Sulphonium Ylids as Possible Intermediates in Terpenoid Biosynthesis

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IN the biosynthesis of squalene[1] two mechanistic routes have been considered involving sulphonium ylid intermediates. One of these possibilities[2] (route *a*) involves a Stevens' rearrangement [three-centre process; see arrows of (I)] of an intermediate (I) containing two farnesyl residues. The other possibility (route *b*) involves an allylic rearrangement[3–7] [five-centre process; see arrows of (II)] of an intermediate (II) containing one farnesyl residue and one nerolidyl residue.[4,5] The mechanisms [arrows of (I) and (II)] are represented as involving dipolar forms, but the possible importance of tetracovalent sulphur intermediates in such processes has been emphasised by Baldwin, Hackler, and Kelly.[5]

Treatment of digeranyl sulphide (IIIa) with benzyne generated from *o*-fluorophenylmagnesium bromide gave *two* products identified† as the isomeric phenyl sulphides [(Va) 3 parts] and [(VIa), 7 parts]. Reduction of this mixture with lithium–liquid ammonia followed by chromatography gave digeranyl [(Vb), 1 part] and the isomeric diterpenoid hydrocarbon [(VIb), 2 parts]. In contrast, the benzyne-promoted rearrangement of geranyl linalyl sulphide [(IV), prepared by rearrangement of digeranyl disulphide (IIIb) with

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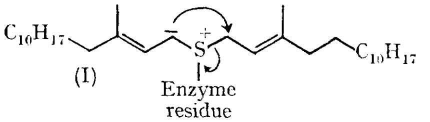
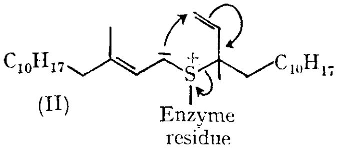
† All new compounds have been fully characterised by analytical and spectroscopic data.

triphenylphosphine[8]] took a substantially unidirectional course and yielded *one* major product [(Va), ~19 parts] with small amounts of the isomer [(VIb), ~1 part]. Similar reduction of this mixture gave digeranyl (Vb).

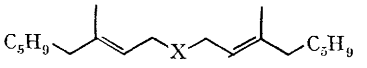
Although it is appreciated that these reactions are distant models for biochemical processes,[1,2] it may be noted that the benzyne-promoted rearrangement of digeranyl sulphide (IIIa) illustrates the simultaneous operation of processes related to routes (*a*) and (*b*), whereas the corresponding rearrangement of geranyl linalyl sulphide (IV) exemplifies route (*b*). The rearrangement (IIIa) → (VIa) provides a plausible analogy for the postulates which can be made[6,9] to account for the biosynthesis of the atypical monoterpenoids isolated from *Santolina chamaecyparissus*[10] and the biosynthetic origin of the atypical terpenoid side chain of bakuchiol.[11] The n.m.r. spectrum of the product (Va) shows that it is a mixture of diastereoisomers and this emphasises the need for caution in judging whether these benzyne-promoted rearrangements are concerted processes. Concerted processes related to type (I), (see arrows) are formally symmetry-forbidden, whereas processes of the type [(II), see arrows] are allowed.[4] Furthermore, the reaction between sulphides and *o*-fluorophenylmagnesium bromide is assumed to involve benzyne formation leading to sulphonium ylid intermediates,[12,13] but other possibilities can be envisaged. These results are not related to the recent suggestion[14] that thiamine pyrophosphate is involved in the biosynthesis of squalene from farnesyl pyrophosphate.



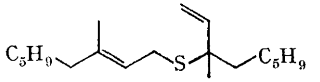
(I)



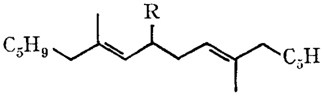
(II)



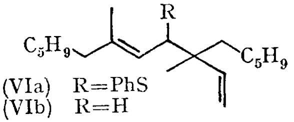
(IIIa) X=S ; (IIIb) X=S-S



(IV)



(Va) R=PhS; (Vb)R=H



(VIa) R=PhS
(VIb) R=H

Added in proof: Two publications (J. E. Baldwin, R. E. Hackler, and D. P. Kelly, *J. Amer. Chem. Soc.*, 1968, **90**, 4758; J. E. Baldwin and D. P. Kelly, *Chem. Comm.*, 1968, 899) describing similar results have appeared since this Communication was submitted.

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