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SYNTHETIC APPLICATION OF LITHIATION REACTIONS—VI[a]

NEW SYNTHESIS OF LINEAR FUROQUINOLINE ALKALOIDS[b]

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Abstract—Using organolithiation and Wittig reactions, a new and general synthesis of the linear furoquinoline alkaloids, dictamnine, pteleine, evolitrine and γ-fagarine is described.

A common feature of the known (until 1967) syntheses[1-4] of the furoquinoline alkaloids is that the quinoline ring is built along with an appropriate carbon chain at 3 position, which is then modified into the furan ring. This is necessary because incorportion of a carbon chain later at 3-position of the quinoline ring, through an electrophilic aromatic substitution reaction is difficult.

A new synthesis of the furoquinoline alkaloids was reported[5] from this laboratory in 1967. In this on a preformed quinoline ring, a carbon chain was introduced at 3-position through aromatic lithiation reaction.[6†] The side chain was then constructed to the linear furan ring. Thus the alkaloid dictamnine was synthesised by lithiation of 2,4-dimethoxy quinoline followed by treatment of the organolithium compound with ethylene oxide, and then by hydrolysis, cyclisation and oxidation (Fig 1). The new method was then extended[7a-b] to the synthesis of other furoquinoline alkaloids, pteleine and γ-fagarine.

In the above method the yield up to the synthesis of the dihydro compound was good. However further oxidation to the alkaloids, by dehydrogenation or by successive treatment with NBS and NEt_3 did not give good yields. An alternate method was then sought which would obviate the final oxidation step. This has now been achieved and is described. The scheme of the new synthesis is shown in Fig 2.

The 2,4-dichloroquinolines (**1**) were prepared by treatment of a mixture of the corresponding anilines and malonic acid with $POCl_3$. The dichlorocompounds were converted to the dimethoxy derivatives by reaction with NaOMe. In one case (m-anisidine) an isomeric mixture of the chlorocompounds was obtained which was first reacted with NaOMe and then separated into the two trimethoxy quinolines **2c** and **2e**.

Attempts to introduce a formyl group at 3-position of the 2,4-dimethoxy quinolines (**2**) by Vilsmeyer–Haack reaction led only to complex mixture. The formyl derivatives (**3**) were, however, prepared smoothly in 50–70% yield, by lithiation of the 2,4 dimethoxy quinolines followed by treatment with N-methyl formanilide.

The formyl derivatives were condensed with methoxymethylenetriphenylphosphorane, prepared from methoxymethyltriphenylphosphonium chloride and KOt-Bu. Mixtures of *cis* and *trans* enol ethers (**4** and **5**) were obtained in 70–80% yield, which were separated into their *cis* and *trans* isomers by careful chromatography. However, for further reaction, since separation was not obligatory, the mixtures were used as such. On refluxing with dil HCl (in most cases 2%), they were selectively hydrolysed to the 2 - hydroxy - 4 - methoxy 3-quinolinyl acetaldehydes (**6**) in 60–80% yield.

[a] Part V: N. S. Narasimhan and B. H. Bhide, *Tetrahedron* **27**, 6171 (1971).

[b] For a preliminary communication, see *Tetrahedron Letters* 843 (1973).

†Recently Grundon and co-workers have also introduced a carbon chain at 3-position of the quinoline ring by lithiation.[6]

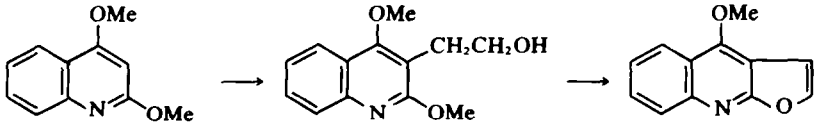

Fig 1.

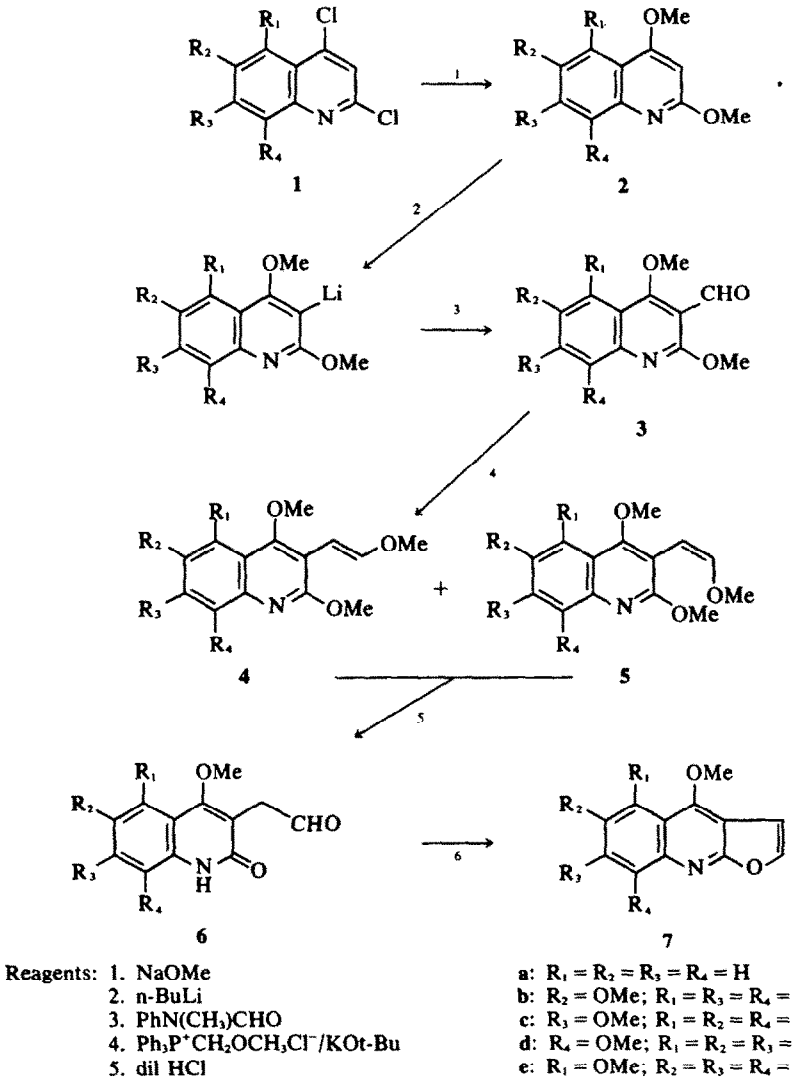

Fig 2.

In a recent work,[6] Grundon *et al* have reported the m.p. of the crude quinolinyl acetaldehyde (**6a**) as 154–157°. By the present method this has been obtained as a compound m.p. 209–210°. The identity of the compound was established by spectral and chemical data. Thus in the IR the compound has bands at 2720, 1680 cm^{-1} (–CHO) and 1640 cm^{-1} (amide). In the NMR the compound shows only one singlet (3H) corresponding to one –OMe. The other important signals in the NMR are at 3·63 (2H, d, J = 3 Hz, $-CH_2CHO$); 9·60 (1H, t, J = 3 Hz, $-CH_2CHO$), 11·73 (1H, broad, NH). The above data indicated structure **6a** for the compound. Chemically the compound was reduced by $NaBH_4$ to the known 3-(β-hydroxy ethyl)-4-methoxy 2-quinolone, m.p. 184°, which was further cyclised to dihydrodictamnine, m.p. 104° (superposable IR).

Finally the 2-hydroxy-4-methoxy-3-quinolinyl acetaldehydes were cyclised by PPA to the alkaloids. The yield was 70–90% (except in the case of evolitrine where it was 20%). In a partial modification of the synthesis, the enol ethers (**4a–5a** and **4b–5b**) themselves were reacted with PPA. The corresponding alkaloids were obtained, but in poorer yield.

EXPERIMENTAL

All m.ps. are uncorrected, IR spectra were measured as nujol mulls, and UV in MeOH soln, chemical shifts are expressed in ppm down field from TMS. n-BuLi used was in ether soln prepared according to H. Gilman.[8]

Dictamnine (**7a**)

2,4-*Dimethoxy*-3-*formylquinoline* (**3a**). A soln of 2,4-dimethoxyquinoline (11 g, 0·058 mole) in ether (150 ml) was cooled to 0° and treated with n-BuLi (from 1·4 g Li and 10 g n-BuBr, 0·087 mole) in ether. After stirring (45 min) in the cold the metalation mixture was treated with a soln of N-methyl formanilide (8·5 ml, 0·063 mole) in ether (25 ml), stirred at 0° for 30 min and at room temp for 45 min. The mixture was hydrolysed with water (70 ml) and the residue (16 g), obtained from the ether extract, chromatographed over silica gel to give the starting compound (2·5 g) from the initial benzene eluates. Further elution with the same solvent furnished, on crystallisation from benzene, 2,4-dimethoxy-3-formyl quinoline as light yellow needles (6·5 g; 67·7% on the basis of recovered 2,4-dimethoxy quinoline), m.p. 82° (Lit.[9] m.p. 76°). ν max 1650 cm^{-1} (–CHO); λ max 234, 247, 265, 294 and 342 nm (log ϵ 4·49, 4·37, 3·67, 3·98 and 3·22), NMR (CCl_4), δ 4·08 (6H, s, 2X–OMe); 7·07–7·62 (4H, m, aromatic H's); 9·23 (1H, s, –CHO); (Found: C, 66·45; H, 5·30. $C_{12}H_{11}O_3N$ requires; C, 66·35; H, 5·10%).

2,4-*Dimethoxy*-3(2-*methoxyvinyl*) *quinoline* (**4a** *and* **5a**. To an ice cold suspension of methoxymethyl-triphenylphosphonium chloride (6·86 g, 0·02 mole) in ether (70 ml) in N_2 atmosphere was added t-BuOK (2·24 g, 0·02 mole) in t-BuOH (20 ml, freshly distilled over calcium hydride). After 20 min, when the red colour of the ylide had fully developed, a soln of **3a** (2·17 g, 0·01 mole) in ether (40 ml) was introduced at an even rate (5 min). The mixture was stirred for 3 h and decomposed with water. The residue (11·6 g), obtained from ether extract, on chromatography over silica gel gave a liquid from the initial light petroleum eluates, which on distillation yielded **4a** (1·1 g, 48·7%), b.p. 145°/25 mm; ν max 1640 cm^{-1} (enol ether); λ max 249·5, 258, 281, 292·5, 302 and 339 nm (log ϵ 4·62, 4·57, 4·22, 4·33, 4·34 and 4·00); NMR (CCl_4), δ 3·73, 3·91 and 4·11 (3H each, s, 3X–OMe); 5·95 and 7·6 (1H each, d, J = 13 Hz, *trans* –CH=CH–), 7·21–7·91 (4H, m, aromatic H's); (Found: C, 68·33; H, 6·23. $C_{14}H_{15}O_3N$ requires: C, 68·55; H, 6·16%).

Further elution with light petroleum gave another liquid, which on distillation furnished **5a** (0·850 g; 37·6%), b.p. 140°/0·25 mm; ν max 1650 cm^{-1} (enol ether); λ max 226·5, 288·5 and 319 nm (log ϵ 4·55, 3·81 and 3·67); NMR (CCl_4), δ 3·57, 3·87 and 4·03 (3H each, s, 3X–OMe); 5·28 and 6·07 (1H each, d, J = 7 Hz, *cis* –CH=CH–); 7·1–8·1 (4H, m, aromatic H's); (Found: C, 68·45; H, 6·15. $C_{14}H_{15}O_3N$ requires C, 68·55; H, 6·16%).

2 - *Hydroxy* - 4 - *methoxy* - 3 - *quinolinyl acetaldehyde* (**6a**). A mixture of **4a** and **5a** (0·9 g), obtained from the total light petroleum eluate in the previous experiment, was refluxed with HCl (20%, 15 ml) for 45 min. Neutralisation ($NaHCO_3$) and extraction with chloroform gave a colourless solid, which on crystallisation from MeOH afforded **6a** as needles (0·48 g, 60·2%), m.p. 209–210° (Lit.[6] m.p. 154–7°); ν max 2720, 1680 cm^{-1} (–CHO) and 1640 cm^{-1} (amide CO); λ max 259, 268·5, 277, 311, 321 and 333 nm (log ϵ 2·17, 2·01, 2·05, 2·14, 2·01 and 3·76); NMR (DMSO-d_6), δ 3·63 (2H, d, J = 3 Hz, $-CH_2CHO$); 3·9 (3H, s, –OMe); 7·0–7·33 (4H, m, aromatic H's), 9·60 (1H, t, J = 3 Hz, $-CH_2-CHO$); 11·73 (1H, broad, s, –NH); (Found: C, 66·48; H, 5·48. $C_{12}H_{11}O_3N$ requires; C, 66·35; H, 5·1%).

Dictamnine (**7a**). A mixture of orthophosphoric acid (1 ml) and P_2O_5 (1 g) was heated on waterbath for 2 h. To the clear soln **6a** (100 mg) was added, heated at 120–125° for 5 h, cooled and poured in water. Neutralisation ($NaHCO_3$) and extraction with chloroform gave a solid, which on chromatography over neutral alumina furnished a white solid from benzene eluates. Crystallisation from benzene followed by sublimation (bath temp 130°/1·5 mm) afforded dictamnine, as white needles (76 mg; 87·1%) m.p. 131–2°, identical (m.p. mixed m.p., UV, IR and NMR) with an authentic sample.

Evolitrine (**7c**)

Mixture of 2,4-*dichloro*-5-*methoxy and* 2,4-*dichloro*-7-*methoxy quinolines*. A mixture of *m*-anisidine (6·1 g), malonic acid (7·8 g) and freshly distilled $POCl_3$ (60 ml) was refluxed for 40 h, cooled, poured over crushed ice with vigorous stirring, kept overnight and made alkaline with 5N NaOH. The residue was filtered and extracted with ether. Removal of solvent gave a solid, which was passed through a column of neutral alumina in benzene, to give a white solid. This melted over a range. Crystallisation from benzene-light petroleum, furnished a solid (6·1 g), which analysed correctly for the dichloromethoxyquinoline. The melting however occurred over a range at 120–5° (Lit.[10] m.p. of 2,4-dichloro-7-methoxyquinoline was 132°); (Found: C, 52·47; H, 3·06, $C_{10}H_7ONCl_2$ requires: C, 52·86; H, 3·09%). The solid was actually a mixture of 2,4-dichloro-5-methoxyquinoline and 2,4-dichloro-7-methoxyquinoline, and was separated after conversion into the trimethoxy compounds.

2,4,5-*Trimethoxy quinoline* (**2e**) *and* 2,4,7-*trimethoxyquinoline* (**2c**). The above mixture of 2,4-dichloro-5-methoxy and 2,4-dichloro-7-methoxyquinolines (6 g) and NaOMe (from Na 4 g, in 80 ml MeOH) was refluxed for 22 h; cooled and poured in ice-cold water. The ppt obtained was chromatographed over silica gel in light petroleum. The initial eluates gave a compound, which was crystallised from light petroleum to furnish, 2,4,7-trimethoxy quinoline as white needles (2·8 g, 48·4%), m.p. 82°; λ max 267, 286·5, 299, 305, 312 and 326 nm (log ϵ 2·75, 2·64, 2·81, 2·75, 2·99 and 2·99); NMR ($CDCl_3$), δ 3·9, 3·93 and 4·03 (3H each, s, 3 X–OMe); 6·05 (1H, s, C_3H); 6·90 (1H, dd, J = 8 and 2 Hz, C_6H); 7·12 (1H, d, J = 2 Hz, C_8H); 7·82 (1H, d, J = 8 Hz, C_5H); (Found: C, 65·44; H, 5·98. $C_{12}H_{13}O_3N$ requires: C, 65·74; H, 5·98%).

Further elution with light petroleum gave a compound which on crystallisation from hexane yielded 2,4,5-trimethoxy quinoline as white needles (0·600 g, 10·4%) m.p. 142°, λ max 277, 284, 307 and 318 nm (log ϵ 3·72, 3·67, 3·24 and 3·23); NMR ($CDCl_3$), δ 3·9, 3·92 and 4·00 (3H each, s, 3X–OMe); 6·13 (1H, s, C_3H); 6·7 (1H, dd, J = 8 and 2 Hz, C_6H); 7·4 (2H, m, C_7H and C_8H); (Found: C, 66·04, H, 5·91. $C_{12}H_{13}O_3N$ requires: C, 65·74; H, 5·98%).

3-*Formyl*-2,4,7-*trimethoxyquinoline* (**3c**). 4·4 g of **2c** was lithiated with n-BuLi in ether soln. After stirring in the cold for 1·5 h, the metalation mixture was treated with N-methyl formanilide, stirred in the cold for 30 min and at room temp for 2 h. Further work up gave **3c** (2·65 g, 53·4%) m.p. 126°, needles from hexane, ν max 1660 cm^{-1} (–CHO); λ max 232, 243, 260, 305, 319 and 332 nm (log ϵ 4·50, 4·50, 4·21, 4·14, 4·25 and 4·10); NMR ($CDCl_3$), δ 3·92 (3H, s, –OMe); 4·1 (6H, s, 2X–OMe); 6·95 (1H, dd, J = 8 and 2 Hz, C_6H); 7·05 (1H, d, J = 2 Hz, C_8H); 7·95 (1H, d, J = 8 Hz, C_5H); 10·35 (1H, s, –CHO); (Found: C, 63·54; H, 5·19, $C_{13}H_{13}O_4N$ requires: C, 63·15; H, 5·30%).

cis *and* trans 3-(2-*Methoxy vinyl*)-2,4,7-*trimethoxyquinolines* (**4c** *and* **5c**). 1·12 g of **3c** in ether soln was reacted with the ylide. The mixture was stirred for 2 h. Further work up and chromatography gave in the

initial light petroleum fractions **4c** (0·490 g, 35·5%), m.p. 85°, white cubes from light petroleum. ν max 1625 cm^{-1} (enol ether); λ max 235, 237, 252·5, 261·5, 287·5, 297, 329 and 340 nm (log ϵ 4·51, 4·51, 4·46, 4·49, 4·09, 4·11, 4·12 and 4·10); NMR (CCl_4), δ 3·71, 3·89, 3·90 and 4·08 (3H each, s, 4X-OMe); 5·9 and 7·53 (1H each, d, J = 13 Hz, *trans* –CH=CH–); 6·9 (1H, dd, J = 9 and 2 Hz, C_6H); 7·08 (1H, d, J = 2 Hz, C_8H); 7·7 (1H, d, J = 9 Hz, C_5H); (Found: C, 65·3; H, 6·44. $C_{15}H_{17}O_4N$ requires: C, 65·44; H, 6·22%).

Further elution with benzene gave **5c** (0·450 g, 32·6%), white prisms from light petroleum, m.p. 72°; ν max 1638 cm^{-1} (enol ether); λ max 232, 249, 283 and 321 nm (log ϵ 5·53, 5·36, 3·89 and 3·93); NMR (CCl_4), 3·58 (3H, s, –OMe); 3·81 (6H, s, 2X–OMe); 3·95 (3H, s, –OMe); 5·17 and 5·98 (1H each, d, J = 7 Hz, *cis* –CH=CH–); 6·75 (1H, dd, J = 8 and 2·5 Hz, C_6H); 6·95 (1H, d, J = 2·5 Hz, C_8H); 7·7 (1H, d, J = 8 Hz, C_5H); (Found: C, 65·27; H, 6·34. $C_{15}H_{17}O_4N$ requires: C, 65·44; H, 6·22%).

4,7-*Dimethoxy*-2-*hydroxy*-3-*quinolinyl acetaldehyde* (**6c**). 800 mg of a mixture of **4c** and **5c** was refluxed with 2% HCl for 20 min. to yield compound **6c** (580 mg, 80·7%), white needles from $CHCl_3$–MeOH, m.p. 206–8°; ν max 1700 cm^{-1} (–CHO) and 1640 cm^{-1} (amide CO); (Found: C, 63·40; H, 5·29. $C_{13}H_{13}O_4N$ requires: C, 63·15; H, 5·30%).

Evolitrine. 100 mg of **6c** was heated with PPA at 125–130° for 2 h to give evolitrine (18 mg, 19·4%), rosettes of needles from chloroform-light petroleum, m.p. 114° (Lit.[13] m.p. 114–5°); ν max 1610, 1570, 1450, 1440, 1400, 1355, 1260, 1242, 1215, 1155, 1088, 1030, 954, 838, 810, 742, and 715 cm^{-1}; λ max 245·0, 307, 318 and 332 nm (log ϵ 5·02, 4·15, 4·13 and 4·07), NMR ($CDCl_3$), δ 3·97 and 4·40 (3H each, s, 2X–OMe); 6·97 (1H, d, J = 2·5 Hz, furan βH); 7·53 (1H, d, J = 2·5 Hz, furan αH); 7·17 (1H, dd, J = 9 and 2 Hz, C_6H); 7·30 (1H, d, J = 2 Hz, C_8H); 8·07 (1H, d, J = 9 Hz, C_5H). (Found: C, 68·28; H, 4·67. $C_{13}H_{11}O_3N$ requires: C, 68·11; H, 4·87%).

UV and NMR were in agreement with reported[13,14] values.

Pteleine (**7b**)

3-*Formyl*-2,4,6-*trimethoxyquinoline* (**3b**), 4·4 g of **2b** was lithiated with n-BuLi in ether soln. After stirring in the cold for 1·5 h, the metalation mixture was treated with N-methyl formanilide, stirred in the cold for 30 min and at room temp for 1 h. Further work up gave **3b** (2·9 g, 58·4%), m.p. 110–1°, needles from hexane; ν max 1660 cm^{-1} (–CHO); λ max 233, 245, 293, 327, 340 and 367 nm (log ϵ 4·59, 4·58, 3·08, 3·30, 3·39 and 3·31); NMR (CCl_4), δ 3·89 (3H, s, –OMe); 4·1 (6H, s, 2X–OMe); 7·22 (1H, dd, J = 8 and 2 Hz, C_7H); 7·29 (1H, d, J = 2 Hz, C_5H); 7·60 (1H, dd, J = 8 and 1 Hz, C_8H); (Found: C, 63·23; H, 5·73. $C_{13}H_{13}O_4N$ requires: C, 63·15; H, 5·60%).

cis *and* trans 3-(2-*Methoxy vinyl*)-2,4,6-*trimethoxyquinolines* (**4b** *and* **5b**). 2·47 g of **3b** in ether soln was reacted with the ylide. The mixture was stirred for 1 h. Usual work up and chromatography gave in the initial light petroleum fractions **4b** (1·15 g, 41·8%), m.p. 65°, b.p. 205–10° (bath)/0·9 mm; ν max 1630 cm^{-1} (enol ether); λ max 246, 252, 297, 306, 336 and 350 nm (log ϵ 4·68, 4·70, 3·15, 3·15, 4·06 and 4·06); NMR (CCl_4), δ 3·71 (3H, s, –OMe); 3·87 (6H, s, 2 X–OMe); 4·05 (3H, s, –OMe); 5·9 and 7·58 (1H each, d, J = 13 Hz, *trans* –CH=CH–); 7·05 (1H, dd, J = 10 and 2·5 Hz, C_7H); 7·11 (1H, d, J = 2·5 Hz, C_5H); 7·61 (1H, d, J = 10 Hz, C_8H); (Found: C, 65·82; H, 6·27. $C_{15}H_{17}O_4N$ requires: C, 65·44; H, 6·22%).

Further elution with light petroleum–benzene (1:1) gave **5b** (0·980 g; 35·6%), b.p. 200–5° (bath)/0·9 mm; ν max 1640 cm^{-1} (enol ether); NMR (CCl_4), δ 3·6, 3·83, 3·87 and 3·97 (3H each, s, 4X–OMe); 5·28 and 6·07 (1H each, d, J = 7 Hz, *cis* –CH=CH–); 7·07 (1H, dd, J = 8·5 and 2·5 Hz, C_7H); 7·2 (1H, d, J = 2·5 Hz, C_5H); 7·6 (1H, d, J = 8·5 Hz, C_8H); (Found: C, 65·19; H, 6·47. $C_{15}H_{17}O_4N$ requires: C, 65·44; H, 6·22%).

4,6-*Dimethoxy*-2-*hydroxy*-3-*quinolinylacetaldehyde* (**6b**). 200 mg of a mixture of **4b** and **5b** was refluxed with 2% HCl for 45 min to yield compound **6b** (150 mg, 83%), white needles from $CHCl_3$–MeOH, m.p. 198–9°; ν max 1705 cm^{-1} (–CHO) and 1640 cm^{-1} (amide CO), (Found: C, 63·01; H, 5·11. $C_{13}H_{13}O_4N$ requires: C, 63·15; H, 5·30%).

Pteleine. 200 mg of **6b** was heated with PPA at 120° for 2 h to furnish pteleine (130 mg, 73·3%); yellowish needles from benzene-light petroleum, m.p. 133–4° (Lit.[11] m.p. 134·5°), ν max ($CHCl_3$) 3·4 (m), 4·24 (m), 6·16 (s), 6·33 (s), 6·49 (m), 6·64 (m), 6·83 (s), 7·07 (s), 7·33 (s), 7·67 (s), 7·9 (m), 8·1 (s), 8·23 (s), 8·65 (s), 9·00 (s), 9·17 (s), 9·68 (m), 10·1 (m), 10·20 (m), 11·78 (w), 12·06 (m), 13·58 (m) μ; λ max 293·5, 304·5, 330·5 and 346 nm (log ϵ 4·00, 4·07, 3·82 and 3·85); NMR ($CDCl_3$), δ 4·06 and 4·53 (3H each, s, 2X–OMe); 7·06 (1H, d, J = 2·5 Hz, furan βH); 7·67 (1H, d, J = 2·5 Hz, furan αH); 7·43 (1H, dd, J = 9 and 2·5 Hz, C_7H); 7·53 (1H, d, J = 2·5 Hz, C_5H); 8·00 (1H, d, J = 8 Hz, C_8H). (Found: C, 67·92; H, 5·29. $C_{13}H_{11}O_3N$ requires: C, 68·11; H, 4·94%).

IR, UV and NMR were in agreement with reported[11,12] values.

γ-*Fagarine* (**7d**)

3-*Formyl*-2,4,8-*trimethoxyquinoline* (**3d**). 4·4 g of **2d** was lithiated in THF soln with n-BuLi in ether. After stirring in the cold for 20 min, the metalation mixture was treated with N-methyl formanilide, stirred for 1 h in the cold and 1 h at room temp. Further workup gave **3d** (1·0 g, 40·3% on the basis of compound reacted), m.p. 161°, orange needles from benzene-light petroleum; ν max 1660 cm^{-1} (–CHO); λ max 244·5, 265, 294, 302, 305, 320 and 355 nm (log ϵ 4·35, 4·31, 3·78, 3·76, 3·73, 3·23 and 3·47); NMR ($CDCl_3$), δ 4·03, 4·12 and 4·2 (3H each, s, 3X–OMe); 7·03 (1H, dd, J = 8 and 2 Hz, C_7H); 7·27 (1H, apparent triplet, J = 8 Hz, C_6H); 7·7 (1H, dd, J = 8 and 2 Hz, C_5H); 10·5 (1H, s, –CHO), (Found: C, 63·20; H, 5·64, $C_{13}H_{13}O_4N$ requires C, 63·15; H, 5·30%).

cis *and* trans 3-(2-*Methoxyvinyl*)-2,4,8-*trimethoxyquinolines* (**4d** *and* **5d**). 1·12 g of **3d** in THF soln was reacted with the ylide. The mixture was stirred for 2 h. Usual work up and chromatography gave in the initial light petroleum–benzene (1:1) fractions **4d** (0·480 g, 34·8%); b.p. 210–220° (bath)/0·14 mm; ν max 1625 cm^{-1} (enol ether); NMR (CCl_4), δ 3·7, 3·85, 3·95 and 4·11 (3H each, s, 4X–OMe); 5·92 and 7·62 (1H, each, d, J = 13 Hz, *trans* –CH=CH–); 6·8 (1H, dd, J = 8 and 2 Hz, C_7H); 7·1 (1H, apparent triplet, J = 8 Hz, C_6H); 7·4 (1H, dd, J = 8 and 2 Hz, C_5H); (Found: C, 65·18; H, 6·39. $C_{15}H_{17}O_4N$ requires: C, 65·44; H, 6·22%).

Benzene elution gave **5d** (0·445 g, 32·2%), white needles from light petroleum, m.p. 85°; ν max 1650 cm^{-1} (enol ether); λ max 243, 265, 288 and 325 nm (log ϵ 4·55, 4·35, 3·85 and 3·50); NMR (CCl_4), δ 3·61, 3·83, 3·93 and 4·03 (3H each, s, 4X–OMe); 5·23 and 6·05 (1H each, d, J = 7 Hz, *cis* –CH=CH–); 6·77 (1H, dd, J = 8 and 2 Hz, C_7H); 7·05 (1H, apparent triplet, J = 8 Hz, C_6H); 7·45 (1H, dd, J = 8 and 2 Hz, C_5H); (Found: C, 65·09; H, 6·37. $C_{15}H_{17}O_4N$ requires: C, 65·44; H, 6·22%).

4,8-*Dimethoxy*-2-*hydroxy*-3-*quinolinyl acetaldehyde*

(**6d**). 200 mg of mixture of **4d** and **5d** was refluxed with 2% HCl for 30 min to yield compound **6d** (157 mg, 87·4%), white needles from MeOH, m.p. 120–5°. ν max 1710 cm^{-1} (–CHO) and 1638 cm^{-1} (amide CO) (Found: C, 63·23; H, 5·21. $C_{13}H_{13}O_4N$ requires: C, 63·15; H, 5·30%).

γ-Fagarine. 100 mg of **6d** was heated with PPA at 150–60° for 2 h to furnish γ-fagarine (62 mg, 66·9%), pale yellow prisms from light petroleum, m.p. 141° (Lit.[13] m.p. 140–1°). ν max 3150, 1600, 1515, 1445, 1370, 1337, 1302, 1261, 1235, 1189, 1158, 1095, 978, 865, 810, 768, 750, 745 and 722 cm^{-1}; λ max 309, 324 and 335 nm (log ϵ 3·95, 3·92 and 3·88); NMR ($CDCl_3$), δ 4·07 and 4·4 (3H each, s, 2X–OMe); 7·03 (1H, d, J = 2·5 Hz, furan βH); 7·63 (1H, d, J = 2·5 Hz, furan αH); 7·03 (1H, dd, J = 8 and 2 Hz, C_7H); 7·33 (1H, apparent triplet, J = 8 Hz, C_6H); 7·83 (1H, dd, J = 8 and 2 Hz, C_5H). (Found: C, 67·84; H, 5·13. $C_{13}H_{11}O_3N$ requires: C, 68·11; H, 4·84%).

IR, UV and NMR were in agreement with reported[13,15] values.

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