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THE SYNTHESIS OF PTELEFOLONE AND O-METHYLPTELEFOLONIUM IODIDE

J. L. Gaston and M. F. Grundon*
School of Physical Sciences, The New University of Ulster,
Coleraine, Northern Ireland.

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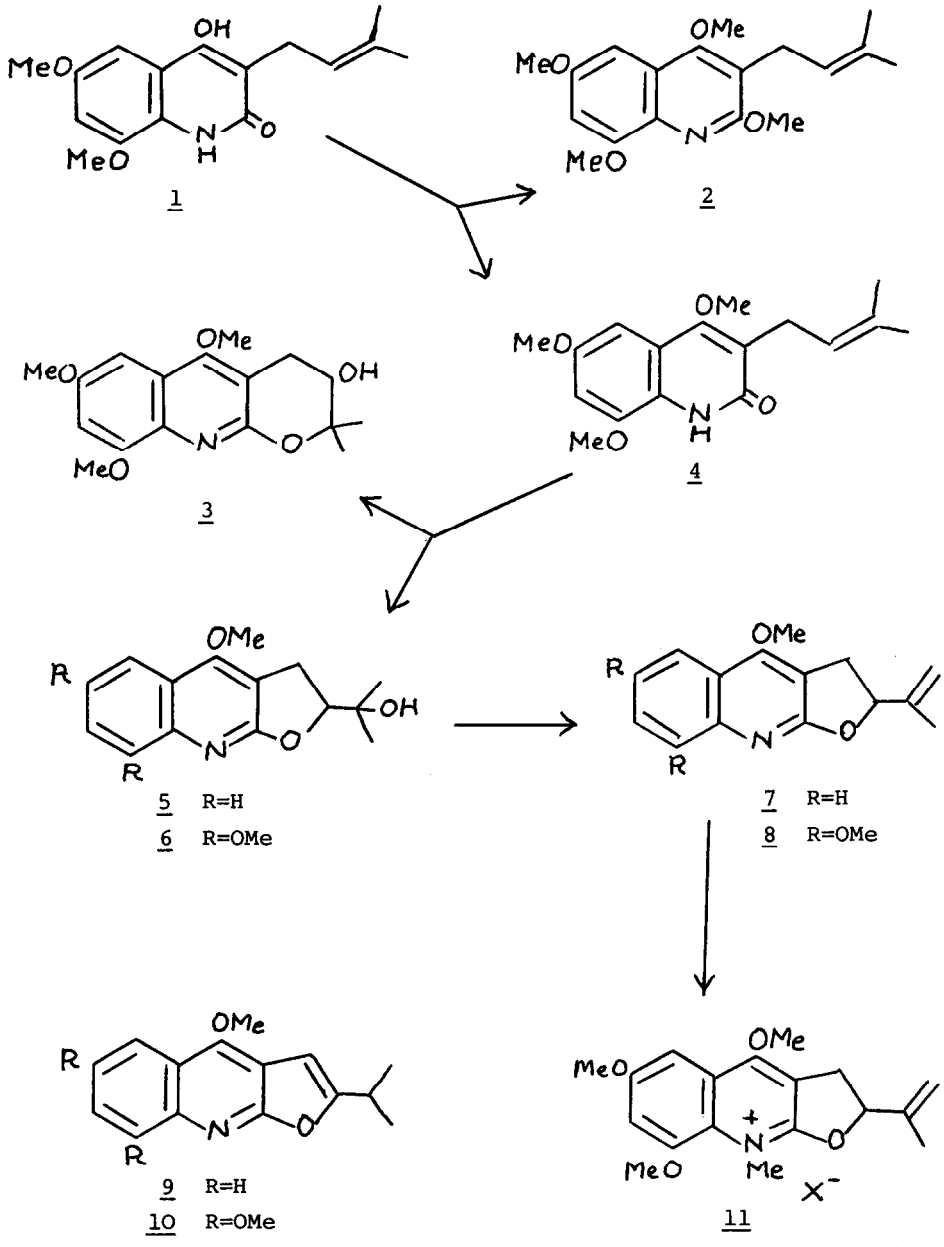
A unique group of hemiterpenoid quinoline alkaloids containing terminal double bonds was isolated by Reisch and co-workers[1,2] from the hop tree, Ptelea trifoliata L., and the constitutions were established by spectroscopy. Four structural types, exemplified by alkaloids 11, 18, 19 and 20 have been identified, other members of the group differing only in the pattern of oxygenated substituents in the aromatic ring. 3-Prenyl-2-quinolones, cf. 4 and 12 and hydroxyisopropyldihydrofuroquinolones, cf. 6 and 15, are plausible biosynthetic precursors and are also constituents of P. trifoliata[3,4]; we now report biomimetic syntheses of the Ptelea alkaloids, O-methylptelefolonium cation (11) and ptelefolone (18) based on dehydration of hydroxyisopropyldihydrofuroquinolones 6 and 15, respectively.

The 4-hydroxy-3-prenyl-2-quinolones 1 and 12 were prepared from aromatic amines by the method developed previously for compounds of this type[5]. Reaction of 2-quinolone 1 with diazomethane furnished a mixture of the tetramethoxyquinoline 2 and the trimethoxy-2-quinolone 4. Treatment of the latter compound with m-chloroperoxybenzoic acid gave the dihydropyranoquinoline 3 (31%) and its furo-isomer (6) (26%). A mixture of the exo-olefin 7 and the furoquinoline 9 was obtained from the dihydrofuroquinoline 5 by reaction with triphenyl phosphite dibromide and potassium carbonate[6], but application of this procedure to the 6,8-dimethoxydihydrofuroquinoline 6 resulted in nuclear bromination and other reactions. Dehydration to the required terminal olefin 8 (20%) was effected by means of thionyl chloride and pyridine; the isomeric isopropylfuroquinoline (10) was not formed in this reaction but was obtained quantitatively by acid-catalysed dehydration of quinoline 6. The exo-olefin 8 afforded a methiodide (11;X=I) with an n.m.r. spectrum corresponding to that recorded for O-methylptelefolonium cation isolated as the chloride from P. trifoliata[2].

In contrast to compound 1, the N-methyl-2-quinolone 12 was readily prepared and purified and was a more useful synthetic intermediate. Reaction with diazomethane gave the Ptelea alkaloid 13 in almost quantitative yield. Treatment of the 3-prenyl-2-quinolone 12 with a peroxy acid furnished the dihydrofuro-4-quinolone 15 (50%); when sodium hydroxide was used during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6 R=OMe
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7 R=H
8 R=OMe
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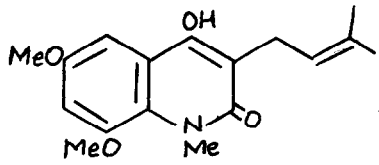
11



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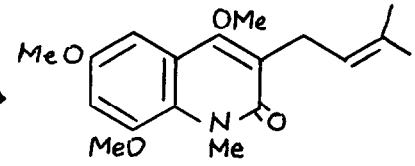

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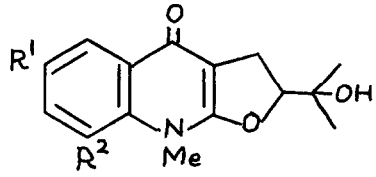
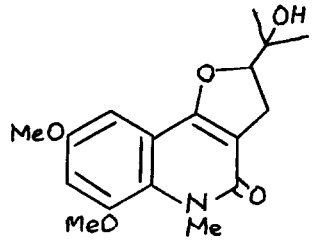


14 R^1=H, R^2=OMe

15 R^1=R^2=OMe



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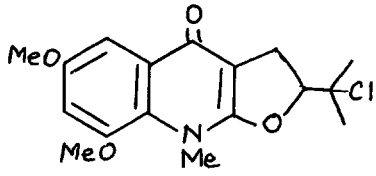
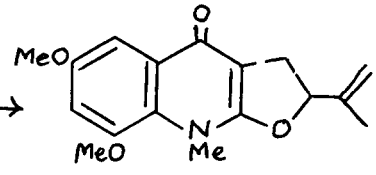
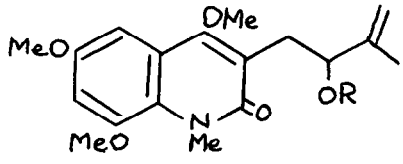


17



18



19 R=H

20 R=Me

isolation, the major product was the angular isomer 16, formed apparently by rearrangement of the linear 4-quinolone 15 as observed for the 8-methoxy analogue, balfourodine (14)[7]. Reaction of the 4-quinolone 15 with triphenyl phosphite dichloride in acetone gave the chloro-derivative 17 (47%), which with pyridine was converted in good yield into the alkaloid, ptelefolone (18); the thermodynamically more stable endo-olefin, cf. 10, was not detected.

Of the nine alkaloids of P. trifoliata containing a chiral centre adjacent to an exo-double bond, cf. 11, 18, 19 and 20 most are optically inactive perhaps because of rapid racemisation of the allylic system during isolation. Ptelefolone (18), however, was obtained as an enantiomer, $[\alpha]_D$ + 7°($CHCl_3$)[1], and in order to study the stereochemistry of the alkaloids we attempted an asymmetric synthesis of ptelefolone. The 3-prenyl-2-quinolone 12 with (+)-(S)-peroxycamphoric acid gave the furoquinolone 15, $[\alpha]_D$ + 1.1-2.2°, containing by analogy with similar asymmetric reactions[8] a preponderance of the (R)-enantiomer; the angular derivative 16, $[\alpha]_D$ + 1.5°, was also isolated. Partial reaction of the tertiary alcohol 15 with triphenyl phosphite dichloride in pyridine led to the formation of racemic ptelefolone and racemic chloro--derivative and to the recovery of the tertiary alcohol with over 50% reduction of optical activity. Thus, it appears that racemisation occurs readily during conversion into the tertiary chloride.

The structures of the compounds described were determined by elemental analysis and by spectroscopic data.

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