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REACTION OF ALLYLSULPHENIC ACID WITH ALKYNES TO GIVE THIOLAN 1-OXIDE DERIVATIVES

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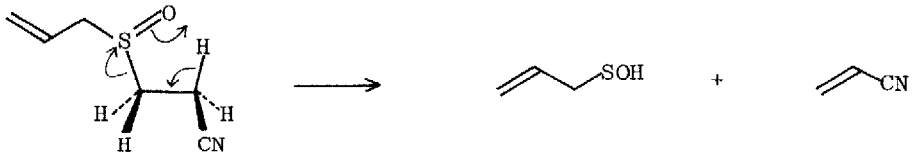
Summary. Thermolysis of 1-allylsulphinyl-2-cyanoethane in alkynes initiated five consecutive pericyclic reactions which led to the formation of thiolan 1-oxide derivatives.

The ready availability of alkenyl sulphoxides by the regiospecific addition of sulphenic acids to alkynes[1] encouraged us to investigate a new way of making thiolan derivatives in which the rearrangement of alkenyl allyl sulphoxides played a key role. Motivation for the investigation was provided by a requirement for suitably functionalized compounds for elaboration into thiaprostanoids. We envisaged (Scheme I) that allylsulphenic acid *(2)* would add to an alkyne to give an alkenyl allyl sulphoxide *(4)* which could undergo a thio-Claisen rearrangement to give a sulphine *(5)*. Rearrangement of the sulphine could then furnish a mixture of alkenyl sulphenic acids *(6-9)* three of which *(6-8)* are capable of intramolecular sulphenic acid-olefin addition to give thiolan 1-oxide derivatives *(10)* and *(11)* and the thiolen 1-oxide derivative *(12)*.

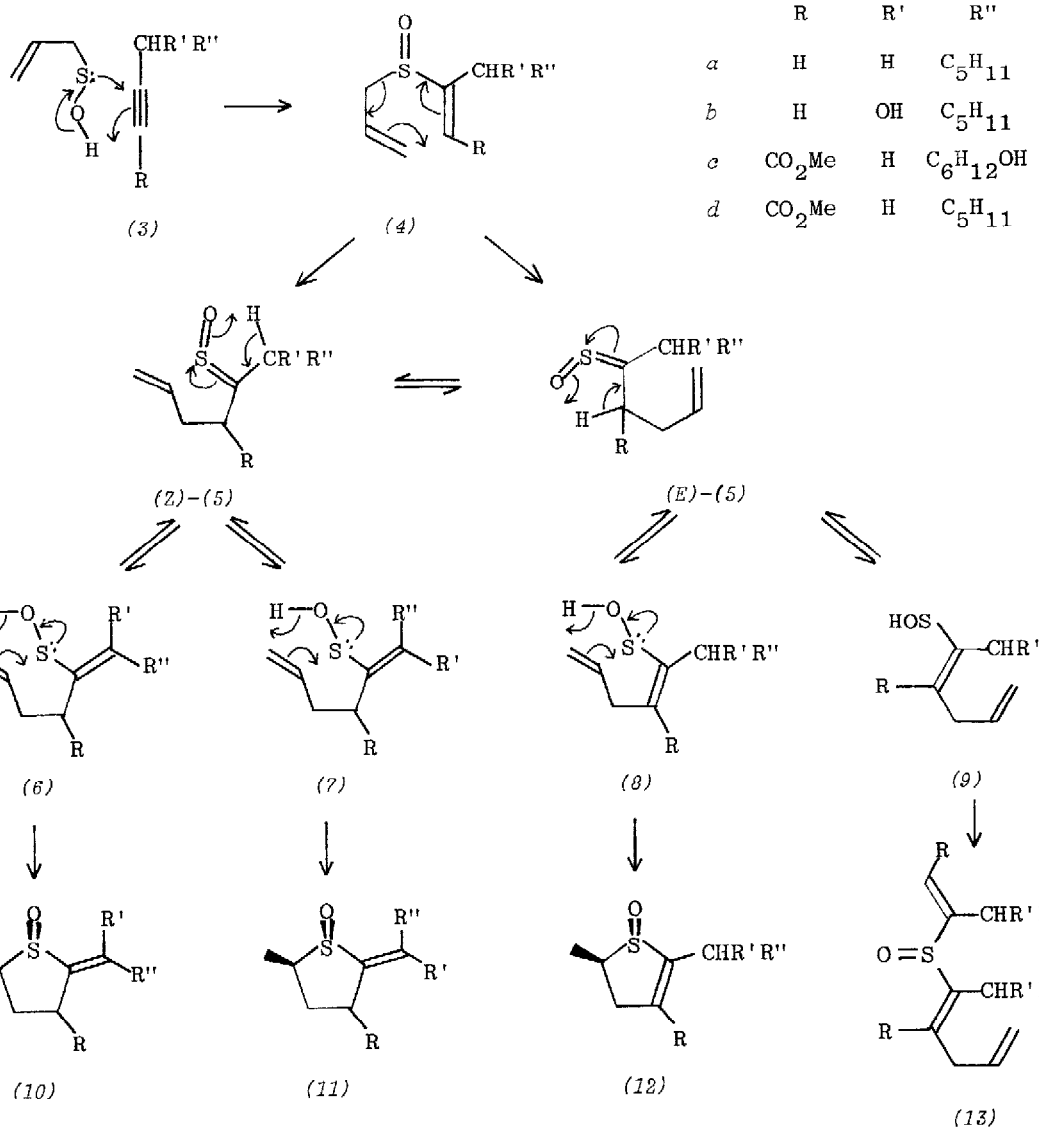
Allyl sulphenic acid *(2)* was generated[2] by thermolysis of 1-allylsulphinyl-2-cyanoethane *(1)*[3] which was prepared by treatment of sodium 1-cyanoethane-2-thiolate[4] in sequence with allyl bromide and sodium metaperiodate. Thermolysis of *(1)* in oct-1-yne *(3a)* at 126° for 1.5h gave, after chromatography on silica, the thiolen 1-oxide *(12a)* (15%) (NMR, δ 1.41,d, J 7Hz, C-5 Me; δ 6.11, t of d, J 4Hz, J' 1.5Hz, $-CH_2-CH=$) and an inseparable mixture of the thiolan 1-oxide derivatives *(10a)* and *(11a)* (15% combined yield) (NMR, δ 1.42 and 1.39, both d, J 7Hz, C-5 Me; δ 6.40, t, J 8Hz, >C=CH- in *(10a)*; δ 6.06, t, J 7Hz,>C=CH- in *(11a)*). The adduct *(4a)* could not be detected and evidently rearranged at 126°.[5] This was expected, since the rearrangement of allyl 2-naphthyl sulphoxide was complete after 2h at 120°;[6] it proceeded faster than that of allyl 2-naphthyl sulphide; and allyl vinyl sulphides rearrange more readily than allyl aryl sulphides.[7]

The sulphine *(5a)* may exist in *(E)* and *(Z)* forms which should rapidly interconvert at 126° (cf. ref. 8). Subsequent rearrangement of *(E)*-*(5a)* furnishes the alkenyl sulphenic acids *(8a)* and *(9a)*, whilst *(Z)*-*(5a)* rearranges to *(6a)* and *(7a)*. The reverse process, the rearrangement of alkenyl sulphenic acids to sulphines, has been demonstrated recently,[9] and it was interpreted in terms of a [1,4] sigmatropic reaction. These observations suggest that the alkenyl sulphenic acids *(6a)*-*(9a)* may interconvert under the reaction conditions. We have obtained evidence for double bond isomerization in alkenyl sulphenic acids by



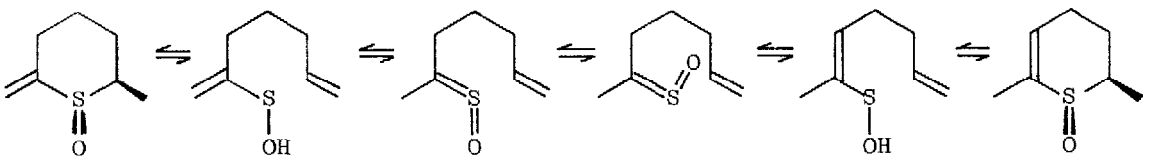
(1) (2)

SCHEME I


R R' R''
a H H C_5H_{11}
b H OH C_5H_{11}
c CO_2Me H $C_6H_{12}OH$
d CO_2Me H C_5H_{11}
(3)
(4)
(Z)-(5)
(E)-(5)
(6)
(7)
(8)
(9)
(10)
(11)
(12)
(13)

equilibrating *cis*-6-methyl-2-methylenethian 1-oxide *(14)*[10] with *cis*-2,6-dimethyl-2-thien 1-oxide *(15)* in xylene at 140° for 18h. Starting severally from the pure isomers a 1:6 mixture of *(14)* and *(15)* was obtained. This is rational in terms of the reactions outlined in Scheme II. The crucial role of the 6-methyl group in the interconversion was demonstrated by the stability of 2-methylenethian 1-oxide under these conditions.

SCHEME II



(14) *(15)*

The intramolecular additions of the sulphenic acids *(6a)-(8a)* to give *(10a)-(12a)* finds analogy in the cyclization of other unsaturated sulphenic acids to give derivatives of thiolan 1-oxide[11] and related compounds.[12] The *cis* relationship between the methyl group and sulphinyl oxygen in *(10a)-(12a)* is a consequence of the stereoelectronic requirements of the sigmatropic reaction.[11,12]

No evidence was forthcoming about the fate of the alkenyl sulphenic acid *(9a)* derived from *(1)* and oct-1-yne *(3a)*, but thermolysis of *(1)* in oct-1-yn-3-ol *(3b)* at 126° for 2.5h gave *(12b)* (7%) and the compound *(13b)* (4%), the formation of which is rational in terms of the intermolecular addition of *(9b)* to oct-1-yn-3-ol *(3b)*. Similarly, thermolysis of *(1)* in methyl 10-hydroxydec-2-ynoate *(3e)* at 140° for 3h gave the thiolan 1-oxide derivative *(12e)* (30%) and the adduct *(13e)* (12%) derived from reaction of the alkenyl sulphenic acid *(9e)* with *(3e)*. No exocyclic isomers *(10e)* and *(11e)* were detected, and their apparent absence suggested that conjugation with the methoxycarbonyl group caused *(8e)* to preponderate among the alkenyl sulphenic acids. However, this simple explanation is inadequate, because thermolysis of *(1)* in methyl non-2-ynoate *(3d)* at 130° for 3h gave a mixture of the exocyclic isomers *(10d)* and *(11d)* (23% combined yield) together with the endocyclic isomer *(12d)* (17%). A similar result was obtained when *(1)* and *(3d)* were heated in octanol, and the compounds *(10d)-(12d)* were stable on prolonged heating at 140° in xylene and in octanol. Evidently the sulphoxides *(10d)-(12d)* do not revert to the sulphenic acids *(6d)-(8d)* respectively, as indicated by the lack of incorporation of deuterium after treatment with boiling xylene-D_2O and DMF-D_2O for 18h (cf. ref. 6, 12a). The reluctance of the sulphoxides to rearrange reversibly to unsaturated sulphenic acids stands in marked contrast to the relative facility of analogous processes in penicillin sulphoxides[12a] and thiazoline sulphoxides.[13] The influence of the 10-hydroxy group in directing equilibration towards *(8e)* remains unexplained.

The moderate yields of thiolan derivatives from 1-allylsulphinyl-2-cyanoethane and alkynes are compensated by the convenience of the method, and the average yield for each of the five consecutive rearrangements (e.g. 79% for *(12e)*) is acceptable in view of the known propensity of simple sulphenic acids[2] and alkyl sulphines[9,14] to decompose even at 30°.

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