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REACTION OF UNSATURATED SULFOXIDES WITH ALKYLLITHIUMS

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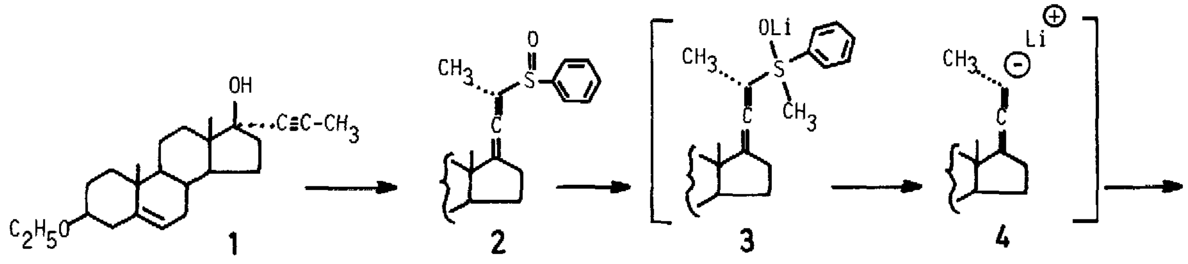
Summary: Nucleophilic attack of methyllithium on allene sulfoxides offers a stereospecific access to sulfur-free allenes. Reaction of phenylsulfinyl substituted diene 15 leads via a benzilic-type rearrangement to phenyl substituted diene 18.

The rapidly expanding chemistry of unsaturated sulfoxides offers a useful methodology of forming new carbon-carbon bonds by either Michael addition[1)] or deprotonation followed by alkylation[2)]. As Durst[3)] and others[4)] pointed out in this context, nucleophilic addition to sulfur has to be regarded as a further potential reaction path which may explain formation of by-products or complete failure of the original synthetic scheme.

In our communication we wish to demonstrate that nucleophilic attack on the sulfur atom of unsaturated sulfoxides can result in synthetically useful transformations which are not easily foreseen.



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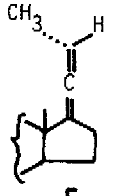

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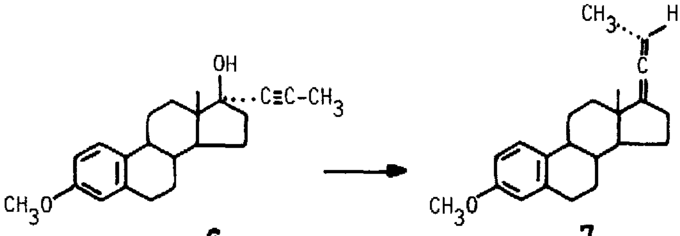
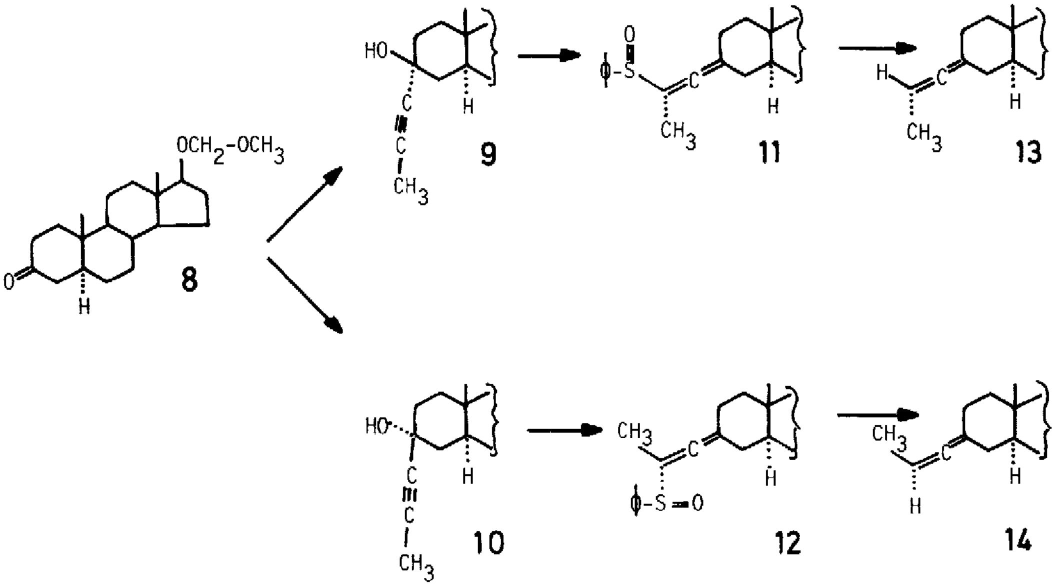


6 7

Allene sulfoxide 2, obtained by reaction of propynyl carbinol 1[5] with phenyl sulfenyl chloride[6] is almost instantaneously converted to the desulfurized allene 5 on treatment with methyl lithium at -70°C (4 equiv. of CH_3Li, THF, 10 min). The formation of 5 can be explained by the intermediacy of tetra-coordinate species 3, which undergoes carbon-sulfur bond cleavage to form anion 4, which is probably protonated by methyl phenyl sulfoxide to give a 72% yield of 5. As Durst[3] showed in the case of various alkyl phenyl and dialkyl sulfoxides, dissociation of type 3 intermediates is controlled by the leaving group quality of the substituents on sulfur. Allene anion 4, according to the pK_a value of its conjugate acid, represents a much better leaving group than methyl or phenyl anion so that almost exclusive formation of 5 is observed.

Although the stereospecific production of 5 was an expected result, since configurational stability of type 4 vinyl anions is generally accepted, we performed the same sequence of reactions with the estrone derivative 6, because allene 7 as well as its 21-isomer are known compounds obtained by other methodology[7,8].

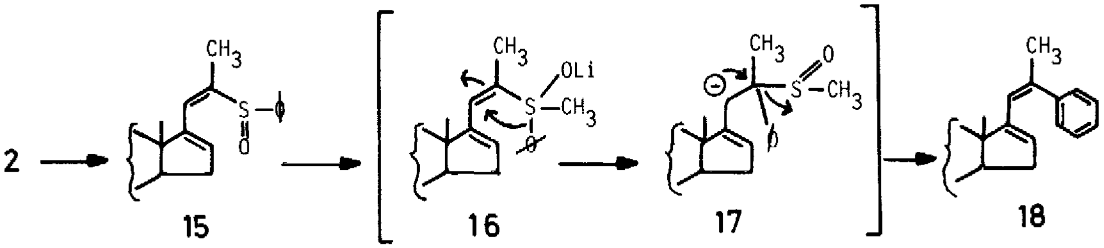
To our surprise the physical data of 7, on comparison with the literature values, corresponded to the 21β-methyl isomer according to the assignment by Van Dijck et al.[8] This result would clearly rule out the mechanism we postulated for the formation of 5 and 7. So, in order to make absolutely sure that the reaction (2 - 5) is kinetically controlled and stereospecific, we treated keto-ether 8 with propynyl lithium and obtained an isomeric mixture containing 70% of 9 and 30% of 10. The mixture was separated by fractionate crystallization from ethyl acetate/ether abd both isomers were individually subjected to the reaction sequence described above. Isomer 9 led to exclusive formation of allene 13 whereas isomer 10 gave allene 14 as the sole product. The overall yields were almost quantitative so that there can be no more doubt that this transformation takes a perfectly stereospecific course.



As far as compound 7 is concerned, this result will demand a revision of stereochemical and mechanistic conclusions drawn by the Organon group[8-10] and confirms an earlier assignment made by Rona and Crabbe[7].

In order to examine the effect of structural modification we converted 2 by thermal isomerization (toluene, reflux, 15h) into 15[11,12] which upon treatment with methyllithium (1,5 equi of CH_3Li, THF, 10 min, -70°C) unexpectedly gave the phenyl-substituted diene 18 in a 68% yield[12]. The most plausible explanation for the formation of 18 is outlined in the scheme below. Tetracoordinate species 16 undergoes a benzilic-type rearrangement with formation of allyl anion 17 and subsequent elimination of methyl sulfinyl group to produce 18.

This experiment shows that, for a prediction of the final products, it is obviously not sufficient to take into account the different pK_a values of the sulfur ligands. The possible intermediacy of an allyl anion such as 17 may represent a driving force resulting in a completely different reaction mode.



References and Notes

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5. Compounds 1, 6, 9 and 10 were prepared by addition of propynyl lithium to their respective keto-precursors in analogy to a procedure described by: E.P. Oliveto in J. Fried and J.A, Edwards. Organic Reactions in Steroid Chemistry, Vol. II, Van Nostrand Reinhold Comp., New York 1972, p. 139.

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11. Compound 15 is obtained as a 60:40 mixture of diastereomers isomeric with respect to sulfu configuration
12. Nuclear Overhauser experiments support the assignments made for compounds 15 (20.21Z-configuration) and 18 (20.21Z-configuration).
13. All compounds were characterized by ^1H-nmr and ir spectra as well as elemental analysis
14. Melting points and specific rotations:

compound	m. p.	$[\alpha]_D^{25}$ (CH_2Cl_2, c=0,5)
1	221-223	-112,1
2	144-145	- 62,8 (single isomer, S-configuration undetermined)
5	99-101	- 90,9
7	69- 70	- 15.2
9	158-159	+ 9.6
10	154-155	+ 15.3
13	73- 75	+ 15.4
14	92 -94	+ 25.0
18	148-150	- 84.3

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