The Absolute Configuration of Some Quinoline Alkaloids

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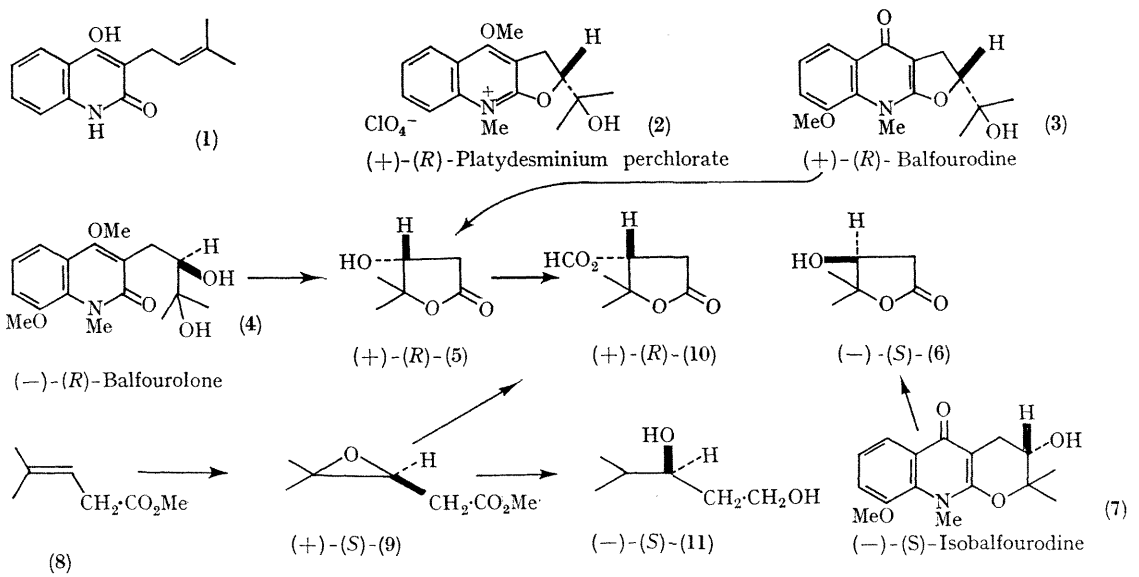
Summary The absolute configurations of some furano- and pyrano-quinoline alkaloids have been established by ozonolysis.

IN a recent biosynthetic study,[1] we showed that the isopropylfuranoquinoline alkaloid, platydesminium salt (2), is derived in *Skimmia japonica* Thunb. from the dimethylallylquinoline (1) presumably by oxidative cyclisation and the same general route is likely to apply to related quinoline alkaloids, for example balfourodine (3) and isobalfourodine (7). Any detailed schemes for oxidative cyclisation must be consistent with the relative stereochemistry of chiral compounds occurring together in the same plant and in this connection, we studied[2] the relative configuration of the alkaloids balfourodine (3) and isobalfourodine (7) found in *Balfourodendron riedelianum* Engl. Our conclusions depended on assumptions of the mechanisms of reactions employed and confirmation is clearly desirable. We now report a direct determination of the relative configuration of a group of furano- and pyrano-quinoline alkaloids involving exhaustive ozonolysis in chloroform at 0° followed by oxidation with 30% hydrogen peroxide to give lactone (5) or (6) in *ca.* 50% yield. (+)-Balfourodine (3) and (−)-balfourolone (4) afforded the (+)-lactone (5), whereas (−)-isobalfourodine (7) gave the (−)-lactone (6). The three alkaloids were prepared by asymmetric synthesis.[2] The (+)-lactone (5) was obtained by ozonolysis of (+)-platydesminium perchlorate (2) isolated† from *Skimmia japonica*.[3] A similar technique was applied recently to natural coumarins by Lemmich and Nielsen[4] who also



synthesised the (±)-lactone (*cf.* 5); the i.r. spectrum of our lactone was identical with that of the synthetic compound.† These results support our previous assignment of relative stereochemistry to balfourodine, isobalfourodine, and balfourolone.[2]

The absolute configuration of the (−)-(*S*)-lactone (6) was assigned by Lemmich and Nielsen[4] on the basis of the known stereochemistry of a coumarin from which it was derived. Since the lactone is clearly a key compound in the determination of the absolute configuration of natural aryl compounds containing oxygenated isoprenoid groups, we now report an independent method of establishing the configuration of the (+)-lactone (5). This method involves asymmetric synthesis of the formate ester (10) and correlation with the diol (11) of known configuration.[5]

The methyl ester (8) was synthesised by the method of Rogan.[6] Treatment with (+)-peroxycamphoric acid gave the (+)-epoxide (9), which was converted with formic acid into the (+)-formate ester (10); the same (+)-ester was obtained from the (+)-lactone (5). The (+)-epoxide (9) with diborane and lithium borohydride[7] gave (−)-(*S*)-4-methylpentane-1,3-diol (11). The structure of this diol was confirmed by comparison with the racemate prepared from isobutyraldehyde and ethyl bromoacetate followed by reduction of the Reformatsky product with lithium aluminium hydride. On the reasonable assumption that inversion occurs in step (9) → (10) and that configurations are retained in the formation of the diol, (9) → (11), and during esterification of the lactone, (5) → (10), absolute configurations can be assigned as in the Chart. Application of the sequence rules then show that (+)-balfourodine (3), (−)-balfourolone (4), and (+)-platydesminium perchlorate (2) have (*R*)-configurations, and (−)-isobalfourodine (7) the (*S*)-configuration.

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