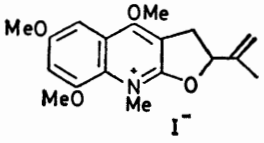
Quinoline Alkaloids. Part 20.[1,2] Synthesis of Ptelefolone and *O*-Methylribaline. Ring Closure of Epoxides of 3-Prenylquinolones

By **John L. Gaston** and **Michael F. Grundon,*** School of Physical Sciences, The New University of Ulster, Coleraine, Northern Ireland

2-(1-Hydroxy-1-methylethyl)-6,8-dimethoxy-9-methyl-2,3-dihydrofuro[2,3-*b*]quindiolin-4(9*H*)-one (5a) and its 8-monomethoxy-analogue *O*-methylribaline (5d) were prepared from 3-prenylquinolones. Reaction of the *N*-methyl-4-quinolone (5a) with triphenyl phosphite dichloride gave ptelefolone (9) and the asymmetric synthesis of the alkaloid was explored. Ring closure of epoxides of 3-prenylquinolones in basic and non-basic media is discussed.

In a previous paper[1] we discussed the significance of hemiterpenoid quinoline alkaloids of *Ptelea trifoliata* containing terminal double bonds, and described the first synthesis of a member of the group, *O*-methylptelefolonium iodide (1). We now report the synthesis of the *N*-methyl-4-quinolone, ptelefolone (9).



(1)

The plan of synthesis (Scheme 1) involved the preparation of the 3-prenylquinolone (2a) from *N*-methyl-2,4-dimethoxyaniline and diethyl (3-methylbut-2-enyl)-malonate, conversion into the dihydrofuroquinolin-4-one (5a) and then dehydration to ptelefolone; these three stages are discussed separately. We also describe a synthesis of *O*-methylribaline (5d) and include a general account of the ring closure of epoxides derived from 3-prenylquinolones.

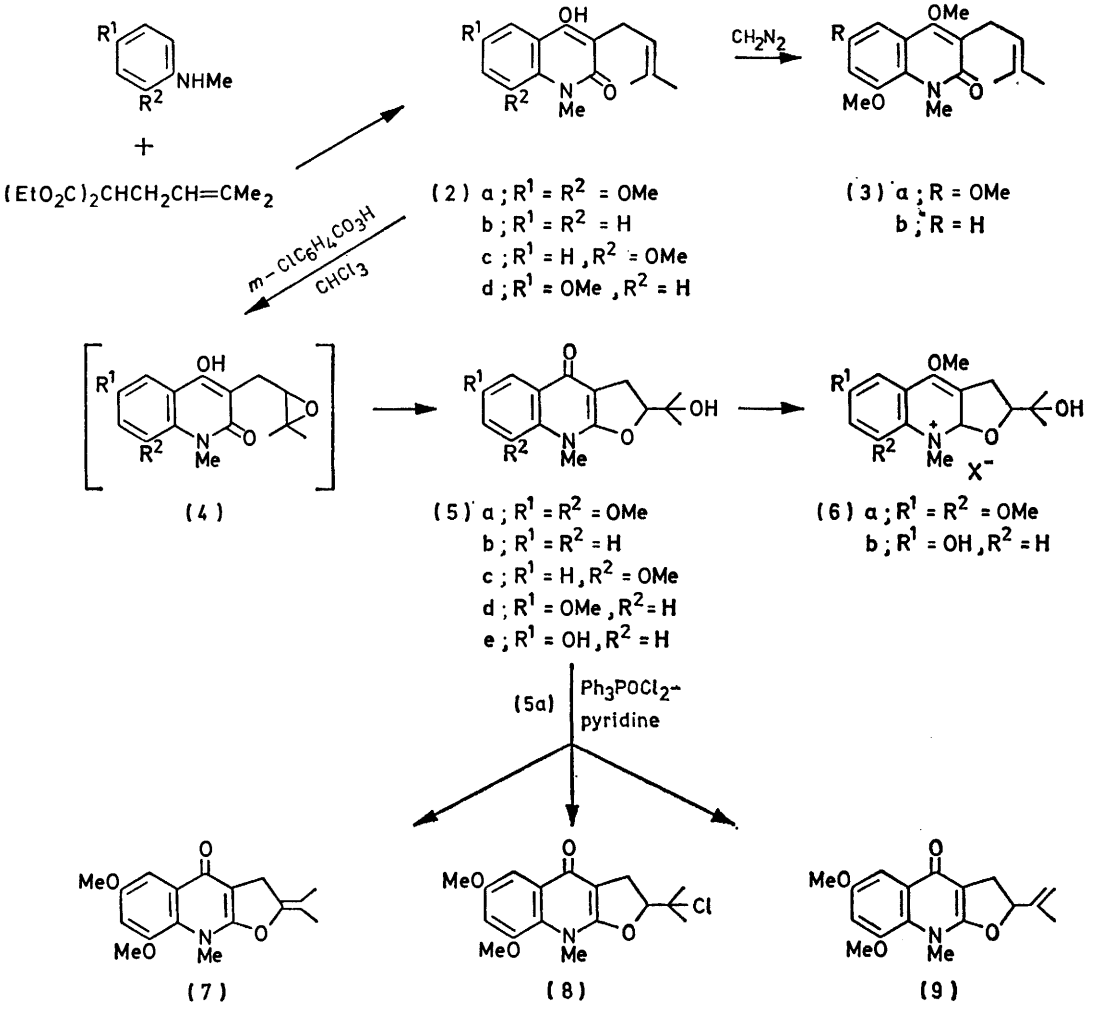
3-*Prenylquinolones* (2).—The required 2,4-dimethoxy-*N*-methylaniline was prepared previously[3] by methylation of *N*-acetyl-2,4-dimethoxyaniline followed by hydrolysis, but the formylation–reduction route to *N*-methylanilines[4] appeared to be more attractive and was applied to the present case. In contrast to the method used earlier,[5] reaction of 2,4-dimethoxyaniline with formic acid in refluxing toluene gave the *N*-formyl derivative in good yield. Reduction of the *N*-formylamine with lithium aluminium hydride on a small scale gave *N*-methyl-2,4-dimethoxyaniline almost quantitatively, but on a larger scale the product was shown by separation of picrates to contain 2,4-dimethoxy-*NN*-dimethylaniline (10—12%); the dimethylamine presumably arises through intermolecular transfer of a formyl group during the hydride reaction and subsequent reduction of the *N*-formyl-*N*-methylamine. The secondary amine was not readily purified by distillation and was used in an impure state for subsequent reactions, since the contaminating tertiary amine does not infere.

The 4-hydroxy-*N*-methyl-3-prenyl-2-quinolones (2b)[6-8] and (2c)[9] were prepared (26—27% yield) by reaction of the appropriate *N*-methylanilines with diethyl (3-methylbut-2-enyl)malonate in boiling diphenyl ether, and application of this procedure to 2,4-dimethoxy-*N*-methylaniline and to 4-methoxy-*N*-methylaniline gave the corresponding quinolones (2a) (20%) and (2d) (37%) respectively; structures were confirmed by the acidity of the compounds and by spectroscopy (see Experimental section). Reaction of the 4-hydroxy-2-quinolone (2a) with diazomethane afforded the 4-methoxy-derivative (3a); the n.m.r. data for this compound (see Experimental section) corresponded with that for a constituent of *P. trifoliata* for which the same structure was proposed.[10]

Dihydrofuroquinolinones (5).—Compounds of this type, (5b) and (5c), were obtained previously by oxidative cyclisation of 4-hydroxy-*N*-methyl-3-prenyl-2-quinolones (2b)[11] and (2c)[9] respectively. Reaction of the 2-quinolone (2a) with *m*-chloroperbenzoic acid in chloroform and isolation of the basic fraction through extraction with 2M-hydrochloric acid gave the linear furoquinoline (5a) as the sole product of oxidative cyclisation; an alternative work-up, using sodium carbonate to remove acidic by-products, resulted in the isolation of a second product, the angular furoquinolone (11a). The structures of the isomers were confirmed by i.r. and n.m.r. spectroscopy; an i.r. absorption at 1 650 cm^{-1} was typical of the 2-quinolone group in the angular compound (11a), and the n.m.r. spectrum of the linear furoquinolone showed a resonance at τ 2.5, characteristic of a proton at C-5 deshielded by a neighbouring carbonyl group in a 4-quinolone. The fact that the angular furoquinolone was obtained only when base was used during isolation suggests that the linear furoquinolone is the primary product and is converted into the isomer by base-catalysed rearrangement. Such a rearrangement was observed in the 8-methoxy-compound (5c),[12] and on treatment with sodium methoxide at ambient temperature the 6,8-dimethoxy-derivative (5a) behaves similarly and is converted into its angular isomer (11a) (Scheme 2).

Prolonged boiling of the *N*-methylfuroquinolinone (5a) with methyl iodide resulted in *O*-methylation to give the quinolinium iodide (6a; X = I). The structure of this compound was indicated by the n.m.r. spectrum, which showed three-proton singlets at τ 5.47, 5.67, 5.95, and 6.50, and by an alternative method of preparation involving treatment of the 4-methoxyquinoline derivative

(17a) with methyl iodide at ambient temperature. The *O*-methylation reaction, however, did not give consistent results and refluxing the furoquinolinone (5a) with methyl iodide alone or with methanol sometimes gave its hydriodide salt rather than the quinolinium iodide. The methylribaline (56%) (5d); since the latter compound has been correlated with ribalinidine (14a) and ribalinium cation (6b) as well as with ribaline (5e) [7,14] the preparation provides synthetic confirmation of the structures of the three alkaloids. Reaction of *O*-methylribaline with

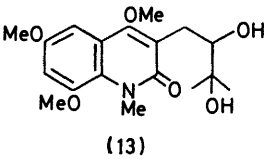


SCHEME 1

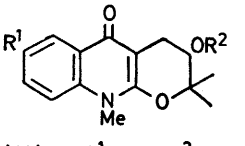
hydriodide gave an n.m.r. spectrum with three 3-proton singlets in the τ 5—7 region and with aqueous sodium carbonate was converted into the furoquinolinone (5a). Although the quinolinium cation (6a) has not been isolated from the plant, there is evidence that it is a constituent of *P. trifoliata*. Thus, Reisch and his co-workers [13] obtained an inseparable mixture of quinolinium salts from this species and showed that treatment with aqueous sodium hydroxide gave the diol (13), which is the expected base-cleavage product of compound (6a).

The phenolic quinoline alkaloid, ribaline (5e), was isolated from *Balfourodendron riedelianum* as its (+)-enantiomer and as the racemate; both (+)- and (±)-ribaline were converted into their *O*-methyl derivatives.[7] We now find that reaction of the 4-hydroxy-2-quinolone (2d) with *m*-chloroperbenzoic acid furnishes (±)-*O*-sodium methoxide afforded the angular furoquinolone (11b).

Ring Closure of Epoxides of 3-Prenylquinolones.—Although epoxides of 2,4-dimethoxy-3-prenylquinolines



(13)

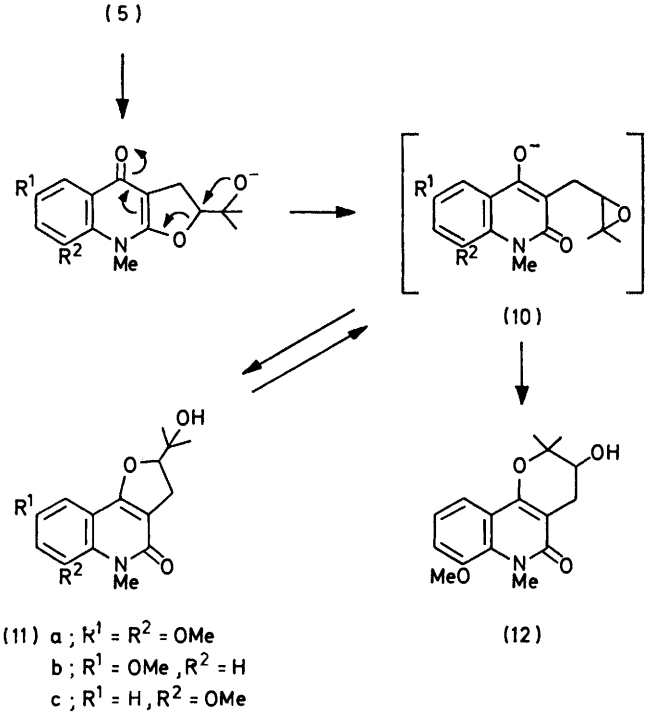


(14) a; R1 = OH, R2 = H
b; R1 = H, R2 = Ac

are easily obtained,[15,16] epoxides in which the oxygen functions are not protected undergo cyclisation readily, and only two such compounds, (19a) and (19b), have

been reported.[12,17] Knowledge of ring closure of epoxides of 3-prenylquinolones is derived mainly from studies of the oxidative cyclisation of 2,4-dihydroxy-3-prenylquinoline derivatives; a sufficient number of examples are now known to warrant discussion of the reaction in an attempt to evaluate the stereoelectronic factors involved.

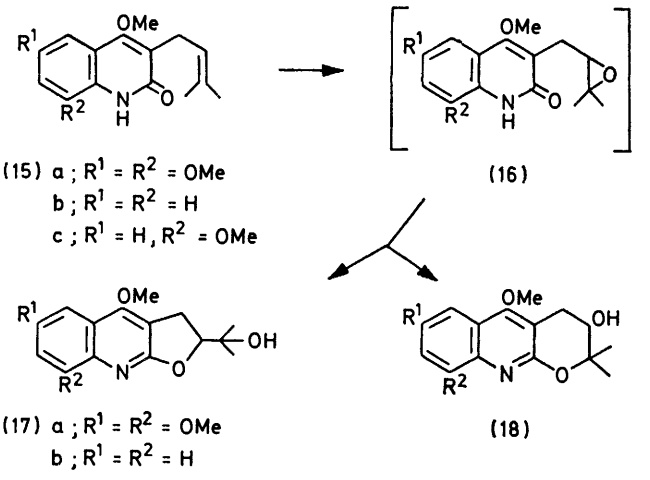
Treatment of the 4-methoxy-3-prenyl-2-quinolones (15a), (15b), and (15c) with peracids under non-basic conditions gives a mixture of dihydrofuro- (17) and dihydropyrano-quinolines (18) (Scheme 3).[18] Apparently ring closure of an intermediate epoxide (16) involves the



SCHEME 2

nucleophilic oxygen of the 2-quinolone group and occurs by a 5-*exo*- or 6-*endo*-process; Baldwin [19] suggests that in the opening of three-membered rings to form cyclic structures *exo*-modes are generally preferred on stereochemical grounds, but the lack of discrimination in this case may be attributed to a competing electronic effect whereby ring closure at the tertiary carbon atom of an epoxide ring to give pyrano-derivatives is favoured.

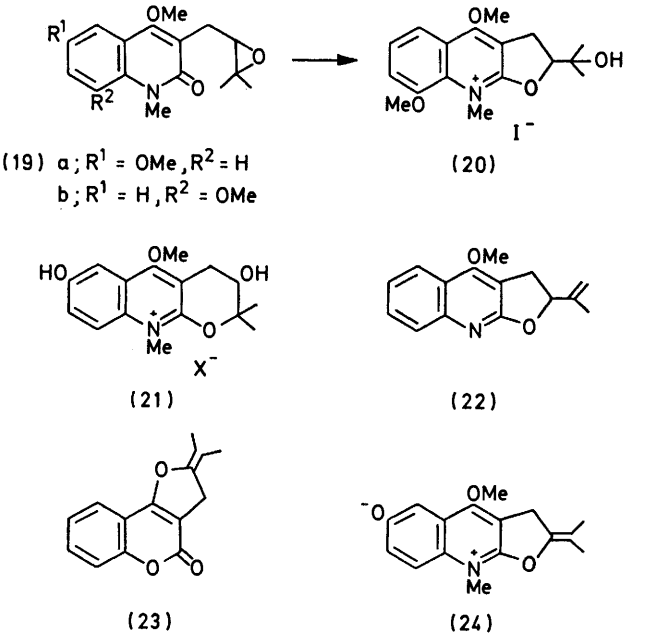
N-Methyl-2-quinolones behave differently. Thus, reaction of 4-hydroxy-*N*-methyl-3-prenyl-2-quinolones (2a—d) with peracids in chloroform affords *N*-methyldihydrofuroquinolinones (5); dihydropyranoquinolinones were not obtained in these reactions and the participation of the 4-hydroxy-group leading to compounds with angular annelation was not observed.[9,11] In the presence of strong acid, a medium that would be expected to favour the formation of pyranoquinolines, epoxidation of the *N*-methyl-2-quinolone (3b) gave the dihydrofuroquinoline (20) quantitatively; [9] the predicted intermediate epoxide (19b) was prepared by



SCHEME 3

another method and with hydrogen iodide also gave the furoquinoline (20) only.[12] The reluctance of the epoxide (19b) and epoxides derived from *N*-methyl-3-prenyl-2-quinolones to form pyrano-derivatives may be due to unfavourable non-bonded interactions between the *N*-methyl group and the terminal $=CMe_2$ group in the transition state. Although a complete study has not been made, there is no evidence to suggest that the formation of furoquinolinones is controlled by the thermodynamic instability of the pyranoquinolinone; indeed, the pyranoquinolinium cation (21) is a constituent of *Ruta graveolens* [20] and rearrangement of the furoquinolinone (5b) with acetic anhydride and sodium acetate furnishes the pyranoquinolinone (14b).[8]

Information about base-catalysed ring closure of epoxides of 4-hydroxy-*N*-methyl-3-prenyl-2-quinolones is derived from studies of the rearrangement of furoquinolinones (5). As described above, the furoquinol-



ines (5a) and (5d) with strong base at ambient temperature give the angular isomers (11a) and (11b), respectively, and similar reactions of the analogous compounds (5b) and (5c) have been reported.[10,11,21] In the 8-methoxy-series rigorous treatment of the furoquinolinone (5c) with base furnishes the angular pyranoquinolinone (12); it was shown that the epoxide (10; $R^1 = H$, $R^2 = OMe$) was a common intermediate, the angular furoquinolinone (11c) being formed under kinetic control, while the pyranoquinolinone (12) is thermodynamically more stable (Scheme 2).[12] To summarise, comparison between the acid- and base-catalysed ring-closures indicates that the 4-hydroxyepoxide (4) gives only linear furoquinolinones whereas the formation of the anionic species (10) in the presence of base leads to angular products; in the latter case there is clearly no stereochemical interaction with the *N*-methyl group inhibiting the production of the pyranoquinolinone.

Dehydration of the Tertiary Alcohol (5a).—Problems associated with the conversion of dihydrofuroquinolines and related compounds into terminal olefins were discussed previously.[1] Triphenyl phosphite dibromide and potassium carbonate in acetone was shown to be an effective reagent for this purpose, the 4-methoxyquinoline (17b) giving a mixture of olefins in which the terminal olefin (22) was the major product.[1] In the 6,8-dimethoxyquinoline group of compounds this reagent leads to bromination of the quinoline nucleus, but we find that the use of triphenyl phosphite dichloride avoids this difficulty. Reaction of the hydroxy-derivative (5a) with triphenyl phosphite dichloride in refluxing pyridine gave the required terminal olefin, (±)-ptelefolone (9) (32%); the structure of the compound was confirmed by comparison of n.m.r. and mass spectral data with those recorded for (+)-ptelefolone isolated from *P. trifoliata*.[22] A second product of the reaction was shown to be the tertiary chloride (8) by its n.m.r. spectrum, which was similar to that of the alcohol (5a) except that the CH and CMe_2 resonances occurred at lower field, and by its partial conversion by boiling pyridine into ptelefolone (9). The tetrasubstituted olefin (7) was a minor constituent of the reaction of the hydroxy-derivative (5a) with triphenyl phosphite dichloride; the n.m.r. spectrum, which indicates the absence of a methine group and shows singlets at τ 6.55 (CH_2) and at 8.26 and 8.37 ($=CMe_2$), is comparable to that of the furocoumarin (23).[23] Apparently the only other example of a tetrasubstituted olefin in the hemiterpenoid quinoline series of compounds is the zwitterion (24), obtained by acid-catalysed dehydration of the dihydrofuroquinoline alkaloid, pteleatinium cation.[24]

Attempted Asymmetric Synthesis of Ptelefolone.—Although all the hemiterpenoid quinoline alkaloids of *P. trifoliata* containing a terminal double bond have a single chiral centre, several were isolated as racemates,[25] and ptelefolone had a specific optical rotation of $[\alpha]_D$ +1.9°.[22] A possible explanation of this lack of optical activity, or its unexpectedly low level in ptelefolone, is that racemisation of the allylic system occurred during isolation of the alkaloids; in order to study the racemisation of ptelefolone we planned to carry out an asymmetric synthesis of the alkaloid by preparation and subsequent dehydration of optically active hydroxy-derivative (5a).

Reaction of the 3-prenylquinolone (2c) with chiral peracids furnished the dihydrofuroquinolinone balfourodine (5c) with up to 10% optical induction, based on the specific optical rotation of the alkaloid.[26] The 6,8-dimethoxy-3-prenylquinolone (2a) and (+)-(*S*)-peroxycamphoric acid in chloroform gave the optically active dihydrofuroquinolinone (5a); fractional crystallisation provided the racemate and chromatography of the more soluble fractions gave a sample having $[\alpha]_D$ +53.7°. The absolute stereochemistry of balfourodine has been established,[26] and by analogy with its asymmetric synthesis from (*S*)- and from (*R*)-peracids, the (+)-dihydrofuroquinolinone (5a) has an *R*-configuration. When base was used in the work up of the asymmetric epoxidation reaction, the angular dihydrofuroquinolinone (11a) containing an excess of the (+)-enantiomer was obtained.

Application of the triphenyl phosphite dichloride reaction to the (+)-dihydrofuroquinolinone (5a) and separation of the products by chromatography gave ptelefolone (9) and the tertiary chloride (8) with neither compound showing appreciable optical activity. Although one of the products of the reaction, the tetrasubstituted olefin (7), allows a possible route for racemisation, the mechanism of the process is not yet clear and will be the subject of further investigation.

EXPERIMENTAL

N.m.r. spectra were determined with Perkin-Elmer R12 (60 MHz) or R32 (90 MHz) spectrometers using tetramethylsilane as an internal standard. Mass spectra were recorded on a Varian MS9 spectrometer. Optical rotations were measured on a Perkin-Elmer 121 electronic polarimeter capable of measurement to $\pm 1 \times 10^{-3}$ degrees.

2,4-*Dimethoxy*-N-*methylaniline*.—A solution of freshly distilled 2,4-dimethoxyaniline (25.5 g) and formic acid (97%, 6.5 ml) in toluene (100 ml) was refluxed for 3 h and then evaporated. Crystallisation of the residue from benzene gave *N*-formyl-2,4-dimethoxyaniline in needles (24.8 g, 82%), m.p. 140—141 °C (lit.,[5] 140—141 °C).

A suspension of lithium aluminium hydride (2.0 g) in tetrahydrofuran (50 ml) was added to a solution of *N*-formyl-2,4-dimethoxyaniline (10 g) in tetrahydrofuran (200 ml) under nitrogen at a rate that kept the mixture refluxing. After the mixture had been kept at ambient temperature for 3 h, water (2 ml) was added followed by 4M-sodium hydroxide (8 ml) and then water (4 ml). Filtration, extraction of the filtrate with dichloromethane, and evaporation gave 2,4-dimethoxy-*N*-methylaniline as an oil (9.8 g, 90%), b.p. 92—99 °C at 0.6 mmHg, containing 10% 2,4-dimethoxy-*NN*-dimethylaniline (n.m.r.). A portion in ethanol was added to a hot solution of picric acid in ethanol; the precipitate, m.p. 156—158 °C (from methanol), was converted with sodium carbonate into 2,4-dimethoxy-*NN*-dimethylaniline, τ ($CDCl_3$) 6.15 (3 H, s) and 6.24 (3 H, s) (2 × OMe), and 7.28 (6 H, s, NMe_2). The mother-liquors

from the crystallisation gave 2,4-dimethoxy-*N*-methylaniline, τ ($CDCl_3$) 6.26 (3 H, s) and 6.32 (3 H, s) (2 × OMe), and 7.22 (3 H, s, NMe).

4-*Hydroxy*-6,8-*dimethoxy*-N-*methyl*-3-(3-*methylbut*-2-*enyl*)-2-*quinolone* (2a).—A solution of 2,4-dimethoxy-*N*-methylaniline (containing *ca.* 10% of the *NN*-dimethyl derivative) (10 g) and diethyl (3-methylbut-2-enyl)malonate (14 g) in diphenyl ether (30 ml) was refluxed for 3 h, and the solvent was removed. The residue in dichloromethane was extracted with 2M-sodium hydroxide, and the alkaline solution was acidified and extracted with dichloromethane to give the 2-quinolone (2a) as needles (3.3 g, 20%) (from aqueous ethanol), m.p. 166—168 °C, τ ($CDCl_3$) 2.84 (1 H, d), 3.30 (1 H, d), 4.60 (1 H, t, $-CH_2-CH=$), 6.06 (3 H, s) and 6.12 (6 H, s) (2 × OMe and *N*Me), 6.46 (2 H, d, $-CH_2-CH=$), and 8.2 (6 H, br s, 2 × Me), *m/e* 303 (36%, M^+) and 260 (100). A satisfactory elemental analysis was not obtained.

4-*Hydroxy*-6-*methoxy*-N-*methyl*-3-(3-*methylbut*-2-*enyl*)-2-*quinolone* (2d).—Reaction of 4-methoxy-*N*-methylaniline (13.7 g) with diethyl (3-methybut-2-enyl)malonate (22.8 g) as described for the preparation of (2a), gave the 2-*quinolone* (2d) as prisms (7.5 g, 37%) (from ethanol), m.p. 171—172 °C, τ (CD_3OD) 2.4—2.8 (3 H, m, ArH), 4.75 (1 H, t, $-CH_2-CH=$), 6.11 (3 H, s) and 6.30 (3 H, s) (OMe and NMe), 6.57 (2 H, d, $-CH_2CH=$), and 8.20 (3 H, s) and 8.31 (3 H, s) (2 × Me) (Found: C, 70.4; H, 6.9; N, 5.2. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%).

4,6,8-*Trimethoxy*-N-*methyl*-3-(3-*methylbut*-2-*enyl*)-2-*quinolone* (3a).—An excess of an ethereal solution of diazomethane was added to the 4-hydroxy-2-quinolone (2a) (100 mg) in methanol (5 ml). After 5 min, the excess of reagent was destroyed with acetic acid, 2M-sodium carbonate was added, and extraction with methylene chloride gave the trimethoxy-2-quinolone (3a) as an oil (98 mg) (lit.,[9] m.p. 69—71 °C), $\nu_{max.}$ (film) 1 650 cm^{-1}, τ ($CDCl_3$) 3.1 (1 H, d, ArH), 3.3 (1 H, d, ArH), 4.7 (1 H, t, $-CH_2CH=$), 6.05(s) and 6.03(s) (12 H, 3 × OMe and NMe), 6.6 (2 H, d, $-CH_2CH=$), and 8.11(s) and 8.20(s) (6 H, CMe_2) [lit.,[9] $\nu_{max.}$ (KBr) 1 640 cm^{-1}, τ ($CDCl_3$) 3.1, 3.3, 4.7, 6.03, 6.05, 6.6, 8.1, and 8.3.]

2-(1-*Hydroxy*-1-*methylethyl*)-6,8-*dimethoxy*-9-*methyl*-2,3-*dihydrofuro*[2,3-b]*quinolin*-4(9H)-*one* (5a).—(*a*) The 2-quinolone (2a) (100 mg) in chloroform (10 ml) was added to a solution of *m*-chloroperbenzoic acid (114 mg) in chloroform (10 ml) at 0 °C. The solution was allowed to reach ambient temperature, kept for 3 days, and extracted with 2M-hydrochloric acid. The extract was basified with 2M-sodium carbonate and extracted with dichloromethane to give the *furoquinolinone* (5a) (55 mg, 51%), m.p. 213—215 °C (from methanol–ether), $\nu_{max.}$ (KBr) 1 620 cm^{-1} (4-quinolone carbonyl), τ ($CDCl_3$), 2.5 (1 H, d, 5-H), 3.38 (1 H, d, 7-H), 5.20 (1 H, t, $-CH_2CH-O-$), 6.12 (6 H, s, 2 × OMe), 6.18 (3 H, s, NMe), 6.75 (2 H, d, $-CH_2CH-O-$), and 8.65(s) and 8.75(s) (6 H, CMe_2), *m/e* 319 (100%, M^+), 286 (10), and 276 (36) (Found: C, 63.9; H, 6.6; N, 4.4. $C_{17}H_{21}NO_5$ requires C, 63.9; H, 6.6; N, 4.4%).

(*b*) The 2-quinolone (2a) (10.3 g) was oxidised with (+)-peroxycamphoric acid (13.4 g), $[\alpha]_D$ +53° (lit.,[28] +52°), active oxygen content 83%, as described in (*a*) above to give the furoquinolinone (5a) (4.7 g). Crystallisation from methanol–ether gave the compound (2.0 g) with $[\alpha]_D$ +0.5°, Evaporation of the solution, preparative t.l.c. of the residue on silica with chloroform–methanol (10 : 1) and isolation of the main band at R_F 0.5 gave the furoquinolinone (1.5 g), $[\alpha]_D$ +47°; chromatography on Fluorosil gave a sample having $[\alpha]_D$ +53.7°.

2-(1-*Hydroxy*-1-*methylethyl*)-6,8-*dimethoxy*-5-*methyl*-2,3-*dihydrofuro*[3,2-c]*quinolin*-4(5H)-*one* (11a).—(*a*) A solution of the linear furoquinolinone (5a) (30 mg) in methanol (10 ml) containing sodium methoxide (200 mg) was kept for 20 h. Addition of water and extraction with chloroform gave the *angular furoquinolinone* (11a) as needles (21 mg), m.p. 151—152 °C (from methanol–ether), $\nu_{max.}$ (KBr) 1 650 cm^{-1} (2-quinolone carbonyl), τ ($CDCl_3$) 3.32 (2 H, m, ArH), 5.13 (1 H, t, $-CH_2CH-O-$), 6.13 (9 H, br s, 2 × OMe and NMe), 6.84 (2 H, d, $-CH_2CH-O-$), and 8.63(s) and 8.72(s) (6 H, CMe_2), *m/e* 319 (100%, M^+), 304 (18), and 286 (22) (Found: C, 63.8; H, 6.6; N, 4.3. $C_{17}H_{21}NO_5$ requires C, 63.9; H, 6.6; N, 4.4%).

(*b*) Reaction of the 2-quinolone (2a) (5 g) with (+)-peroxycamphoric acid (10 g) in chloroform as described above, extraction of the solution with 2M-sodium hydroxide, and work-up of the chloroform solution gave a product which crystallised from methanol–ether to give the angular furoquinolone (11a) (155 mg), identical (mixed m.p. and n.m.r.) with an authentic sample. Evaporation of the methanol–ether solution and preparative t.l.c. of the residue on silica with chloroform–methanol (10 : 1) afforded the angular furoquinolinone (11a) (100 mg) R_F 0.5, $[\alpha]_D$ +1.48°, and the linear furoquinolinone (5a) (70 mg), R_F 0.4, $[\alpha]_D$ +2.2°.

Reaction of the Furoquinolinone (5a) *with Methyl Iodide.*—(*a*) Refluxing the furoquinolinone (5a) with methyl iodide for 48 h gave 2-(1-*hydroxy*-1-*methylethyl*)-4,6,8-*trimethoxy*-9-*methyl*-2,3-*dihydrofuro*[2,3-b]*quinolinium iodide* (6a; X = I) as needles, m.p. 210—215 °C (decomp.) (from methanol–ether), τ (CD_3OD) 2.69 (1 H, d, ArH), 2.86 (1 H, d, ArH), 4.72 (1 H, t, $-CH_2-CH-O-$), 5.47 (3 H, s, $\overset{+}{N}Me$), 5.67 (3 H, s), 5.95 (3 H, s), and 6.05 (3 H, s) (3 × OMe), and 8.57(s) and 8.67(s) (6 H, CMe_2) (Found: C, 47.6; H, 5.3; N, 3.1. $C_{18}H_{25}INO_5$ requires C, 46.9; H, 5.2; N, 3.0%).

The quinolinium iodide was deposited when a solution of the tertiary base (17a) in methyl iodide was kept at 20 °C for 10 h.

(*b*) In other experiments, reaction of the furoquinolinone (5a) with refluxing methyl iodide alone or with methanol gave the *hydriodide* as prisms, m.p. 180—185 °C (from methanol–ether), τ (CD_3OD) 2.76 (1 H, d, ArH), 3.07 (1 H, d, ArH), 4.82 (1 H, t, $-CH_2CH-O-$), 5.82 (3 H, s), 6.03 (3 H, s), and 6.10 (3 H, s) (2 × OMe and $\overset{+}{N}Me$), and 8.57(s) and 8.67(s) (6 H, CMe_2), *m/e* 219 (100%, M^+ — HI) (Found: C, 46.8; H, 5.0; N, 3.2. $C_{17}H_{22}INO_5$ requires C, 45.6; H, 5.0; N, 3.1%).

Treatment of the hydriodide with 2M-sodium carbonate gave the furoquinolinone (5a).

(±)-*O-Methylribaline* (5d).—Treatment of the 2-quinolone (2d) (3.2 g) with *m*-chloroperbenzoic acid in chloroform, as described for the reaction of 2-quinolone (2a) [see (*a*) above], gave (±)-*O*-methylribaline (5d) (1.86 g, 56%), m.p. 225—226 °C (from methanol–ether) (lit.,[7] 226—227 °C), τ($CDCl_3$) 2.15 (1 H, d, ArH), 2.7—2.9 (2 H, m, ArH), 5.2 (1 H, t, $-CH_2CH-O-$), 6.1 (3 H, s) and 6.33 (3 H, s) (OMe and NMe), 6.8 (2 H, d, $-CH_2CH-O-$), and 8.65(s) and 8.75(s) (6 H, CMe_2), *m/e* 289 (100%, M^+), 256 (22), and 246 (24) (Found: C, 66.3; H, 6.6; N, 5.0. Calc. for $C_{16}H_{19}NO_4$: C, 66.4; H, 6.6; N, 4.8%).

2-(1-*Hydroxy*-1-*methylethyl*)-6-*methoxy*-5-*methyl*-2,3-*dihydrofuro*[3,2-c]*quinolin*-4(5H)-*one* (11b).—Reaction of the linear furoquinolinone (5d) (200 mg) with sodium methoxide as described for the analogue (5a) gave the *angular furo-*

quinolinone (11b) as needles (157 mg), m.p. 175—176 °C (from ethyl acetate), τ($CDCl_3$) 2.8—2.95 (3 H, m, ArH), 5.16 (1 H, t, $-CH_2CH-O-$), 6.15 (3 H, s) and 6.45 (3 H, s) (OMe and NMe), 6.83 (2 H, d, $-CH_2CH-O-$), and 8.6(s) and 8.7(s) (6 H, CMe_2), *m/e* 289 (66%, M^+), 256 (33), and 230 (100) (Found: C, 66.2; H, 6.6. $C_{16}H_{19}NO_4$ requires C, 66.4; H, 6.6%).

Reaction of the Furoquinolinone (5a) *with Triphenylphosphite Dichloride*.—A solution of the 4-quinolone (5a) (400 mg) and an excess of triphenylphosphite dichloride [27] in dry pyridine was refluxed for 24 h and evaporated. The residue was chromatographed on silica, eluting first with chloroform and then with methanol. Preparative t.l.c. of the latter fraction on silica with chloroform–methanol (10 : 1) gave (±)-ptelefolone (9) as a gum (120 mg, 32%), R_F 0.5, τ ($CDCl_3$) 2.52 (1 H, d, 5-H), 3.35 (1 H, d, ArH), 4.63 (1 H, t, $-CH_2-CH-O-$), 4.93(s) and 5.03(s) (2 H, $=CH_2$), 6.1(s) and 6.2(s) (9 H, 2 × OMe and NMe), 6.72 (2 H, d, $-CH_2CH-O-$), and 8.23 (3 H, s, Me–C=), *m/e* 301 (87%, M^+) and 286 (100) [lit.,[22] for (+)-ptelefolone, m.p. 70—71 °C, τ 2.45, 4.7, 4.85, 5.0, 6.1, 6.7, and 8.2, *m/e* 301(87%) and 286 (100)]. A second t.l.c. fraction, R_F 0.2, was apparently the chloride (8) (215 mg, 51%), m.p. 175—177 °C (needles from methanol–isopropyl ether), τ ($CDCl_3$) 2.47 (1 H, d, 5-H), 3.31 (1 H, d, ArH), 4.88 (1 H, t, $-CH_2-CH-O-$), 6.05(s), 6.07(s), and 6.10(s) (9 H, 2 × OMe and NMe), 6.65 (2 H, d, $-CH_2-CH-$), and 8.24(s) and 8.34(s) (6 H, $-C(Cl)Me_2$). When the reaction was repeated with the 4-quinolone (5a) (100 mg) and worked up by washing a chloroform solution of the product with 2M-sodium carbonate and crystallisation of the product, *2-isopropylidene-6,8-dimethoxy-9-methyl-2,3-dihydrofuro-*[2,3-b]*quinolin-4(9H)-one* (7) was obtained as needles (12 mg), m.p. 190—191 °C (from methanol–ether), τ(CD_3OD) 2.8 (1 H, d) and 3.4 (1 H, d) (ArH), 6.2 (9 H, br s, 2 × OMe and NMe), 6.55 (2 H, br s, CH_2), and 8.26(s) and 8.37(s) (6 H, $=CMe_2$), *m/e* 301 (10%, M^+), 300 (10), and 299 (35) (Found: C, 67.8; H, 6.2; N, 4.9. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.4; N, 4.7%).

Application of the reaction to the (+)-4-quinolone (5a) gave optically-inactive ptelefolone (9) and chloride (8).

Reaction of the chloride (8) (100 mg) with refluxing pyridine for 36 h and preparative t.l.c. of the product gave (±)-ptelefolone (9) (12 mg).

Preliminary work on the synthesis and rearrangement of *O*-methylribaline was carried out by Catherine M. Kirkpatrick. We thank the Department of Education for Northern Ireland for a postgraduate studentship (to J. L. G.).

[9/1908 *Received*, 3rd *December*, 1979]

REFERENCES

[1] Part 19, J. L. Gaston, M. F. Grundon, and K. J. James, *J.C.S. Perkin I*, 1980, 1136.
[2] Preliminary report, J. L. Gaston and M. F. Grundon, *Tetrahedron Letters*, 1978, 2629.
[3] J. D. Loudon and J. Ogg, *J. Chem. Soc.*, 1955, 739.
[4] M. Clerc-Borg and C. Mentzer, *Bull. Soc. chim. France*, 1953, 814.
[5] G. R. Pettit, M. V. Kalnins, T. M. H. Liu, E. G. Thomas, and K. Parent, *J. Org. Chem.*, 1961, **26**, 2563.
[6] F. Bohlmann and V. S. Bhaskar Rao, *Chem. Ber.*, 1969, **102**, 1774.
[7] R. A. Corral and O. O. Orazi, *Tetrahedron*, 1973, **29**, 205.
[8] M. F. Grundon and S. A. Surgenor, unpublished work.
[9] E. A. Clarke and M. F. Grundon, *J. Chem. Soc.*, 1964, 4196.
[10] J. Reisch, K. Szendrei, I. Novák, E. Minker, J. Körösi, and K. Csedo, *Tetrahedron Letters*, 1972, 449.
[11] M. F. Grundon and S. A. Surgenor, *J.C.S. Chem. Comm.*, 1978, 624.
[12] K. J. James and M. F. Grundon, *J.C.S. Perkin I*, 1979, 1467.
[13] J. Körösi, K. Szendrei, I. Novák, J. Reisch, G. Blazso, E. Minker, and M. Koltai, *Herba Hung.*, 1976, **15**, 9 (*Chem. Abs.*, 1976, **85**, 30,608).
[14] R. A. Corral and O. O. Orazi, *Tetrahedron*, 1965, **21**, 909.
[15] R. M. Bowman and M. F. Grundon, *J. Chem. Soc.* (*C*), 1967, 2368.
[16] R. M. Bowman, G. A. Gray, and M. F. Grundon, *J.C.S. Perkin I*, 1973, 1051.
[17] R. A. Corral and O. O. Orazi, *Tetrahedron*, 1966, **22**, 1153.
[18] R. M. Bowman and M. F. Grundon, *J. Chem. Soc.* (*C*), 1966, 1504.
[19] J. E. Baldwin, *J.C.S. Chem. Comm.*, 1976, 734.
[20] K. Szendrei, J. Reisch, I. Novák, L. Simon, Zs. Rozsa, E. Minker, and M. Koltai, *Herba Hung.*, 1971, **10**, 131 (*Chem. Abs.*, 1973, **79**, 15, 853).
[21] H. Rapoport and K. G. Holden, *J. Amer. Chem. Soc.*, 1960, **82**, 4395.
[22] J. Reisch, K. Szendrei, V. Papay, I. Novák, and E. Minker, *Tetrahedron Letters*, 1970, 3365.
[23] K. Yamamoto, H. Irie, and S. Uyeo, *Yakugaku Zasshi*, 1971, **91**, 257 (*Chem. Abs.*, 1971, **74**, 125509).
[24] L. A. Mitscher, M. S. Bathala, G. W. Clark, and J. L. Beal, *Lloydia*, 1975, **38**, 109; *cf.* M. F. Grundon, in 'The Alkaloids,' ed. M. F. Grundon, Specialist Periodical Reports, The Chemical Society, London, 1977, vol. 7, p. 86.
[25] J. Reisch, K. Szendrei, I. Novák, E. Minker, and V. Papay, *Tetrahedron Letters*, 1969, 3803; J. Reisch, K. Szendrei, V. Papay, E. Minker, and I. Novák, *ibid.*, 1970, 1945.
[26] R. M. Bowman, J. F. Collins, and M. F. Grundon, *J.C.S. Perkin I*, 1973, 626.
[27] D. G. Coe, S. R. Landauer, and H. N. Rydon, *J. Chem. Soc.*, 1954, 2281.
[28] N. A. Milas and A. McAlevy, *J. Amer. Chem. Soc.*, 1933, **53**, 349.