vanadium oxytrifluoride. Negligible reaction occurred and the phenanthridine was recovered unchanged, which suggested that the hydroxylation step occurs with some intermediate species, not the final phenanthridine product. As a result of some cyclizations (see **3j** in the experimental section) carried out during the later stages of this investigation, interest in hydroxymethylation was rekindled, and some variations to the standard experimental procedure were investigated. In these experiments a reversed order of addition was explored, wherein the substrate **2a** was added to more than six equivalents of vanadium oxytrifluoride which was either suspended in dichloromethane/trifluoroacetic acid or dissolved by incorporation of ethyl acetate. Although neither modification enhanced the formation of the presumed hydroxymethylphenanthridine, the yield of the parent phenanthridine was markedly improved from the original

* Vanadium oxytrifluoride has low solubility in solvents with which it does not react, such as trifluoroacetic acid or dichloromethane; the addition of 1–2 moles of ethyl acetate causes a marked increase in solubility, apparently without deleterious effects upon the potency of the reagent.
† An unfavourable portent; successful coupling reactions require initial formation of radical cations whose existence is often indicated by formation of green, blue, or violet species at some stage during the reaction.

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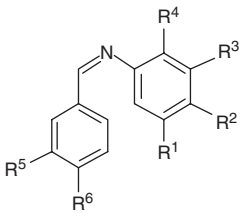

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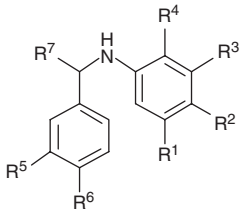

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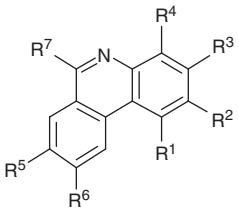

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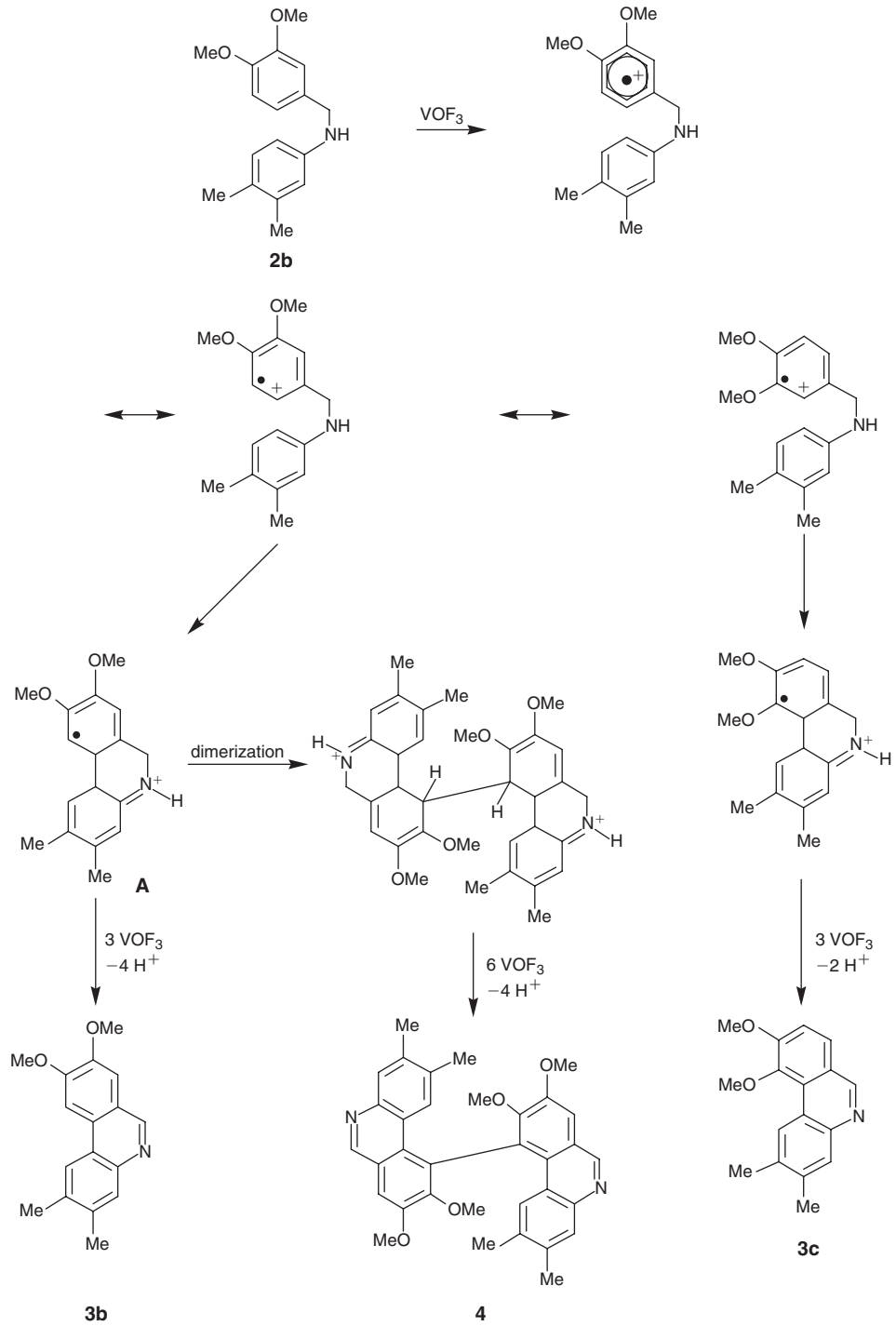
	R^1	R^2	R^3	R^4	R^5	R^6	R^7
1a	H	Me	H	Me	$-OCH_2O-$		H
1b	H	Me	Me	H	OMe	OMe	H
1c	H	CF_3	H	H	OMe	OMe	H
2a	H	Me	H	Me	$-OCH_2O-$		H
2b	H	Me	Me	H	OMe	OMe	H
2c	H	CF_3	H	H	OMe	OMe	H
2d	H	Cl	H	Cl	$-OCH_2O-$		H
2e	H	H	Cl	Cl	OMe	OMe	H
2f	H	Cl	H	Cl	OMe	OMe	H
2g	H	Cl	H	Cl	$-OCH_2O-$		$P(O)(OEt)_2$
2h	H	Me	H	Me	$-OCH_2O-$		$P(O)(OEt)_2$
2i	H	Me	H	Me	$-OCH_2O-$		P(O)(OH)(OEt)
3a	H	Me	H	Me	$-OCH_2O-$		H
3b	H	Me	Me	H	OMe	OMe	H
3c	Me	Me	H	H	OMe	OMe	H
3d	H	CF_3	H	H	OMe	OMe	H
3e	H	Cl	H	Cl	$-OCH_2O-$		H
3f	H	H	Cl	Cl	OMe	OMe	H
3g	H	Cl	H	Cl	OMe	OMe	H
3h	H	Cl	H	Cl	$-OCH_2O-$		$P(O)(OEt)_2$
3i	H	Me	H	Me	$-OCH_2O-$		$P(O)(OEt)_2$
3j	H	CH_2OH	H	Me	$-OCH_2O-$		$P(O)(OEt)_2$

Scheme 1.

41% to 80% or more. It seems likely that the yields from some of the cyclizations described below which were only carried out by the original protocol would have been significantly increased had they been revisited using the methodology of reversed order of addition.

A similar absence of cyclization was observed with the Schiff's base **1b** obtained from the reaction between veratraldehyde and 3,4-dimethylaniline. Once again, prior reduction (with sodium borohydride[9]) to the benzylamine **2b** enabled the cyclization to be carried out successfully. Although a combined yield of approximately 68% of phenanthridine-containing material was obtained, it was distributed between several products. In each of the compounds produced, the site of reaction was consistent with an electrophilic substitution directed by substituent groups on the rings. Thus, coupling of the methoxylated ring of **2b** took place *para*- to a methoxyl group and *ortho*- to the amino substituent in the other ring. In this substrate, the aniline has two *ortho*-positions free to provide potential coupling sites. It is noteworthy that while a majority of the product arose from reaction at the relatively less hindered *ortho*-position to give **3b** (40% yield), a substantial proportion



Scheme 2.

of the coupling nevertheless occurred at the more hindered *ortho*-position, despite two flanking substituents, to give the phenanthridine **3c** in 21% yield. In addition to these isomeric phenanthridines a modest quantity (7%) of an apparently dimeric product (**4**, Scheme 2) was also formed. The small number of peaks observed in the ^{1}H NMR spectrum of **4** argued for formation of a symmetrically coupled product, and the site at which the linkage occurs was assigned on the basis of NOE experiments. Once formed, the phenanthridine nucleus appears to be resistant to further transformation by vanadium oxytrifluoride. Therefore, it is improbable that **4** arises merely from dimerization of the phenanthridine product **3b**. Rather, it seems more likely that the benzylamine **1a** forms a mono-cation radical (**A**, Scheme 2) which dimerizes to an appreciable extent before further conversion into the dication radical can take place.

The synthesis of phenanthridines by cyclization of Schiff's bases appears to be inhibited by the presence of the electron-withdrawing imine bond linking the two rings. This has the effect of depleting the aromatic rings of electron density, and this effect is enhanced by extensive protonation within the highly acidic reaction medium. Consequently, prior oxidation

to a Schiff's base is not likely to be an enabling step on an oxidative path to phenanthridines from *N*-arylbenzylamines. Even so, this unproductive oxidation may still occur as a competing pathway during an otherwise successful cyclization. For example, the trifluoromethyl-substituted benzylamine **2c** gave the phenanthridine **3d** together with substantial quantities of veratraldehyde and 4-trifluoromethylaniline. Presumably these products arise from partial oxidation of **2c** to the imine **1c**, followed by hydrolytic cleavage of the imine to its components during the subsequent aqueous acidic workup. In contrast with the indeterminate products observed with the Schiff's base **1a**, in this instance the regenerated aniline is sufficiently robust to survive the aqueous oxidative medium relatively unscathed.

Vanadium oxytrichloride has electron-abstracting properties similar to the trifluoride, and has also been used to effect coupling between aromatic rings.[12] A brief investigation with *N*-arylbenzylamines which had already been cyclized successfully with the trifluoride usually showed that inferior results were obtained.

Formation of 6-Substituted Phenanthridines

Following a series of successful phenanthridine cyclizations, it was of additional interest to determine whether 6-substituted phenanthridines might be prepared by this procedure since they are less accessible by classic methodology.[7] It was decided that a phosphoryl substituent would offer the challenge of keeping this substituent intact during the vigorous reaction conditions. It had the added attraction that no 6-phosphorylated phenanthridines have been reported and would thus be attractive candidates for biological testing. It is known[10] that phosphites add readily to Schiff's bases and it was expected that, with judicious selection of ring substituents, the resulting benzylamine would be a suitable substrate to test the procedure.

Warming a mixture of piperonaldehyde, 2,4-dichloroaniline, and two equivalents of diethyl phosphite at 85°C for 8 h afforded the phosphonate **2g** as a candidate for cyclization. Gratifyingly, this substituent survived the conditions required for cyclization to give the first example of a 6-phosphono-substituted phenanthridine **3h**, albeit in low yield (16%, based on reacted starting material). The rate-retarding effect of the phosphonate substituent was initially underestimated and under the standard reaction conditions much of the starting material (57%) was recovered. By a similar procedure, fusion of piperonaldehyde, 2,4-dimethylaniline, and two equivalents of diethyl phosphite gave the corresponding diethyl phosphonate **2h**. While phosphonic esters are usually relatively resistant to hydrolysis, it was found that even under these mild reaction conditions a significant quantity of the corresponding monoethyl ester **2i** was isolated, presumably from the action of water generated during the initial condensation. This partially hydrolyzed material was easily separated from the main product **2h** by extraction of the mixture with aqueous sodium carbonate. However, the monoester **2i** failed to give a phosphorylated phenanthridine with vanadium oxytrifluoride and produced only a low yield of the dephosphorylated material **3a**, previously obtained by cyclization of **2a**. On the other hand, the diester **2h** cyclized readily in the presence of a little more than four equivalents of vanadium oxytrifluoride, with retention of the phosphorus substituent, to give the phosphorylated product **3i** in 59% yield. A small amount (8%) of the analogous dephosphorylated phenanthridine **3a** was also recovered.

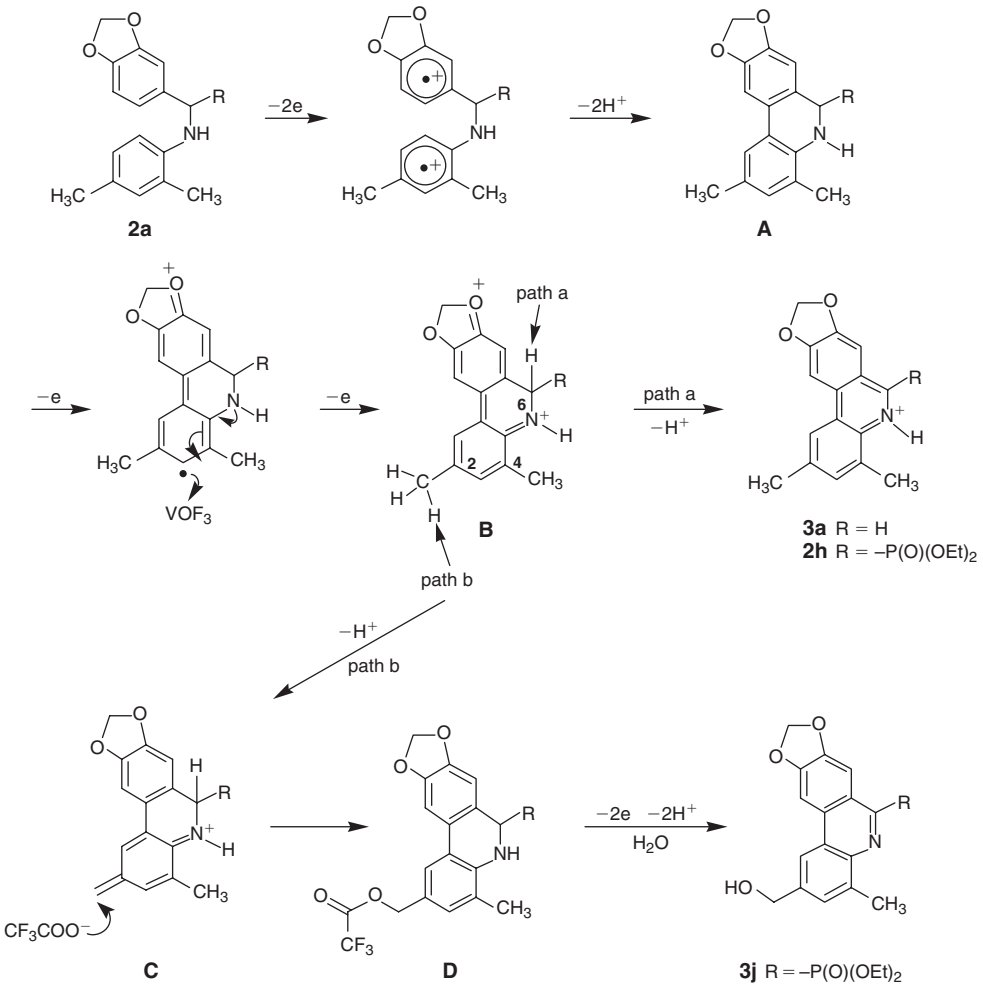
During chromatographic purification of **3i**, traces of what appeared to be a closely related material were isolated. This minor constituent had very similar spectroscopic properties except that one of the original methyl substituents was no longer apparent in the ^{1}H NMR spectrum but was replaced by a methylene group at δ 4.83, apparently as the result of further reaction. Acting on the assumption that this material was most likely to be the result of over-oxidation, we repeated the cyclization using six equivalents of vanadium oxytrifluoride instead of four. In addition to the 2,4-dimethyl product **3i** (22%), a major phenanthridine product **3j** (52%) was obtained in which the 2-methyl group had been selectively hydroxylated. Presumably, during the course of the reaction, in the presence of abundant oxidant, selective trifluoroacetoxylation of the 2-methyl group occurs (see Scheme 3 and related discussion), and the hydroxymethyl product **3j** is the final outcome from hydrolysis of a trifluoroacetate ester during workup in a basic medium.

It is interesting to note that the benzylisoquinoline alkaloid laudanosine has been cyclized with two molar equivalents of vanadium oxytrifluoride to give 4-hydroxyglaucine[11] (40% yield), possibly by a mechanistically related hydroxylation at a benzylic position.

Mechanism and Scope

In the current study, it is unlikely that oxidation to the imine (Schiff's base) is the first step, since attempts to oxidize either the imine **1a** or **1b** failed to produce any phenanthridine product. By contrast, it is noteworthy that some success has been achieved in a vanadium oxytrifluoride mediated synthesis of a benzophenanthridine from the corresponding 1-naphthylamine derived Schiff's base, albeit in 'extremely variable' yields.[13] On the other hand, anodic oxidation, which sometimes gives[14] products resembling those obtained with electron-abstracting inorganic oxidants, failed to give any benzophenanthridine. Interestingly, reduction to the *N*-naphthylbenzylamine followed by anodic oxidation also failed to produce any cyclized material. The effect of vanadium oxytrifluoride on the benzylamine was not reported.[13]

It is generally agreed[15] that cation radicals are formed as reactive intermediates during coupling between aromatic rings during reactions of this type as well as within related electrochemical processes. Despite this knowledge it is usually not possible to decide whether a given coupling has occurred from an initial reaction between an electrophilic cation radical and an aromatic ring or, alternatively, as a result of pairing between two radical cations followed by proton expulsion. As an example, one can speculate upon the processes which may take place during the cyclization of **2a** to give the phenanthridine **3a**. It appears[16] that oxidative coupling of non-phenolic aromatics, either by action of



Scheme 3.

a chemical agent or by an electric current is initiated by removal of an electron from the aromatic sextet of an electron-rich aromatic ring. The ring in which the cation radical has formed (possibly stabilized by complexation with a vanadyl species) may then undergo nucleophilic attack by an unchanged aromatic ring followed by proton expulsion. Oxidation of the resultant radical to a cation followed by another proton loss gives the final product by an ECE (electron abstraction–coupling–electron abstraction) mechanism (for example **2b** to **3b**, Scheme 2). Alternatively, each aromatic nucleus may be converted into a cation radical followed by radical coupling and expulsion of two protons in an EEC process (**2a** to **3a**, Scheme 3). Usually it is difficult to distinguish between these pathways, although the electrochemically induced ECE mechanism may favour intermolecular coupling.[17] Following formation of the electron-rich tetrahydrophenanthridine (**A**; R = H, Scheme 3), sequential removal of two electrons to generate the dicationic species (**B**; R = H, or an equivalent canonical form) seems unexceptional. Elimination of the proton at C6 (**B**, path a) would then lead to the phenanthridine salt (**3a**; R = H).

During some of these cyclizations, small quantities of 2-hydroxymethyl products apparently arise by transformation of an aromatic methyl substituent. This may occur as follows. A minor pathway may be present wherein a proton is abstracted from the intermediate dication (**B**; R = H) at the 2-methyl group (path b, Scheme 3) rather than C6 (path a, Scheme 3) to give **C**. This could then add a trifluoroacetate anion to give the dihydrophenanthridine **D**, which is readily oxidized further to a phenanthridine and then finally hydrolyzed to a benzyl alcohol during the alkaline workup. Notably, cyclization of the phosphonate **2h** led to substantial amounts of a hydroxymethylphenanthridine product **3j**. Previously, it had been found that the addition of vanadium oxytrifluoride in excess of the four equivalents required to form the phenanthridine **3a** did little to affect the trace of the accompanying hydroxymethyl compound. On the other hand, while the phosphonate starting material and four equivalents of oxidant readily gave the phenanthridine **3i** and some (8%) of the 2-hydroxymethyl product **3j**, the addition of six equivalents raised the yield of **3j** to 52%. It may be that the presence of the bulky phosphonate at C6 (Scheme 3) makes deprotonation via path a (**B**, R = P(O)(OEt)$_2$) relatively less ready, allowing path b (**B**, R = P(O)(OEt)$_2$) to assume a dominant role in this instance.

An attempt was made to verify the intervention of a mechanism where a potentially reversible C–H dissociation such as the one implied in Scheme 3, path b, might occur.

Thus, the cyclization of **2a** was reinvestigated but using a solution in deuterated trifluoroacetic acid rather than trifluoroacetic acid. However, no appreciable loss or diminution of any of the previously observed ^{1}H NMR signals indicating incorporation of deuterium in the product, **3a**, was seen.

As successful cyclization is dependent upon removal of an electron from an aromatic sextet, the synthesis is limited to aromatic nuclei which are relatively electron rich in order to achieve a necessary minimum ionization potential, a value probably[16] in the order of +1.2 V. This requirement can be readily accommodated by the presence of two alkoxy groups or by an amino substituent on one ring. In the latter instance, some mild electron-withdrawing substituents may then be tolerated on the same ring as shown by the cyclization of **2c**–**2f** to form **3d**–**3g**.

Experimental

Melting points were determined on a Reichert Kofler hot-stage micro-melting point apparatus and are uncorrected. Microanalyses were performed by Campbell Microanalytical Laboratory, University of Otago, New Zealand. Infrared spectra were recorded on a Perkin Elmer 842 spectrophotometer using KBr disks. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50.3 MHz respectively on a Bruker AC-200 spectrometer, or at 250 and 62.9 MHz on a Bruker AC250 instrument. Phosphorus NMR spectra were recorded relative to 85% phosphoric acid as an external standard. Chemical shifts (δ) are measured in ppm. High-resolution chemical ionization mass spectra were obtained on a Jeol JMS-DX303 mass spectrometer. Low-resolution mass spectra were recorded on a Fisons Instruments VG Platform quadrupole using either atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI) in the positive and/or negative ion mode with a cone voltage of 30 eV for both APCI and ESI, with either 1 : 1 acetonitrile/water or methanol as solvent. Radial thin-layer chromatography was performed on a Harrison Research Chromatotron (7924T) using 4-mm thick silica plates (silica gel 60 PF254, Merck No. 7749). Light petroleum refers to the fraction with a bp of 40–60°C. Trifluoroacetic acid, when used for NMR, was in a 10% concentration v/v in $CDCl_3$.

(Benzo[1,3]dioxol-5-ylmethylene)(2,4-dimethylphenyl)amine ***1a***

Piperonaldehyde and 2,4-dimethylaniline in equimolar quantities were heated under reflux in benzene for 4 h and the solution was evaporated under reduced pressure. Recrystallization of the residue from isopropyl alcohol gave the *product* as pale yellow prisms, mp 67–68°C (Found: C 76.0, H 6.3, N 5.6. $C_{16}H_{15}NO_2$ requires C 75.8, H 6.0, N 5.5%). δ_H ($CDCl_3$) 2.34 (6H, s, 2 Me), 6.04 (2H, s, CH_2), 6.8–7.3 (5H, m, 5 ArH), 7.59 (1H, s, ArH) 8.25 (1H, s, ArH).

Reaction of ***1a*** *with Vanadium Oxytrifluoride*

The Schiff's base **1a** (1.3 g, 5.1 mmol) was dissolved in a mixture of trifluoroacetic acid (4 mL) and dichloromethane (6 mL) at 0°C and treated with a solution of vanadium oxytrifluoride (1.3 g, 10.5 mmol) dissolved in a mixture of ethyl acetate (3 mL) and trifluoroacetic acid (7 mL). The orange solution was stirred at 0°C for 30 min and then at room temperature for 30 min without any significant change in colour. It was then stirred into a mixture of 5% aqueous citric acid (50 mL) and dichloromethane (10 mL) at 0°C. An orange-yellow mixture was observed briefly which rapidly changed to red then purple, particularly within the dichloromethane layer. After 5 min, examination of the dichloromethane phase by TLC showed no significant amount of phenanthridine; only piperonaldehyde and a highly coloured polar material were evident.

(3,4-Dimethoxybenzylidene)(3,4-dimethylphenyl)amine ***1b***

This was recrystallized from ethanol to give the *product* as pale yellow needles, mp 123–124°C (Found: C 75.6, H 7.0, N 5.5. $C_{17}H_{19}NO_2$ requires C 75.8, H 7.1, N 5.2%). δ_H ($CDCl_3$) 2.27, 2.29 (each 3H, each s, 2 Me), 3.95, 3.99 (each 3H, each s, 2 OMe), 6.92 (1H, d, *J* 8.0, ArH), 7.0–7.4 (4H, m, 4 ArH), 7.63 (br s, ArH), 8.38 (1H, s, ArH). This Schiff's base failed to give any phenanthridine product when treated with vanadium oxytrifluoride.

(Benzo[1,3]dioxol-5-ylmethyl)(2,4-dimethylphenyl)amine ***2a***

Method A

Dimethylamine borane (1 g, 17.0 mmol) was added to a solution of piperonaldehyde (3.0 g, 20.0 mmol) and 2,4-dimethylaniline (2.4 g, 19.8 mmol) in acetic acid (20 mL) with cooling to maintain the temperature at less than 25°C. The solution was stirred until it became colourless, heated on a steam bath (2 min), and diluted with water to a faint turbidity. When the mixture had cooled, the crystalline precipitate was collected by filtration and recrystallized from isopropyl alcohol to give the *product* (4.1 g, 80%) as colourless blades, mp 98–99°C (Found: C 75.1, H 6.7, N 5.6. $C_{16}H_{17}NO_2$ requires C 75.3, H 6.7, N 5.5%). δ_H ($CDCl_3$) 2.14, 2.23 (each 3H, each s, 2 Me), 4.26 (2H, s, CH_2), 5.9 (2H, s, OCH_2O), 6.52 (1H, d, *J* 8.8, ArH), 6.76–6.91 (5H, m, 5 ArH).

Method B

A mixture of piperonaldehyde (16.5 g, 0.11 mol) and 2,4-dimethylaniline (12.1 g, 0.10 mol) was heated at 100°C for 3 h in an open flask. The cooled mixture was dissolved in methanol (180 mL) at 40°C, sodium borohydride (4.0 g, 0.11 mol) was added in portions, and the temperature of the mixture raised to 60°C for 2 h. The mixture was cooled, water (300 mL) added, and the precipitate collected by filtration. The crude product was stirred with a mixture of ether (100 mL) and aqueous hydrochloric acid (2 M, 100 mL). The aqueous solution and the ethereal layer were separated from an oily material at the interface and the ether solution was re-extracted with hydrochloric acid (2 M, 2 × 50 mL). The oil was dissolved in ethyl acetate (100 mL), which was further extracted with hydrochloric acid (2 M, 100 mL). The combined aqueous extracts were neutralized by the addition of sodium bicarbonate, and the precipitate was collected and recrystallized from isopropyl alcohol to give colourless needles identical with the product obtained above (14.9 g, 53%).

The following benzylamines were obtained by in-situ preparation of the Schiff's bases followed by reduction (method B).

(3,4-Dimethoxybenzyl)(3,4-dimethylphenyl)amine ***2b***

Veratraldehyde (3.3 g, 0.02 mol) and 3,4-dimethylaniline (2.4 g, 0.02 mol) were heated together at 100°C for 4 h. Addition of ethanol (80 mL) followed by sodium borohydride (1 g, 0.026 mol) gave the *product* (4.1 g, 76%) as colourless needles, mp 115–116°C, from isopropyl alcohol (Found: C 75.3, H 7.9, N 5.2. $C_{17}H_{21}NO_2$ requires C 75.3, H 7.8, N 5.2%). δ_H ($CDCl_3$) 2.18, 2.21 (each 3H, each s, 2 Me), 3.79 (1H, m, N*H*CH_2), 3.89 (each 3H, s, 2 OMe), 4.2 (2H, d, *J* 5.4, NHC*H*$_2$), 6.6–7.0 (6H, m, 6 ArH).

(3,4-Dimethoxybenzyl)(4-trifluoromethylphenyl)amine ***2c***

This was recrystallized from isopropyl alcohol to give the *product* as colourless prisms (58%), mp 99–101°C (Found: C 61.9, H 5.3, N 4.6. $C_{16}H_{16}F_3NO_2$ requires C 61.7, H 5.2, N 4.5%). δ_H ($CDCl_3$) 3.86, 3.87 (each 3H, each s, 2 OMe), 4.29 (2H, s, CH_2), 4.45 (1H, br s, NH), 6.64 (2H, d, *J* 8.8, 2 ArH), 6.82–6.94 (3H, m, 3 ArH), 7.39 (2H, d, *J* 8.8, 2 ArH).

(Benzo[1,3]dioxol-5-ylmethyl)(2,4-dichlorophenyl)amine ***2d***

This was obtained by heating piperonaldehyde (4.5 g, 0.03 mol) with 2,4-dichloroaniline (4.9 g, 0.03 mol) followed by reduction with sodium borohydride (2 g, 0.053 mol) in ethanol to afford the *product* (5.4 g, 61%) as colourless needles from isopropyl alcohol, mp 63–64°C (Found: C 56.7, H 3.6, N 4.6%. $C_{14}H_{11}Cl_2NO_2$ requires C 56.8, H 3.7, N 4.7%). δ_H ($CDCl_3$) 4.28 (2H, s, CH_2N), 5.96 (2H, s, OCH_2O), 6.56 (1H, d, *J* 8.8, ArH), 6.78–6.82 (3H, m, 3 ArH), 7.04 (1H, dd, *J* 2.2, ArH), 7.26 (1H, d, *J* 2.2, ArH).

By Method A

Dimethylamine borane (1.3 g, 0.022 mol) was added in portions (0.2 g) over 1 h to a solution of piperonaldehyde (6.0 g, 0.04 mol) and 2,4-dichloroaniline (6.5 g, 0.04 mol) in acetic acid (25 mL) maintained at 20°C. After standing the solution for 2 h, colourless needles began to separate and the whole was left overnight. The next day, the mixture was diluted slowly with water (50 mL), and the solid collected by filtration and recrystallized from ethanol to give colourless needles (8.7 g, 72%) identical with the compound prepared above.

(2,3-Dichlorophenyl)(3,4-dimethoxybenzyl)amine ***2e***

This was recrystallized from cyclohexane to give the *product* as colourless prisms (17.5 g, 56%), mp 110–111°C (Found: C 57.5, H 4.9, N 4.5. $C_{15}H_{15}Cl_2NO_2$ requires C 57.7, H 4.8, N 4.5%). δ_H ($CDCl_3$) 3.88 (6H, s, 2 OMe), 4.33 (2H, s, CH_2), 6.54 (1H, dd, *J* 1.5, 8.1, ArH), 6.79 (1H, dd, *J* 2.4, 8.1, ArH), 6.86–7.06 (4H, m, 4 ArH).

(2,4-Dichlorophenyl)(3,4-dimethoxybenzyl)amine ***2f***

This was recrystallized from light petroleum to give the *product* as colourless prisms (29%), mp 62–64°C (Found: C 57.7, H 5.0, N 4.4. $C_{15}H_{15}Cl_2NO_2$ requires C 57.7, H 4.8, N 4.5%). δ_H ($CDCl_3$) 3.87 (6H, s, 2 OMe), 4.31 (2H, s, CH_2), 6.56 (1H, d, *J* 8.8, ArH), 6.84–6.92 (3H, m, 3 ArH), 7.05 (1H, dd, *J* 2.5, 8.8, ArH), 7.27 (1H, d, *J* 2.5, ArH).

Diethyl [Benzo[1,3]dioxol-5-yl-(2,4-dichlorophenylamino)methyl]phosphonate ***2g***

A mixture of piperonaldehyde (1.5 g, 0.01 mol), 2,4-dichloroaniline (1.6 g, 0.01 mol), and diethyl phosphite (2.8 g, 0.02 mol) was heated at 80°C for 8 h, and then cooled, dissolved in ether (60 mL), and washed with water (3 × 50 mL). The ether solution was evaporated to give a light brown oil which began to crystallize after several hours. The material was collected and recrystallized from benzene to give the *product* (2.7 g, 62%) as fawn needles, mp 110–111°C (Found: C 50.2, H 4.6, N 3.6. $C_{18}H_{20}Cl_2NO_5P$ requires C 50.0, H 4.7, N 3.3%). δ_H ($CDCl_3$) 1.21, 1.29 (each 3H, each t, *J* 7.3, 2 CH_2Me), 3.7–4.2 (4H, m, 2 CH_2Me), 4.64 (1H, d, *J* 24.2, CH), 5.24 (1H, br s, NH), 5.94 (2H, dd, *J* 1.4, 2.6, OCH_2O), 6.37 (1H, d, *J* 8.8, ArH), 6.74 (1H, d, *J* 8.8, ArH), 6.75–7.0 (3H, m, 3 ArH), 7.25 (1H, d, *J* 2.2, ArH).

Diethyl [Benzo[1,3]dioxol-5-yl-(2,4-dimethylphenylamino)methyl]phosphonate ***2h*** *and Ethyl [Benzo[1,3]dioxol-5-yl-(2,4-dimethylphenylamino)methyl]phosphonate* ***2i***

A mixture of piperonaldehyde (6.5 g, 0.04 mol) and 2,4-dimethylaniline (4.8 g, 0.04 mol) in diethyl phosphite (11.4 g, 0.082 mol) was heated at 80°C for 10 h and then stirred into water (100 mL). The mixture was allowed to cool and the supernatant liquid was decanted from a tarry residue that was dissolved in isopropyl alcohol (35 mL). The solution was treated dropwise with water until a faint turbidity appeared, and then stirred at room temperature for 48 h to afford a colourless precipitate which was collected to yield the crude phosphonate diethyl ester (5.3 g). The filtrate was diluted with water (200 mL) and extracted with ether (100 mL), which was then extracted with aqueous sodium carbonate (7%, 2 × 40 mL). The aqueous extract was acidified with concentrated hydrochloric acid. The precipitated oil was collected by extraction with ether (2 × 50 mL), which was then removed by evaporation to afford the *phosphonic acid monoethyl ester* **2i** as a red-brown oil (5.5 g, 38%) that hardened to a glass (Found: *m/z* 364.1318. $C_{18}H_{22}NO_5P \cdot H^+$ requires 364.1308). δ_H ($CDCl_3$) 1.16 (3H, t, *J* 7.3, CH_2Me), 2.20, 2.24 (each 3H, each s, 2 ArMe), 3.37–3.39 (2H, m, CH_2Me), 4.56 (1H, d, *J* 22.6, CHP) 6.43 (2H, br s, OCH_2O), 6.3–6.9 (6H, m, 6 ArH), 9.05 (2H, br, NH and OH). δ_P ($CDCl_3$) 20.5 (d, *J* 0.22).

The ether solution remaining after the sodium carbonate extraction was evaporated and the residue stirred with aqueous isopropyl alcohol to afford a further quantity of the phosphonate diethyl ester (3.4 g) which was combined with the first crop obtained above and recrystallized from benzene to afford the *phosphonic acid diethyl ester* **2h** (7.1 g, 45%) as colourless prisms, mp 81–82°C (Found: C 61.5, H 6.6, N 3.6. $C_{20}H_{26}NO_5P$ requires C 61.4, H 6.7, N 3.5%). δ_H ($CDCl_3$) 1.18, 1.29 (each 3H, each t, *J* 7.3, 2 CH_2Me), 2.18, 2.23 (each 3H, each s, 2 Me), 3.6–4.2 (4H, m, 2 CH_2Me), 4.65 (1H, d, *J* 24.1, CH), 5.93 (2H, dd, *J* 1.5, 4.4, OCH_2O), 6.41 (1H, d, *J* 8.4, ArH), 6.7–7.0 (5H, m, 5 ArH).

*2,4-Dimethyl-[1,3]dioxolo[4,5-*j*]phenanthridine* ***3a***

A solution of the benzylamine **2a** (4.74 g, 0.018 mol) in a mixture of trifluoroacetic acid/dichloromethane (1 : 1, 40 mL) was cooled to −20°C (internal temperature) and treated with a solution of vanadium oxytrifluoride (10.3 g, 0.083 mol) in a mixture of dichloromethane (20 mL), trifluoroacetic acid (20 mL), and ethyl acetate (10 mL). After 5 min, TLC showed a partial reaction, and stirring was continued at −10°C for 15 min. The reaction mixture was poured into a mixture of aqueous citric acid (10%, 100 mL), aqueous sodium metabisulfite (10%, 100 mL), and ice (100 g). After stirring for 15 min, the mixture was chilled and adjusted to pH 8 by the addition of concentrated aqueous ammonia. The organic solvents were allowed to evaporate, and the solid was collected by filtration and stirred with dichloromethane (200 mL), leaving behind some insoluble residue. The solution was filtered, the solvent was removed by evaporation, and the residue was chromatographed upon silica gel using dichloromethane as the initial eluant and progressing to dichloromethane/ethyl acetate (1 : 1). Early fractions returned unchanged benzylamine (0.93 g, 0.004 mol), while crude phenanthridine was obtained by combining the more polar fractions. Evaporation followed by recrystallization of the residual material from ethyl acetate/light petroleum gave the *title compound* as colourless needles (1.96 g, 41%), mp 186–188°C with prior sublimation from 165°C (Found: C 76.6, H 5.2, N 5.6. $C_{16}H_{13}NO_2$ requires C 76.5, H 5.2, N 5.6%). δ_H ($CDCl_3$) 2.57, 2.83 (each 3H, each s, 2 Me), 6.16 (2H, s, CH_2), 7.32, 7.39, 7.89, 8.01 (each 1H, each s, 4 ArH), 9.08 (1H, s, CH=N). δ_C ($CDCl_3$) 18.6, 21.8, 99.8, 101.7, 105.0, 119.3, 122.8, 123.9, 130.0, 130.5, 135.8, 137.1, 141.2, 147.5, 149.4, 150.9.

A later crude fraction (15 mg) had a ^{1}H NMR spectrum suggestive of a monohydroxylated product. δ_H ($CDCl_3$) 2.20 (1H, br, CH_2OH), 2.83 (3H, s, Me), 4.89 (2H, s, CH_2OH), 6.15 (2H, s, OCH_2O), 7.29 (1H, s, ArH), 7.51, 7.82 (each 1H, br s, 2 ArH), 9.05 (1H, s, CH=N).

An attempt to generate the hydroxymethyl compound from the phenanthridine **3a** by treatment with additional vanadium oxytrifluoride returned unchanged phenanthridine.

Preparation of ***3a*** *by Reverse Addition—to Vanadium Oxytrifluoride in Suspension*

A solution of the benzylamine **2a** (1.0 g, 0.004 mol) in a mixture of dichloromethane (5 mL) and trifluoroacetic acid (5 mL) was stirred into a suspension of vanadium oxytrifluoride (3.9 g, 0.31 mol) in a mixture of dichloromethane (5 mL) and trifluoroacetic acid (5 mL) at 0°C. After 15 min, the yellow-green suspension was stirred into a mixture of D-tartaric acid (10 g), sodium metabisulfite (5 g), and ice/water (100 g), and basified after 10 min to pH 9–10 by addition of concentrated ammonium hydroxide. The product was extracted into dichloromethane (2 × 100 mL), and the extract was washed with water and evaporated to dryness to afford a solid which was recrystallized from ethyl acetate to give the phenanthridine (0.79 g, 80%) as colourless needles, mp 187–188°C, identical with the material **3a** prepared above.

Preparation of ***3a*** *by Reverse Addition—to Vanadium Oxytrifluoride in Solution*

The reaction was carried out with the benzylamine **2a** (1.0 g, 0.004 mol) as in the previous experiment, except that complete dissolution of the vanadium oxytrifluoride (4.0 g, 0.032 mol) was effected by prior addition of ethyl acetate (4 mL) to the mixture of dichloromethane (5 mL) and trifluoroacetic acid (5 mL). The reaction gave a homogeneous deep green-brown solution which was worked up in the usual way. Recrystallization of the residue from aqueous ethanol gave the phenanthridine as colourless needles (0.83 g, 83%), mp 186–188°C, identical with the material **3a** prepared above.

*8,9-Dimethoxy-2,3-dimethylphenanthridine **3b**, 8,9-Dimethoxy-1,2-dimethylphenanthridine hydrochloride **3c**, and 8,9,8′,9′-Tetramethoxy-2,3,2′,3′-tetramethyl-[10,10′]biphenanthridine **4***

A solution of the benzylamine **2b** (4.6 g, 0.017 mol) in a mixture of dichloromethane (20 mL) and trifluoroacetic acid (20 mL) was cooled to −20°C while a solution of vanadium oxytrifluoride (9.3 g, 0.075 mol) in a mixture of dichloromethane (5 mL), trifluoroacetic acid (20 mL), and ethyl acetate (10 mL) was added in a thin stream. Following completion of the addition, the cooling bath was removed and the mixture was warmed to 20°C over 15 min and then stirred into a mixture of aqueous citric acid (20%, 100 mL) and ice (100 g). After 10 min, the stirred mixture was kept at a temperature of 10°C and made slightly alkaline by the addition of concentrated ammonia. The mixture was extracted with dichloromethane (2 × 200 mL) and the combined extracts were evaporated under reduced pressure to give a light brown solid (4.6 g). The solid was boiled with methanol (200 mL) for 10 min, cooled, and the *product* **4** was collected as a colourless powder by filtration (0.36 g, 7%), mp > 270°C (Found: C 76.1, H 6.1, N 5.1. $C_{34}H_{32}N_2O_4 \cdot 0.25H_2O$ requires C 76.0, H 6.1, N 5.2%). δ_H ($CDCl_3$) 2.54 (6H, s, 2 Me), 2.96 (6H, s, 2 Me), 3.95, 4.06 (each 6H, each s, 4 OMe), 7.18, 7.53, 8.16 (each 2H, each s, 6 ArH), 8.82 (1H, s, CH=N). δ_C ($CDCl_3$) 21.3, 21.8, 55.9, 56.0, 107.7, 108.4, 123.0, 124.4, 128.8, 131.3, 132.3, 135.3, 138.4, 142.7, 148.6, 150.2, 150.8. *m/z* ($APCI^+$) 533 (M + 1). The assigned structure was supported by NOE experiments, which revealed the following interactions.

Irradiation of each methyl (at δ 2.54 and 2.96) independently resulted in an equal response from two aromatic protons (δ 7.53 and 8.16 respectively). Irradiation of one of the aromatic protons (δ 7.18) showed an interaction with the CH adjacent to the N (δ 8.82), as well as one of the methoxyls (δ 3.95). Irradiation of the CH adjacent to the N (δ 8.82) resulted in a single interaction with one aromatic H (δ 7.18), which had been previously demonstrated to be adjacent to one of the methoxyls (δ 3.95).

The filtrate was evaporated, the residue was dissolved in a mixture of dichloromethane (40 mL) and methanol (10 mL), diluted with ethyl acetate (15 mL), and the temperature raised to boiling point. Solvent was allowed to evaporate until a volume of 50 mL was reached, and evaporation by boiling was continued with a constant volume being maintained by the periodic addition of ethyl acetate. After 1 h, the mixture was allowed to cool, was filtered, and the precipitate was washed lightly with ethyl acetate to give a fawn powder which was recrystallized from ethanol to afford the *product* **3b** as cream needles (1.87 g, 40%), mp 222–224°C (Found: C 76.2, H 6.4, N 5.2. $C_{17}H_{17}NO_2$ requires C 76.4, H 6.4, N 5.2%). δ_H ($CDCl_3$/CF_3COOH) 2.42 (3H, s, ArMe), 2.53 (3H, s, ArMe), 4.02 (3H, s, OMe), 4.24 (3H, s, OMe), 7.30, 7.80, 7.89, 8.14 (each 1H, each s, 4 ArH), 9.31 (1H, s, CH=N). δ_C ($CDCl_3$) 19.9, 20.0, 55.8, 55.9, 101.2, 107.4, 121.2, 121.4, 121.6, 127.6, 129.6, 135.8, 137.1, 142.5, 149.2, 150.5, 152.4.

The mother liquors were evaporated, the residue was dissolved in hot methanol (40 mL), and concentrated hydrochloric acid (1.4 mL) was added dropwise to give a pale yellow precipitate. Water (10 mL) was added, the mixture was simmered for 2 h, and left to cool. The next day, the precipitate (1.44 g) was collected as a pale yellow crystalline solid (still containing approximately 15% of the other isomer). The hydrochloride was recrystallized from formic acid/methanol (1 : 4) to give pale yellow needles of *8,9-dimethoxy-1,2-dimethylphenanthridine hydrochloride* **3c** (1.09 g, 21%), mp 238–241°C (Found: C 66.9, H 6.1, N 4.7. $C_{17}H_{18}ClNO_2$ requires C 67.2, H 6.0, N 4.6%). δ_H ($CDCl_3$/CF_3COOH) 2.66 (3H, s, ArMe), 3.06 (3H, s, ArMe), 4.15 (3H, s, OMe), 4.24 (3H, s, OMe), 7.26 (1H, s, ArH), 7.78 (1H, d, *J* 8.1, ArH) 8.08 (1H, d, *J* 8.1, ArH), 8.35 (1H, s, ArH), 9.45 (1H, d, *J* 1.9, C*H*=NH^+). δ_C ($CDCl_3$/CF_3COOH) 20.8, 21.7, 56.4, 56.6, 108.1, 110.7, 111.6, 117.2, 118.9, 120.5, 132.0, 133.4, 133.9, 140.8, 144.6, 150.5, 157.1. For NOE studies, a portion of the hydrochloride salt was converted into the free base by shaking it with a mixture of aqueous sodium carbonate and deuterated chloroform. δ_H ($CDCl_3$) 2.54, 2.92, 4.04, 4.06 (each 3H, each s, 2 ArMe, 2 OMe), 7.33 (1H, s, ArH), 7.49 (1H, d, *J* 8.2, ArH), 7.93 (1H, d, *J* 8.2, ArH), 8.13 (1H, s, ArH), 9.02 (1H, C*H*=N). The location of the substituents in **3c** was confirmed by the following NOE interactions. Irradiation of the aromatic singlet at δ 7.33 resulted in an interaction with the CH adjacent to the N (δ 9.02) and one of the methoxyl groups (δ 4.04). Irradiation of the other aromatic singlet (at δ 8.13) gave an interaction with the other OMe (δ 4.06) and a smaller interaction with one of the methyl groups (δ 2.92) from the other ring. Irradiation of one of the methyls (δ 2.54) showed an interaction with one of the aromatic ab pairs (δ 7.49). Irradiation of the other methyl (δ 2.92) showed an interaction with the other methyl and one of the proton singlets (δ 8.13) from the other ring but not with the aromatic ab doublet.

Irradiation of both methoxyls resulted in an interaction with each of the aromatic singlets but was without any effect upon the ab pair.

*8,9-Dimethoxy-2-trifluoromethylphenanthridine **3d***

A solution of the benzylamine **1c** (1.2 g, 3.8 mmol) in dichloromethane/trifluoroacetic acid (1 : 1, 10 mL) at −30°C was treated with a solution of vanadium oxytrifluoride (1.9 g, 15.3 mmol) in ethyl acetate/trifluoroacetic acid (1 : 2, 12 mL). After 10 min, the mixture was worked up as in **3a** and the residue chromatographed over silica gel. Elution with dichloromethane/light petroleum (1 : 1) progressing to dichloromethane/ethyl acetate (1 : 1) successively eluted 4-trifluoromethyl aniline (75 mg) and veratraldehyde (220 mg) followed by crude phenanthridine which was recrystallized from ethanol to give the *product* as colourless needles (0.62 g, 52%), mp 164–166°C (Found: C 62.5, H 3.9, N 4.5. $C_{16}H_{12}F_3NO_2$ requires C 62.5, H 3.9, N 4.6%). δ_H ($CDCl_3$) 4.07, 4.16 (each 3H, each s, 2 OMe), 7.34 (1H, s, ArH), 7.79 (1H, s, ArH), 7.83 (1H, dd, *J* 1.1, 8.0, ArH), 8.20 (1H, d, *J* 8.0, ArH), 8.62 (1H, br s, ArH), 9.18 (1H, s, CH=N). δ_C ($CDCl_3$) 56.0, 56.3, 101.4, 107.7, 119.3, 121.8, 123.4, 124.8 (q, *J* 61), 127.6, 128.2, 130.8, 130.9, 145.1, 150.4, 153.2, 153.5. *m/z* ($APCI^+$) 308 (M + 1).

*2,4-Dichloro-8,9-methylenedioxyphenanthridine **3e***

The benzylamine **2d** (4.4 g, 0.015 mol) in dichloromethane (20 mL) and trifluoroacetic acid (20 mL) was cooled to −20°C and a solution of vanadium oxytrifluoride (9.1 g, 0.073 mol) in a mixture of trifluoroacetic acid (20 mL) and ethyl acetate (10 mL) was added over 5 min. The mixture was allowed to attain room temperature during the next 20 min and then stirred into aqueous citric acid (20%, 100 mL) and ice (100 g). The mixture was stirred and kept at <15°C during the addition of concentrated ammonium hydroxide to pH 8. Dichloromethane (100 mL) was added to the mixture, which was then stirred overnight and filtered. The solid was washed on the filter with water and dichloromethane to give the *product* **3e** (2.5 g, 58%), and a portion was obtained as needles from *N*,*N*-dimethylformamide, mp > 280°C (Found: C 57.4, H 2.3, N 4.9. $C_{14}H_7Cl_2NO_2$ requires C 57.6, H 2.4, N 4.8%). δ_H ($CDCl_3$/CF_3COOH) 6.44 (2H, s, CH_2), 7.73 (1H, s, ArH), 8.01 (1H, d, *J* 2.2, ArH), 8.05 (1H, s, ArH), 8.51 (1H, d, *J* 2.2, ArH), 9.45 (1H, s, C*H*=NH^+). δ_C ($CDCl_3$/CF_3COOH) 101.4, 104.8, 108.0, 121.6, 121.9, 123.1, 126.6, 126.8, 127.5, 131.8, 135.0, 136.5, 146.8, 152.0. *m/z* ($APCI^+$) 292 (M + 1).

*3,4-Dichloro-8,9-dimethoxyphenanthridine **3f***

Vanadium oxytrifluoride (1.6 g, 0.013 mol) dissolved in a mixture of trifluoroacetic acid (10 mL) and ethyl acetate (5 mL) was added to the benzylamine **2e** (1.0 g, 0.0032 mol) in trifluoroacetic acid/dichloromethane (1 : 1, 10 mL) maintained at 0°C. After 30 min, the mixture was worked up as in **3a**. The residue was stirred with ethanol (50 mL) to recover starting material (300 mg was obtained from the ethanol solution) and the residue was crystallized from dichloromethane to yield *the product* **3f** as fawn needles (450 mg, 69%), mp 251–252°C (with prior sublimation from 230°C) (Found: C 58.4, H 3.6, N 4.6. $C_{15}H_{11}Cl_2NO_2$ requires C 58.5, H 3.6, N 4.6%). δ_H ($CDCl_3$/CF_3COOH) 4.17 (3H, s, Me), 4.33 (3H, s, Me), 7.83 (1H, s, ArH), 8.05 (1H, d, *J* 9.14, ArH), 8.09 (1H, s, ArH), 8.65 (1H, d, *J* 9.14, ArH), 9.62 (1H, s, C*H*=NH^+). δ_C ($CDCl_3$/CF_3COOH) 56.4, 57.1, 102.6, 110.1, 119.6, 122.3, 122.5, 123.8, 124.2, 129.7, 131.2, 133.6, 136.7, 147.0, 152.7. *m/z* ($APCI^+$) 308 (M + 1).

*2,4-Dichloro-8,9-dimethoxyphenanthridine **3g***

The benzylamine **2f** (0.81 g, 2.6 mmol) in trifluoroacetic acid/ethyl acetate (2 : 1, 15 mL) at 0°C was treated with vanadium oxytrifluoride (1.42 g, 11.4 mmol) dissolved in trifluoroacetic acid/ethyl acetate (1 : 1, 10 mL) After 15 min, the mixture was worked up in the usual way and the mixture was extracted with dichloromethane. Following evaporation of the solvent, the residue was recrystallized from ethanol/dichloromethane to afford the *product* **3g** as colourless needles (0.38 g, 51%), mp 227–228°C (with prior sublimation) following crystallization from ethanol/dichloromethane (Found: C 58.4, H 3.6, N 4.6. $C_{15}H_{11}Cl_2NO_2$ requires C 58.5.0, H 3.6, N 4.6%). δ_H ($CDCl_3$/CF_3COOH) 4.09 (3H, s, ArMe), 4.15 (3H, s, ArMe), 7.36 (1H, s, ArH), 7.71 (1H, s, ArH), 7.75 (1H, d, *J* 2.2, ArH), 8.26 (1H, d, *J* 2.2, ArH), 9.21 (1H, s, C*H*=NH$^+$). δ_C ($CDCl_3$/CF_3COOH) 56.6, 57.3, 102.8, 110.6, 111.9, 117.6, 120.1, 121.7, 126.2, 127.1, 127.5, 131.5, 132.1, 136.2, 147.3. *m*/*z* (APCI$^+$) 308 (M + 1).

*Reaction of **2b** with Vanadium Oxytrichloride*

Reaction of 3,4-dimethoxybenzyl-(3,4-dimethylphenyl)amine **2b** (4.6 g, 14.7 mmol) with vanadium oxytrichloride (12.9 g, 0.104 mmol) instead of the trifluoride in the manner described above gave 8,9-dimethoxy-2,3-dimethylphenanthridine (1.60 g, 35%), mp 222–224°C, identical with the product **3b** obtained in the earlier experiment. Neither of the other two products, **3c** and **4**, obtained previously were found in isolable quantities.

*Diethyl 2,4-dichloro-[1,3]dioxolo[4,5-*j*]phenanthridin-6-yl)-phosphonate **3h***

The phosphonate **2g** (4.0 g, 9.2 mmol) was dissolved in dichloromethane/trifluoroacetic acid (1 : 1, 40 mL), cooled to −30°C, and a solution of vanadium oxytrifluoride (5.4 g, 43.6 mmol) dissolved in a mixture of trifluoroacetic acid (15 mL) and ethyl acetate (7 mL) was added in a thin stream over 2 min. After 10 min, the mixture was worked up in the usual way. Extraction with dichloromethane (2 × 50 mL), followed by evaporation of solvents gave a reddish gum (4.1 g) which was stirred with ether (40 mL). The precipitate was collected and recrystallized as needles from methanol to afford the *product* **3h** (0.65 g, 16%), based on unrecovered starting material, mp 222–224°C (Found: C 50.6, H 3.6, N 3.2. $C_{18}H_{16}Cl_2NO_5P$ requires C 50.5, H 3.8, N 3.3%). δ_H ($CDCl_3$) 1.45 (6H, t, *J* 7.7, 2 CH_2*Me*), 4.4–4.6 (4H, m, 2 C*H*$_2$Me), 6.21 (2H, s, OCH_2O), 7.77 (1H, d, *J* 1.8, PCC=CH), 7.81 (1H, d, *J* 2.2, ArH), 8.25 (1H, d, *J* 2.2, ArH), 8.36 (1H, s, ArH). δ_C ($CDCl_3$) 16.4 (d, *J* 5.5 Hz), 64.1 (d, *J* 7.2), 100.1, 102.5, 105.5, 120.5, 124.7 (d, *J* 30.1, *C*CP), 126.8 (d, *J* 2.9), 128.8, 129.7 (d, *J* 10.2), 133.7, 136.5, 137.6 (d, *J* 26.8, PC=N*C*), 149.4, 151.9, 152.7 (d, *J* 222.7, N=CP). (The principal phosphorus–carbon coupling values are assigned on the basis of proximity to the phosphorus atom; minor couplings are unassigned.) The filtrate was evaporated and chromatographed over silica to recover starting material (2.3 g).

*Reaction of Benzo[1,3]dioxol-5-yl-(2,4-dimethylphenylamino)-methyl]phosphonic Acid Monoethyl Ester **2i** with Vanadium Oxytrifluoride*

Reaction with four equivalents of vanadium oxytrifluoride at −25 to −30°C in the usual way showed complete consumption of the starting material, but only 290 mg of dephosphorylated phenanthridine **3a** was isolated from the reaction mixture after workup.

*Diethyl (2,4-Dimethyl-[1,3]dioxolo[4,5-*j*]phenanthridin-6-yl)-phosphonate **3i***
*and (2-Diethyl Hydroxymethyl-4-methyl-[1,3]dioxolo[4,5-*j*]-phenanthridin-6-yl)phosphonate **3j***

(a) With Four Equivalents of Vanadium Oxytrifluoride

The benzylamine **2h** (2.61 g, 6.7 mmol) was dissolved in trifluoroacetic acid/dichloromethane (1 : 1, 20 mL) at −30°C and a solution of vanadium oxytrifluoride (3.96 g, 32.0 mmol) in a mixture of trifluoroacetic acid (10 mL) and ethyl acetate (5 mL) was added at such a rate as to keep the internal temperature at −25 to −30°C. Workup of an aliquot showed negligible reaction, the reaction mixture was allowed to warm to 0°C over 30 min when examination of a further aliquot indicated no remaining starting material. The mixture was worked up in the usual way and extracted with dichloromethane (2 × 50 mL). The solvent was removed under reduced pressure and the residue was stirred with ether (40 mL), leaving a colourless solid (1.65 g). The ether was removed and the residue was chromatographed over silica progressing from dichloromethane to dichloromethane/ethyl acetate (1 : 1). The fractions containing less polar material were combined, evaporated, and recrystallized from ethyl acetate to afford the dephosphorylated phenanthridine **3a** (0.13 g, 8%), identical with the sample described previously. A more polar material was contained in the next few fractions which were combined with the solid obtained above by filtration and the material remaining after removal of the solvent was recrystallized from methanol to give colourless woolly needles of the *diethyl ester* **3i** (1.52 g, 59%), mp 200–202°C (Found: C 61.7, H 5.6, N 3.6. $C_{20}H_{22}NO_3P$ requires C 62.0, H 5.7, N 3.6%). δ_H ($CDCl_3$) 1.42 (6H, t, *J* 6.2, 2 CH_2*Me*), 2.51 (3H, s, ArMe), 2.78 (3H, s, ArMe), 4.2–4.4 (4H, m, 2 C*H*$_2$Me), 6.09 (2H, s, OCH_2O), 7.33 (1H, br s, ArH), 7.80 (1H, d, *J* 2.1, ArH), 7.89 (1H, br s, ArH), 8.28 (1H, s, ArH). δ_C ($CDCl_3$) 16.4 (d, *J* 6.3), 18.4, 22.1, 63.5 (d, *J* 6.9), 100.0 (d, *J* 2.3), 101.9, 105.1, 119.2, 123 (d, *J* 31.3), 124.6 (*J* 3.5), 130.6, 130.8, 136.1, 136.4, 140.1 (d, *J* 27.1), 148.2, 149.7 (d, *J* 224.6), 150.9. *m*/*z* (APCI$^+$) 388 (M + 1).

Further elution yielded a more polar compound (210 mg, 8%), ^{1}H NMR of which suggested it was the hydroxymethyl analogue **3j** (see below).

(b) With Six Equivalents of Vanadium Oxytrifluoride

The benzylamine **2h** (2.38 g, 6.1 mmol) in trifluoroacetic acid/dichloromethane (1 : 1, 20 mL) at 0°C was treated with a solution of vanadium oxytrifluoride (4.54 g, 0.036 mol) in trifluoroacetic acid/dichloromethane (1 : 1, 20 mL). After 10 min, the reaction was worked up as described above and extracted with dichloromethane (2 × 50 mL). The residue remaining after removal of the solvent was chromatographed over silica, commencing with dichloromethane as eluent and progressing to dichloromethane/ethyl acetate (1 : 1), successively yielded the following: dephosphorylated phenanthridine **3a** (75 mg), dialkoxyphosphorylated phenanthridine **3i** (0.52 g, 22%; identical with the compound prepared above), and *diethyl ester* **3j** (1.31 g, 52%), mp 201–202°C (Found: C 59.6, H 5.5, N 3.5. $C_{20}H_{22}NO_6P$ requires C 59.8, H 5.6, N 3.4%). δ_H ($CDCl_3$) 1.43 (6H, t, *J* 6.9, 2 CH_2*Me*), 2.66 (3H, s, ArMe), 4.2–4.5 (4H, m, 2 C*H*$_2$Me), 4.83 (2H, s, C*H*$_2$OH), 6.07 (2H, s, OC*H*$_2$O), 7.26 (1H, s, ArH), 7.33 (1H, br s, ArH), 7.80 (1H, br s, ArH), 7.90 (1H, s, ArH). Irradiation of the methylene of the CH_2OH (δ 4.83) caused enhancement of two one-proton singlets (δ 7.26 and 7.80). Irradiation of the aromatic methyl (δ 2.66) caused enhancement of a signal of only one aromatic proton (δ 7.26). δ_C ($CDCl_3$) 16.4 (d, *J* 6.7), 18.4, 63.7 (d, *J* 6.9), 64.5, 99.4, 101.9, 104.2, 116.3, 122.6 (d, *J* 31.4), 123.9, 126.8, 130.4 (d, *J* 10.7), 137.8, 140.2 (d, *J* 26.7), 141.9, 147.6, 148.5 (d, *J* 218.9), 150.5.

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