The Conversion of a Germacrane into Guaiane Derivatives

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THE postulate of Ruzicka,[1] elaborated by Barton and de Mayo,[2] and by Hendrickson,[3] that a cyclodecadiene [*e.g.* (I)] could be the biosynthetic precursor of the selinane sesquiterpenes [*e.g.* (II)] is now amply supported by chemical analogies.[4] No such chemical support exists for generation of the guaiane ring [*e.g.* (XI)] from similar precursors. At the inception of this work no well established cases of this conversion existed (other than in dehydrogenation reactions). Since then the germacranolide, parthenolide, has been cyclised[5] to a guaianolide, the structure being proved by dehydrogenation to an azulene.

In our previous work on the reactions of germacrene[4b] (I) with electrophilic reagents we have shown that little or no guaianes are formed in these reactions† so we turned to the mono-oxides of (I). Reaction of (I) with buffered peracetic acid(1 mol.) gave liquid (IX) and solid (X) mono-oxides whose structures are based on their further transformations. Cyclisation of (IX) with aqueous acid gave two major products, the diol (II) and the alcohol (VII). The structure of (II) was established by oxidation to the ketone (III) which, on Wolff–Kishner reduction, gave (IV) of established structure and stereochemistry.[4b] The stereochemistry of the 1-hydroxy-derivative of (II) was assigned from the $W_{\frac{1}{2}}$ (*ca.* 18c./sec.) of the 1H signal in the n.m.r. spectra of (II) and its derivatives. The structure and stereochemistry of (VII) followed from the presence of a methylene group (1H singlets at τ 5·24 and 5·45) and the preparation of its monoacetate (VIII) by phosphoryloxychloride–pyridine dehydration of the monoacetate (V). This cyclisation is fully in accord with the results obtained in the cyclisation of pyrethrosin.[2,6]

(I)

(II) X=OH, Y=H
(III) X, Y=O
(IV) X=Y=H
(V) X=OAc, Y=H
(VI) X=$OSO_2C_7H_7$ Y=H

(VII) X=OH
(VIII) X=OAc

(IX)

(X)

(XI)

(XII)

(XIII)≡(V)

Reaction of the oxide (X) with acid‡ again gave diol and mono-ol fractions. The diol fraction was shown to be (XI) (3H, s, τ 8·83 and 8·63; 6H, s, τ 8·28) since it behaved as a di-tertiary alcohol and, on dehydration (phosphoryl oxychloride–pyridine) followed by sulphur dehydrogenation, gave *S*-guaiazulene. The structure was confirmed using a reaction modelled on one in the pyrethrosin series,[2] solvolysis of the toluene-*p*-sulphonate (VI) in aqueous dioxan gave the diol (XI) thus establishing the stereochemistry at C(1), C(7), and C(10); that at C(6) follows from hydration on the least-hindered convex side of the molecule. The second solvolysis product was the alcohol (XII) (3H, s, τ 8·85 and 8·40; 6H, s, τ 8·33) which was identical with one of the compounds in the mono-ol fraction from cyclisation of (X).

It is notable that the structures of the cyclisation products from the triene (I) and the oxide (IX) follow from strict application of the Markovnikov (M) rule which, however, predicts that the oxide (V) should cyclise to a [6,2,0] ring system. Instead the more stable [5,3,0] rings of (III) are generated by anti-M addition to the epoxide and M addition to the double bond. The *trans*-decalin (II) is probably thermodynamically more stable than

† Acid-catalysed cyclisation of (1) gives a selinane quantitatively, while reaction with HOBr gives 17 ± 11% of guaiane, the remainder being selinanes.

‡ It has been established that none of the alcohols of either series are interconvertible under the cyclisation conditions.

(XI) but its generation from (X) would require two anti-M additions; thus it appears that in this series there is a balance between steric and electronic effects. The stereochemistry of the cyclisation products can be accounted for by adoption of the 'crown' conformation [already established for the triene (I)[8]] for the epoxides [*e.g.* (XIII)]. The cyclisation of (I) and (IX) to *trans*-decalins is in contrast to the conversion of *cis,trans*-1,5-cyclodecadiene to *cis*-decalins[7] and these differences are undoubtedly explicable by the different conformations of the two series. These results may imply that mono-oxides are involved in the biosynthesis of guaiane derivatives.

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