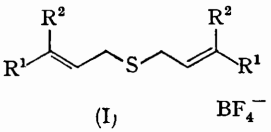
Sigmatropic Reactions of Allylic Sulphur Ylids

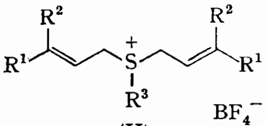
By G. M. BLACKBURN, W. D. OLLIS,* J. D. PLACKETT, C. SMITH, and I. O. SUTHERLAND
(*Department of Chemistry, The University, Sheffield* S3 7HF)

THE biosynthesis of squalene[1] involves a sequence of remarkably stereoselective reactions in which one of the last steps is the generation of the interfarnesyl bond. This C–C bond formation has been shown[2] to involve at one carbon atom inversion of configuration, and at the other retention of configuration plus reduction by the nicotinamide–adenine dinucleotide phosphate coenzyme. The biosynthesis of the symmetrical squalene molecule by an asymmetric process poses interesting mechanistic problems for which there is recognised to be inadequate chemical analogy.[3] We now report a new general reaction of allylic sulphur ylides which may well be relevant to the processes operating during the creation of the interfarnesyl bond.[1,2]

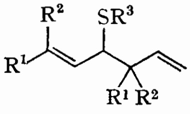
Treatment of the sulphides (I; $R^1 = R^2 = H$), (I; $R^1 = R^2 = Me$), and (I; $R^1 = Ph$, $R^2 = H$)[4] with triethyloxonium fluoroborate in ether gave the corresponding sulphonium fluoroborates (II; $R^3 = Et$). The sulphonium salts (II; $R^1 = R^2 = H$, $R^3 = Et$) and (II; $R^1 = R^2 = Me$, $R^3 = Et$) with



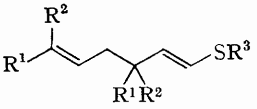
(I)



(II)



(III)



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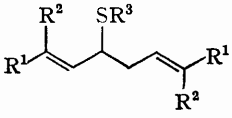

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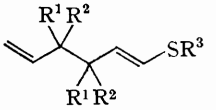
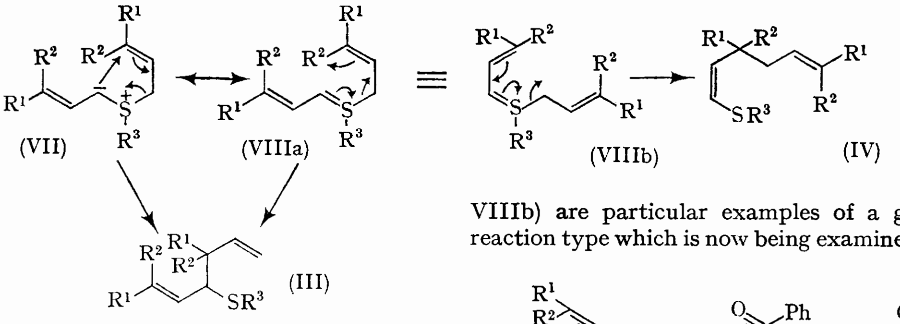


(VI)

sodium hydride in tetrahydrofuran were transformed in high yield (90—95%) to the rearrangement products[†] (III; $R^1 = R^2 = H$, $R^3 = Et$) and (III; $R^1 = R^2 = Me$, $R^3 = Et$) respectively. A similar base-catalysed rearrangement yielding the sulphide (III; $R^1 = Ph$, $R^2 = H$, $R^3 = Et$) was observed under very mild conditions when anhydrous potassium carbonate was added to an ethanolic solution of the sulphonium salt (II; $R^1 = Ph$, $R^2 = H$, $R^3 = Et$).



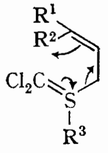
(VII) (VIIIa) (III) (VIIIb) (IV)

The base-catalysed transformation (II → III) could well be represented[5] as an internal nucleophilic displacement reaction involving the ylid (VII). Alternatively, the transformation may be represented as a sigmatropic reaction[‡] involving the covalent formulation (VIIIa) of the ylid intermediate.

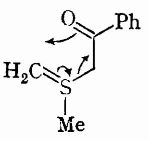
Other transformations of the ylid (VII) could be visualised leading to the possible products (IV), (V), and (VI), in addition to the observed product (III). These expectations were partially realised when alternative routes[6,7] to sulphur ylid intermediates were examined. Thus, the sulphide (I; $R^1 = R^2 = H$) and benzyne gave a mixture of *two* sulphides (III; $R^1 = R^2 = H$, $R^3 = Ph$; 9 parts) and (IV; $R^1 = R^2 = H$, $R^3 = Ph$; 1 part); this reaction has been previously studied,[7] but the products were not separated and they were not fully characterised. The sulphide (I; $R^1 = R^2 = Me$) and benzyne gave a mixture of *three* isomeric sulphides (III; $R^1 = R^2 = Me$, $R^3 = Ph$; 7 parts), (IV; $R^1 = R^2 = Me$, $R^3 = Ph$; 1 part) and (V; $R^1 = R^2 = Me$, $R^3 = Ph$; 2 parts).

The formation of these products may now be considered in relation to the sigmatropic reactions (arrows, VIIIa and VIIIb). The formulae (VIIIa and VIIIb) are different conformations of the ylid (VII) and conservation of orbital symmetry[8] permits the recognition that the observed sigmatropic reactions (VIIIa → III) and (VIIIb → IV) are symmetry-allowed processes. On the other hand, the route to the observed Stevens[9] rearrangement product (V; $R^1 = R^2 = Me$, $R^3 = Ph$) is formally symmetry-forbidden; the other symmetry-forbidden product (VI) has not been observed in these studies.

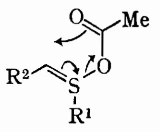
These mechanistic intepretations (VIIIa and VIIIb) are particular examples of a generalised reaction type which is now being examined. Other



(IX)



(X)



(XI)

[†] All new compounds described have been adequately characterised by analytical, infrared, nuclear magnetic resonance, and mass spectral data.

[‡] This was first suggested to us by Dr. J. E. Baldwin (Department of Chemistry, Pennsylvania State University, U.S.A.), who kindly informed us of his independent interest in the base-catalysed transformation of sulphur ylids.

known reactions which may be similarly interpreted include the reaction (IX) of dichlorocarbene with allylic sulphides,[10] the rearrangement (X) of dimethylphenacylidene sulphurane,[11] and the Pummerer rearrangement[12] (XI) of sulphoxides by acetic anhydride. These results and the recognition of a general reaction type are considered relevant to possible mechanisms for the formation of the inter-farnesyl bond in squalene biosynthesis. This general reaction is under further experimental scrutiny.

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