Quinoline Alkaloids. Part XVI.[1] 2,2-Dimethylpyranoquinolines from Base-catalysed Rearrangement of Isoprenyl Epoxides. Synthesis and Biogenesis of Flindersine [2]

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The reaction of 3-isoprenyl-2,4-dimethoxyquinoline epoxides with potassium hydroxide in aqueous dimethyl sulphoxide furnished 2,2-dimethylpyranoquinolines in high yield, and led to a new synthesis of the alkaloid flindersine. A mechanistic study resulted in the isolation of an allylic alcohol intermediate and the detection of a second allylic alcohol, and indicated that quinone methides were involved in the cyclisation step. The biogenesis of flindersine and related compounds is discussed.

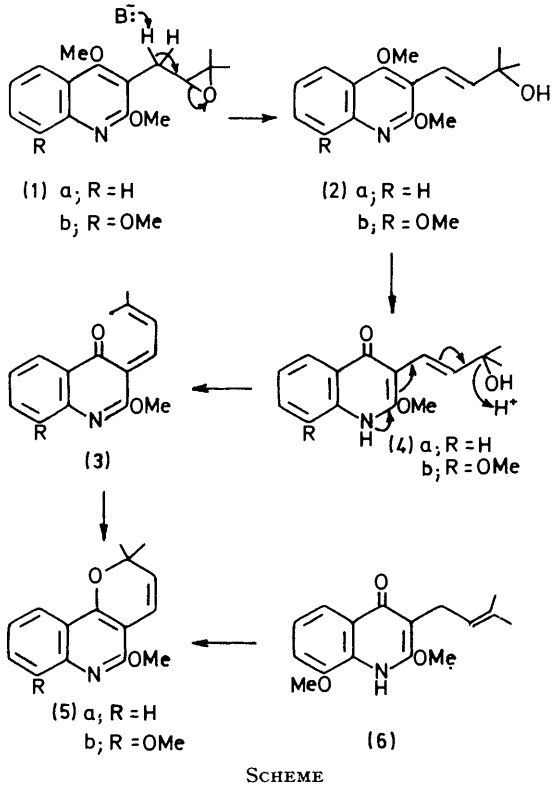
THE ISOPRENYLQUINOLINE EPOXIDES (1) were prepared initially as intermediates in the synthesis of quinoline alkaloids;[3,4] the biosynthetic significance of the epoxides then led us to examine their reactions. We have reported a study of reduction products,[1] and now describe a base-catalysed reaction.

Treatment of the trimethoxyquinoline epoxide (1b) with aqueous potassium hydroxide in dimethyl sulphoxide at 100°, followed by dilution with water, gave a clear solution; neutralisation afforded a solid, $C_{16}H_{17}NO_3$ (74%), which clearly was a 2,2-dimethylpyranoquinoline [(5b) or (7b)]. Thus, the i.r. spectrum was devoid of hydroxy-absorption and showed no strong amide-carbonyl absorption characteristic of quinolones. The n.m.r. spectrum showed two three-proton singlets at τ 5·88 and 5·98 (OMe), two equivalent *C*-methyl resonances at τ 8·48, and two one-proton spin–spin coupled doublets at τ 3·35 and 4·41 (J 10 Hz) attributable to a *cis*-vinylic system. The mass spectrum showed that the most prominent process was loss of a methyl radical to give a fully conjugated ion, *m/e* 256 [see (8)], typical of 2,2-dimethylchromens;[5] a peak at *m/e* 241 (*M*—30) probably is due to extrusion of a methyl radical from the ion (8) to give (9), since a metastable peak was observed at *m/e* 227 ($241^2/256 = 226{\cdot}5$). The dimethoxyquinoline epoxide (1a) reacted with base to give a product (77%) shown by spectroscopy to have the analogous structure (5a) or (7a).

Catalytic reduction of the pyrans derived from the epoxides (1a and b) afforded dihydro-derivatives. The n.m.r. spectra, each showing two two-proton triplets at τ 7·36—8·25 and no resonances due to olefinic protons, were in accord with the presence of dihydropyran rings. Because the reduction product from the dimethoxypyranoquinoline was not identical with the known linear compound (11b),[6] it was assigned structure (10b). Similarly, the monomethoxy-dihydro-derivative (10a) clearly differed from the linear compound (11a); the latter was prepared from the 4-quinolone khaplofoline by methylation with diazomethane. It appeared, therefore, that the pyranoquinolines possessed the angular structures (5), and we decided to confirm this by an independent synthesis. For this purpose we required a 4-hydroxy-2-methoxyquinoline. The selective hydrolysis of a 2,4-dimethoxyquinoline seemed a possible route to this intermediate, since 2,4-dichloroquinolines appear to react preferentially with nucleophiles at the 4-position, and reductive displacement of the 4-methoxy-group of 2,4-dimethoxyquinolines occurs with lithium aluminium hydride.[1] In a model experiment, 2,4,8-trimethoxyquinoline was hydrolysed with potassium hydroxide; the major product (35%) was the 4-hydroxy-2,8-dimethoxyquinoline, which showed i.r. absorption at 3350 and 1620 cm^{-1} indicative of this structure, and 4,8-dimethoxy-2-quinolone (edulitine) was obtained in only 3% yield. Reaction of 2,4,8-trimethoxy-3-(3-methylbut-2-enyl)quinoline with potassium hydroxide also resulted in selective nucleophilic displacement of the 4-methoxy-group to give the 4-quinolone (6). The product was identified by the n.m.r. spectrum, which

[1] Part XV, R. M. Bowman, G. A. Gray, and M. F. Grundon, preceding paper.
[2] Preliminary communication, M. F. Grundon and K. J. James, *Chem. Comm.*, 1970, 666.
[3] R. M. Bowman and M. F. Grundon, *J. Chem. Soc.* (*C*), 1967, 2368.
[4] J. F. Collins, G. A. Gray, M. F. Grundon, D. M. Harrison, and (Mrs.) C. G. Spyropoulos, *J.C.S. Perkin I*, 1973, 94.
[5] D. Lavie, N. Daniele, R. Weitman, and E. Glotter, *Tetrahedron*, 1968, **24**, 3011.
[6] E. A. Clarke and M. F. Grundon, *J. Chem. Soc.*, 1964, 4190.

showed two three-proton singlets at τ 5·82 and 5·95 (OMe), a two-proton doublet at 6·52 (ArCH_2) and an ill-defined one-proton triplet at 4·65 (–CH_2·CH=); the i.r. absorption at 1620 cm^{-1} supports the 4-quinolone structure. The useful synthesis of chromen involving reaction



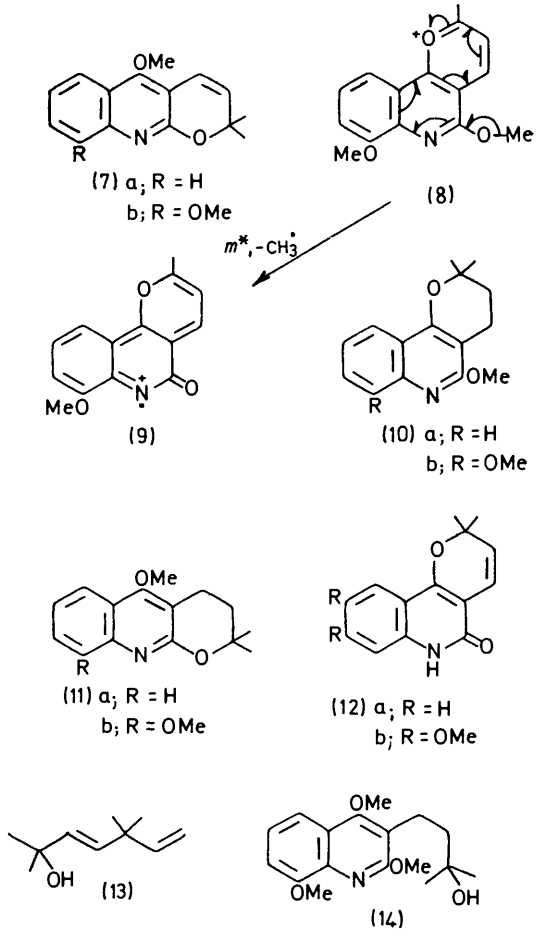
SCHEME

of an allyl phenol with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) [7] was applied to the 4-quinolone (6) and afforded the angular 2,2-dimethylpyranoquinoline (5b) (65%), identical with the product from the epoxide (1b).

The pyran obtained from the dimethoxyquinoline epoxide (1a) was demethylated with hydrobromic acid to give flindersine (12a) (81%), a quinoline alkaloid of established structure.[8] This conversion confirms that this pyranoquinoline is also the angular isomer (5a).

Mechanism of the Reaction.—Since the base-insoluble pyrans (5) are obtained from the epoxides only on neutralisation of the basic medium, they are not the initial products. We decided to study the sequence involved by using deuteriated solvents and following the reaction of the epoxide (1b) by n.m.r. spectroscopy. After 10 min at 90°, resonances attributed to the benzylic methylene group and the oxiran proton (an ABX system) in the epoxide (1b) had disappeared. By stopping the reaction at this point, the *trans*-allylic alcohol (2b) was isolated. Its structure was indicated by i.r. absorption at 3420 (OH) and 978 cm^{-1} (*trans*-disubstituted olefin) and by the n.m.r. spectrum, which showed three methoxy-singlets, a six-proton singlet at τ 8·53 (>CMe_2), and a singlet at 8·08 (OH), which disappeared on addition of deuterium oxide. The signal for the olefinic protons appeared as two unsymmetrical doublets at τ 3·12 (J 17 Hz), behaviour typical of an AB system where δ/J_{AB} is small; [9] the *trans*-allylic alcohol (13) displays a similar effect in the n.m.r. spectrum.[10] Support for structure (2b) for the allylic alcohol was obtained by catalytic hydrogenation to the known tertiary alcohol (14).[1] Satisfactory conditions for preparing the allylic alcohol (2b) (96%) from the epoxide (1b) involved reaction with base at 60° for 4 h; application of this procedure to the dimethoxyquinoline epoxide (1a) furnished the allylic alcohol (2a) (92%). The structure of the latter compound was indicated by n.m.r. and mass spectrometry.

Prolonged reactions of the epoxide (1b) with base in deuteriated solvents resulted in conversion of the intermediate allylic alcohol (2b) into the final product, which



could not be isolated but gave the pyranoquinoline (5b) when the solution was neutralised. The new compound is apparently the 4-quinolone (4b): its n.m.r. spectrum is similar to that of the allylic alcohol (2b) except that

[7] I. M. Campbell, C. H. Calzadilla, and N. J. McCorkindale, *Tetrahedron Letters*, 1966, 5107; G. Cardillo, R. Cricchio, and L. Merlini, *Tetrahedron*, 1968, **24**, 4825.

[8] R. F. C. Brown, G. K. Hughes, and E. Ritchie, *Austral. J. Chem.*, 1956, **9**, 277.

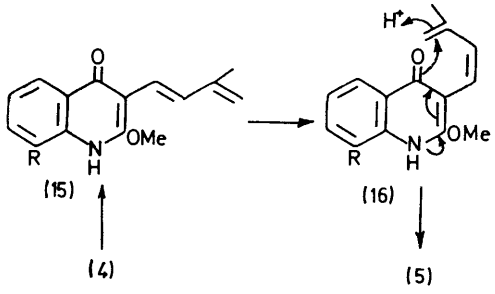
[9] I. Fleming and D. H. Williams, 'Spectroscopic Methods in Organic Chemistry,' McGraw-Hill, New York, 1966, 99.

[10] E. Hayashi, K. Yano, and T. Matsumura, *Tetrahedron Letters*, 1968, 6241; B. Willhalm and A. F. Thomas, *Chem. Comm.*, 1969, 1380.

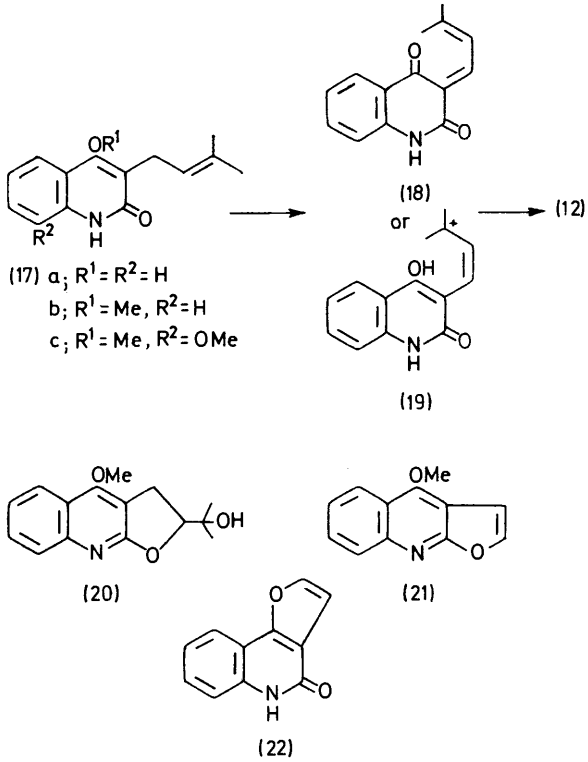
there is one less methoxy-resonance. The presence of a 4-quinolone group is indicated by the solubility of the compound in aqueous base, and by the n.m.r. signal at τ 2·07, arising from the aromatic proton at C-5 deshielded by the 4-carbonyl group. The reaction was applied to the epoxide (1a), and in this case the resultant 4-quinolone (4a) was trapped as its methyl ether (2a) by adding dimethyl sulphate to the alkaline solution.

The foregoing results indicate that the pyranoquinolines (5) are formed from the epoxides (1) *via* the allylic alcohols (2) and (4); the suggested mechanisms are shown in the Scheme. Base-catalysed rearrangements of epoxides to allylic alcohols [*e.g.* (1) ⟶ (2)] have been discussed previously,[11] and *trans*-olefins were found to be the preferred products, as in the present examples. We suggest that when the solutions are neutralised, dehydration of the alcohols (4) and subsequent cyclisaton occurs through quinone methides (3). An alternative mechanism for decomposition of the allylic alcohols (4) involves dehydration to the diene (15), followed by isomerisation of the *trans*-double bond [(15) ⟶ (16)], and finally by cyclisation. This mechanism seems less likely than the quinone methide route, since the formation of pyranoquinolines (5) from allylic alcohols (4) occurs at ambient temperature in slightly acidic medium, whereas the isomerisation of dienes [*e.g.* (15) ⟶ (16)] usually requires more vigorous conditions.[12]

The reactions described constitute an efficient synthesis of pyranoquinolines from isoprenyl epoxides, but the method is not likely to be general for 2,2-dimethylchromens, since a key step [(2) ⟶ (4)] is the hydrolysis of a methoxy-group; this reaction is characteristic of quinolines and related heterocycles (see foregoing discussion), but not of methoxybenzene derivatives.



Biogenesis of Pyranoquinoline Alkaloids.—2,2-Dimethylchromens are widespread amongst aromatic and heterocyclic natural products, and their biosynthesis is thought to proceed by oxidative cyclisation of an *o*-isoprenylphenol *via* a quinone methide [13,14] or through an allylic carbonium ion.[15] Application of these hypotheses to the pyranoquinoline alkaloids flindersine (12a) and ornicine (12b), in which the pyran ring is fused to the heterocyclic system, suggests that their biosynthesis occurs from a 3-isoprenylquinoline (17) through intermediates (18) or (19). The furano-, isopropyldihydrofurano- and dimethyldihydropyrano-quinoline alkaloids,



e.g. (20) and (21), also are known to be derived from 3-isoprenylquinolines,[16] and this large group of over fifty members all have a linear arrangement of the three rings, although angular compounds, *e.g.* (22), are apparently thermodynamically more stable;[4] it appears that prior methylation of the 4-hydroxy-group leads to kinetically controlled formation of linear compounds. The pyranoquinoline alkaloids (12a) and (12b), with linear annulation, provide an intriguing exception. The conversion of *o*-allylphenols into chromens by reaction with DDQ is thought to proceed through a quinone methide and is regarded as an *in vitro* model for the biosynthetic route;[7] the 3-isoprenyl-4-hydroxy-2-quinolone (17a) yields flindersine in this way,[17] and the 4-quinolone (6) behaves similarly (see before). In an attempt to prepare linear pyranoquinolines, we treated the 4-methoxy-2-quinolones, (17b and c) with DDQ, but observed no reaction. A possible explanation for this unexpected result is that formation of a quinone methide from a 2-quinolone would involve disruption of the benzenoid system, in contrast to the case with a

[11] D. M. Burness, *J. Org. Chem.*, 1964, **29**, 1862; A. C. Cope and J. K. Heeren, *J. Amer. Chem. Soc.*, 1965, **87**, 3125; B. Rickborn and R. P. Thummel, *J. Org. Chem.*, 1969, **34**, 3583.

[12] E. E. Schweizer and C. I. Berninger, *J. Org. Chem.*, 1966, **31**, 2907.

[13] A. J. Birch and H. Smith, *Chem. Soc. Special Publ.*, No. 12, 1958, p. 1.

[14] W. D. Ollis and I. O. Sutherland, in ' Recent Developments in the Chemistry of Natural Phenolic Compounds, Pergamon, Oxford, 1961, 84; A. B. Turner, *Quart. Rev.*, 1964, **18**, 347.

[15] R. Aneja, S. K. Muckerjee, and T. R. Seshadri, *Tetrahedron*, 1958, **4**, 256; W. B. Whalley in ref. 14.

[16] J. F. Collins and M. F. Grundon, *Chem. Comm.*, 1969, 621; M. F. Grundon and K. J. James, *ibid.*, 1971, 1311.

[17] F. Piozzi, P. Neuturella, and A. Bellino, *Gazzetta*, 1969, **99**, 711.

4-quinolone intermediate (3). Thus, the *in vitro* evidence rationalises the occurrence of angular rather than linear pyranoquinoline alkaloids, and supports the quinone methide theory of biosynthesis; the alternative allylic carbonium ion intermediate (19) should provide no barrier to the formation of linear compounds after protection of the 4-hydroxy-group.

After the completion of our work, Fourrey *et al.*[18] described the synthesis of pyranocoumarins from allylic alcohols, prepared by photosensitised oxidation of dimethylallyl derivatives. It was suggested that this route could be biogenetically significant, and there is chemotaxonomic evidence for this proposal, for example in the occurrence of a 2,2-dimethylchromen and the corresponding allylic alcohol in *Helianthella uniflora*.[19] The alkaloid flindersine (12a) may arise similarly, or from a quinoline isoprenyl epoxide by a route analogous to the *in vitro* synthesis recorded here.

EXPERIMENTAL

I.r. spectra were measured with a Perkin-Elmer 157 spectrometer, n.m.r. spectra with Perkin-Elmer 60 MHz R12 and R10A spectrometers (unless stated otherwise) with tetramethylsilane as internal standard, and mass spectra with an A.E.I. MS 902 spectrometer.

3-(2,3-*Epoxy*-3-*methylbutyl*)-2,4-*dimethoxyquinoline* (1a).—A solution of 2,4-dimethoxy-3-(3-methylbut-2-enyl)quinoline [4] (2 g) in chloroform (40 ml) was treated with an excess of *m*-chloroperbenzoic acid in chloroform (40 ml). After 4 days at room temperature, the solution was extracted with 2N-sodium carbonate (4 × 50 ml) and evaporated. Chromatography of the product on alumina and elution with light petroleum (b.p. 40—60°)–ether (7 : 3) gave the *epoxide* as an oil (1·87 g, 88%), b.p. 110—115° at 0·05 mmHg, τ ($CDCl_3$) 1·7—2·5 (4H, m, arom.), 6·94 (3H, m, $-CH_2-$ and $-CH<$), 5·80 (3H, s, OMe), 5·91 (3H, s, OMe), and 8·52 (s) and 8·68 (s) (CMe_2), *m/e* 273 (73%, M^+), 258 (9, $M - CH_3$), 244 (12, M — CHO), 230 (100, $M - CH_3 - CO$, *m**), 217 (13, 244 — HCN), 216 (14), 214 (10), 213 (9), 202 (61, $M - C_4H_7O$), 200 (42, 230 — HCHO), 198 (8), and 188 (12) (Found: C, 70·5; H, 7·1; N, 5·1. $C_{16}H_{19}NO_3$ requires C, 70·3; H, 7·0; N, 5·1%).

5,7-*Dimethoxy*-2,2-*dimethyl*-2H-*pyrano*[3,2-c]*quinoline* (5b).—(*a*) A solution of the epoxide (1b) [20] (0·4 g) in dimethyl sulphoxide (40 ml) and 2N-potassium hydroxide (6 ml) was heated at 100° for 15 h, added to water (150 ml), and extracted with chloroform. The aqueous solution was neutralised. Extraction with chloroform gave the *pyranoquinoline* (0·27 g, 75%), m.p. 114—115° [prisms from light petroleum (b.p. 40—60°)], τ ($CDCl_3$) 2·38 (1H q, 5-H), 2·66—3·09 (3H, 6- and 7-H), 3·35 (1H, d, *J* 10 Hz), 4·41 (1H, d, *J* 10 Hz), 5·88 (3H, s, OMe), 5·98 (3H, s, OMe), and 8·48 (6H, s, $>CMe_2$) (Found: C, 71·2; H, 6·6; N, 5·5. $C_{16}H_{17}NO_3$ requires C, 70·8; H, 6·3; N, 5·2%).

(*b*) A solution of 2,4,8-trimethoxy-3-(3-methylbut-2-enyl)quinoline [4] (0·87 g) in methanolic 30% potassium hydroxide was refluxed for 4 h. Evaporation, addition of water, and extraction with ether gave the starting compound (0·68 g). Neutralisation of the basic solution and extraction with ether furnished the 4-quinolone (6) (0·102 g, 12%). A solution of the crude quinolone (72 mg) and DDQ (75 mg) in dry benzene (20 ml) was refluxed for 15 h. After filtration, the solution was washed with 2N-sodium hydroxide (3 × 20 ml) and evaporated to give the pyranoquinoline (46 mg, 65%), m.p. and mixed m.p. 114—115°.

When the 2-quinolones (17b) [4] and (17c) [4] were heated similarly with DDQ in benzene, they were recovered and no new products were detected.

5-*Methoxy*-2,2-*dimethyl*-2H-*pyrano*[3,2-c]*quinoline* (5a).—Reaction of the epoxide (1a) (0·58 g) with potassium hydroxide in aqueous dimethyl sulphoxide as for the epoxide (1b) gave the *pyranoquinoline*, obtained by distillation at 115° and 0·05 mmHg as an oil (0·39 g, 77%), and separating from light petroleum (b.p. 40—60°) in prisms, m.p. 47—48°, τ ($CDCl_3$) 1·89 (1H, q, 5-H), 2·05—2·80 (3H, arom. 6-, 7-, and 8-H), 3·31 (1H, d, *J* 10 Hz), 4·46 (1H, d, *J* 10 Hz), 5·91 (3H, s, OMe), and 8·52 (6H, s, $>CMe_2$), *m/e* 241 (26%, M^+), 226 (100, $M - CH_3$, *m**), 210 (M — OMe), 211 ($M - CH_2O$), 198 (226 — CH_2O), and 183 (4, 226 — CH_3CO) (Found: C, 74·4; H, 6·4; N, 5·6. $C_{15}H_{15}NO_2$ requires C, 74·7, H, 6·3; N, 5·8%).

3,4-*Dihydro*-5-*methoxy*-2,2-*dimethyl*-2H-*pyrano*[3,2-c]-*quinoline* (10a).—A solution of the pyranoquinoline (5a) (0·20 g) in methanol (10 ml) was shaken with platinum and hydrogen at room temperature for 5 h. Filtration and evaporation gave the *dihydro-derivative* as an oil (0·20 g), b.p. 110° at 0·05 mmHg, τ ($CDCl_3$), 1·90 (1H, q, 10-H), 2·00—2·85 (3H, 7-, 8-, and 9-H), 7·36 (2H, t, $ArCH_2{\cdot}CH_2$), 8·25 (2H, t, $ArCH_2{\cdot}CH_2$), 5·91 (3H, s, OMe), and 8·65 (6H, s, $>CMe_2$) (Found: C, 74·0; H, 7·0; N, 5·8. $C_{15}H_{17}NO_2$ requires C, 74·0; H, 7·0; N, 5·8%).

3,4-*Dihydro*-5,7-*dimethoxy*-2,2-*dimethyl*-2H-*pyrano*[3,2-c]-*quinoline* (10b).—The pyranoquinoline (5b) was hydrogenated as for the 5-methoxy-compound (5a) and gave the *dihydro-derivative*, separating from light petroleum (b.p. 40—60°) in prisms, m.p. 107—109°, τ ($CDCl_3$; at 100 MHz) 2·43 (1H, q, $J_{9,10}$ 8, $J_{8,10}$ 1·5 Hz, 10-H), 2·73—3·12 (2H, 8- and 9-H), 5·88 (3H, s, OMe), 5·99 (3H, s, OMe), 7·30 (2H, t, $ArCH_2{\cdot}CH_2$), 8·12 [2H, t, $\frac{1}{2}(J_{AB} + J_{AB'}) = 7$ Hz, $ArCH_2{\cdot}CH_2$], and 8·60 (6H, s, CMe_2) (Found: C, 70·4; H, 6·9; N, 5·0. $C_{16}H_{19}NO_3$ requires C, 70·3; H, 7·0; N, 5·1%).

3,4-*Dihydro*-5-*methoxy*-2,2-*dimethyl*-2H-*pyrano*[2,3-*b*]-*quinoline* (11a).—A solution of khaplofolin [21] (195 mg) in methanol (10 ml) was kept for 12 h with an excess of ethereal diazomethane, and the solution was evaporated. A solution of the residue in ether was washed with 2N-sodium carbonate and evaporated. Chromatography of the products on alumina and elution with ether afforded the *dihydropyranoquinoline*, separating from light petroleum (b.p. 40—60°) in prisms (129 mg, 62%), m.p. 95—96°, τ ($CDCl_3$; 100 MHz) 2·08 (1H, q, 6-H), 2·00—2·78 (3H, 7-, 8- and 9-H), 5·97 (3H, s, OMe), 7·02 (2H, t, $ArCH_2$), 8·07 (2H, t, $ArCH_2{\cdot}CH_2$) and 8·53 (6H, s, $>CMe_2$) (Found: C, 74·1; H, 7·1; N, 5·6. $C_{15}H_{17}NO_2$ requires C, 74·0; H, 7·1; N, 5·8%). Elution with chloroform gave the *N*-methyl derivative as described previously.[21]

2,8-*Dimethoxyquinolin*-4-*ol*.—A solution of 2,4,8-trimethoxyquinoline [22] (0·40 g) in dimethyl sulphoxide (20 ml) containing 2N-potassium hydroxide (5 ml) was heated at

[18] J. L. Fourrey, J. Rondest, and J. Polansky, *Tetrahedron*, 1970, **26**, 3839.

[19] F. Bohlmann and M. Grenz, *Chem. Ber.*, 1970, **103**, 90.

[20] R. M. Bowman, J. F. Collins, and M. F. Grundon, *J.C.S. Perkin I*, 1973, 626.

[21] R. M. Bowman and M. F. Grundon, *J. Chem. Soc.* (*C*), 1966, 1084.

[22] G. H. Patel and C. M. Mehta, *J. Sci. Ind. Res.* (*India*), 1960, **19***B*, 436; N. S. Narisimhan, and M. V. Paradikar *Chem. and Ind.*, 1967, 831; 1968, 515; N. S. Narisimhan, M. V. Paradhar, and R. H. Alurka, *Tetrahedron*, 1971, **27**, 1351.

100° for 2·5 days. The non-acidic products were obtained with ether, and chromatographed on alumina. Elution with ether gave 2,4,8-trimethoxyquinoline (0·20 g), and elution with chloroform–methanol furnished 4,8-dimethoxy-2-quinolone (0·01 g, 3%), m.p. 236—237° (lit.,[23] 236°), identical with a sample of edulitine. Neutralisation of the basic solution and extraction with chloroform gave 2,8-*dimethoxyquinolin*-4-*ol* as a solid separating from light petroleum (b.p. 40—60°)–chloroform in needles of the monohydrate (0·12 g, 35%), m.p. 74° (Found: C, 59·1; H, 5·9; N, 6·2. $C_{11}H_{11}NO_3,H_2O$ requires C, 59·2; H, 5·9; N, 6·3%).

Flindersine (12a).—A mixture of the methoxypyranoquinoline (5a) (0·138 g) and 48% hydrobromic acid (2 ml) was heated at 70° for 4 h, diluted with water, and extracted with chloroform. Evaporation of the solvent gave flindersine in needles (from ether) (0·105 g, 81%), m.p. 192—194° (decomp.) [lit.,[5] 195—196° (decomp.)].

Hydrogenation with a platinum catalyst furnished dihydroflindersine in needles from ether, m.p. 232° (lit.,[22] 233—234°), identical (i.r. and mixed m.p.) with an authentic sample.

N.m.r. Study of the Reactions of the Quinoline Epoxides (1a and b) *with Base*.—In a typical run, the epoxide (1b) (0·100 g) in [$^2H_6$]dimethyl sulphoxide (0·80 g) was treated with 6N-sodium deuteroxide in deuterium oxide (0·15 g) in an n.m.r. tube. The sealed tube was inserted in a n.m.r. spectrometer at 90°, and a spectrum run after 10 min showed that all the epoxide had reacted to give the allylic alcohol (2b). After 3 h, a demethylation reaction was observed, and after 20 h, this reaction was *ca.* 80% complete. The tube was opened, and the contents were diluted with deuterium oxide (0·60 g) and extracted with deuteriochloroform (2 × 0·5 ml). The n.m.r. spectrum of the basic solution showed signals at τ 2·07 (q, 5-H), 2·50—2·87 (6- and 7-H), 2·98br (s, $H-\overset{|}{C}=\overset{|}{C}-H$), 5·87 (s, OMe), 5·94 (s, OMe), and 8·48 (s, $>CMe_2$), consistent with structure (4b). Neutralisation of the solution followed by extraction with chloroform gave the pyranoquinoline (5b).

A similar experiment with the epoxide (1a) gave comparable results.

3-(3-*Hydroxy*-3-*methylbut*-1-*enyl*)-2,4,8-*trimethoxyquinoline* (2b).—A solution of the quinoline epoxide (1b) (0·350 g) in dimethyl sulphoxide (7 ml) containing 2N-potassium hydroxide (1·5 ml) was heated at 55° for 4 h, diluted with water (10 ml), and extracted with ether. The ether solution was washed repeatedly with water and evaporated. Chromatography of the residue on silica gel and elution with light petroleum (40—60°)–ether (3 : 2) furnished the *allylic alcohol* as a solid (0·335 g, 96%), separating from light petroleum (b.p. 40—60°) in prisms, m.p. 81—83°, τ ($CDCl_3$; 100 MHz) 2·34 (1H, q, 5-H), 2·64 (1H, m, 6-H), 2·94 (1H, q, 7-H), 3·14 (2H, dd, J_{AB} 17 Hz, $H-\overset{|}{C}=\overset{|}{C}-H$), 5·80 (s, OMe), 5·93 (s, OMe), 6·07 (s, OMe), 8·08 (s, OH), and 8·53 (s, $>CMe_2$) (Found: C, 67·1; H, 7·0; N, 4·5. $C_{17}H_{21}NO_4$ requires C, 67·3; H, 7·0; N, 4·6%).

The allylic alcohol (2b) (0·250 g) in methanol (50 ml) was shaken with platinum and hydrogen at 18°; after 30 min the catalyst was removed and the solvent was evaporated off. Preparative t.l.c. on silica gel [chloroform–ethyl acetate (4 : 1)] furnished the dihydro-derivative (14) (0·221 g, 88%), separating from light petroleum (b.p. 40—60°) in prisms, m.p. 76—77° (lit.,[1] 78—81°), identical (mixed m.p., i.r. spectra, and t.l.c.) with an authentic sample.

3-(3-*Hydroxy*-3-*methylbut*-1-*enyl*)-2,4-*dimethoxyquinoline* (2a).—Reaction of the epoxide (1a) with potassium hydroxide as for the epoxide (1b) gave the *allylic alcohol* (2a) as an oil (92%), b.p. 120° at 0·05 mmHg, $\nu_{max.}$ 3420 (OH) and 980 cm^{-1} (*trans*-CH=CH–), τ ($CDCl_3$) 1·8—2·7 (4H, m, aromatic), 3·03br (2H, s, –C*H*=C*H*–), 5·84 (s, OMe), 6·04 (s, OMe), 7·97 (s, OH), and 8·54 (s, $>CMe_2$), *m/e* 273 (33%, M^+), 258 (62, M — Me), 255 (12, $M - H_2O$), 230 (13, 258 — CO), 226 (13), 224 (13, 255 — MeO), 217 (M — 59, m^*), 216 (23, 258 — CH_2CO, m^*), 202 (100, $M - C_4H_7O$, m^*), 188 (26, $M - C_5H_9O$), and 159 (11) (Found: C, 70·5; H, 7·1; N, 4·9. $C_{16}H_{19}NO_3$ requires C, 70·3; H, 7·0; N, 5·1%).

Trapping of the 4-*Quinolone* (4a).—The epoxide (1a) (0·76 g) was treated with potassium hydroxide as before, and, after extraction with chloroform, the aqueous basic solution was divided into two equal portions [(*a*) and (*b*)]. Potassium hydroxide (20 g) and dimethyl sulphate (6 ml) were added to solution (*a*), and the mixture was made homogeneous by adding ethanol. The solution was refluxed for 3 h, and water (50 ml) was added. Extraction with chloroform gave the 2,4-dimethoxyquinoline (2a) as an oil (0·082 g), identical with an authentic sample. The basic solution was neutralised, re-basified, and extracted with chloroform to give the pyranoquinoline (5a) (0·04 g).

Neutralisation of solution (*b*) and extraction with chloroform afforded the pyranoquinoline (5a) (0·185 g).

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[23] T. P. Toube, J. W. Murphy, and A. D. Cross, *Tetrahedron*, 1967, **23**, 2061.