Tetrahedron Letters Vol. 21, pp 547 - 550 0040-4039/80/0201-0547$02.00/0

STEREOCHEMISTRY OF METHYLATION OF CYCLIC SULFONIUM YLIDES

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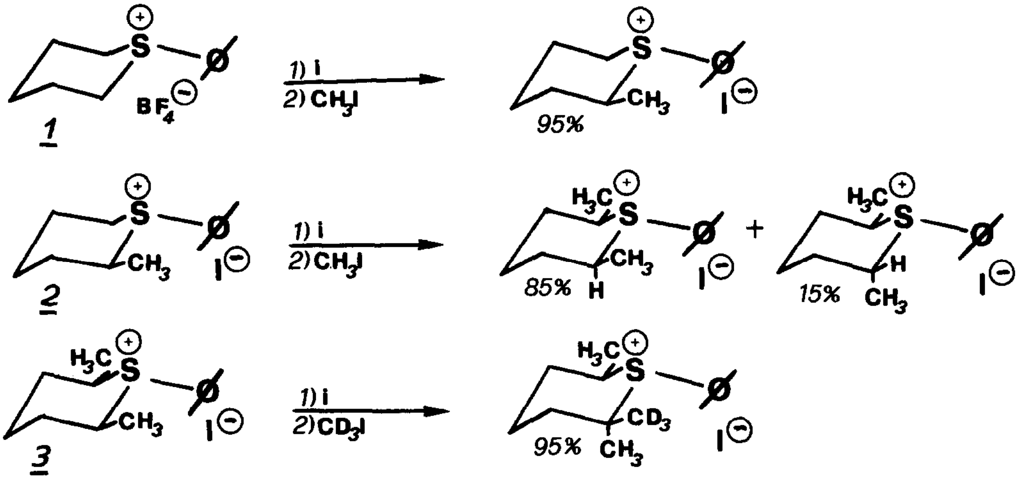
Low temperature methylation of 6-membered sulfonium ylides is highly stereoselective and configurational inversion has been established in at least one case.No appreciable stereoselectivity has been observed in 5-membered ylides.

The stereoselective reactivity of α-lithiosulfoxides toward electrophiles is well known and is being exploited for synthetic purposes(1). All available evidence indicates the steric course is largely,though perhaps not exclusively,(2) dictated by the necessary presence of the metal atom and by its electrical nature(3). Much less attention has been paid to the stereochemical aspects of the reaction of sulfonium ylides with electrophiles. Yet the general problem of the stability of diastereomeric carbanions α to a tricoordinated sulfur function should be more amenable to rationalisation in this case,where the carbanionic species is overall neutral,and is likely to be minimally affected by the presence of ionic solutes and by the nature of the solvent.

That sulfonium ylides may maintain stereochemical integrity is already implied by the highly stereoselective base-catalyzed H/D exchange which has been proven to occur with a variety of sulfonium salts(4). Moreover,it has been shown that diphenylsulfonium cyclopropylide preserves stereochemistry of the carbanionic carbon both in H/D exchange and in the reaction with acetone(5),while evidence has been presented indicating the carbanionic carbon of a bis-sulfonium ylide is pyramidal and has a relatively large barrier to pyramidal inversion(6),a conclusion which is supported by ab initio computation of model sulfonium ylides(7).

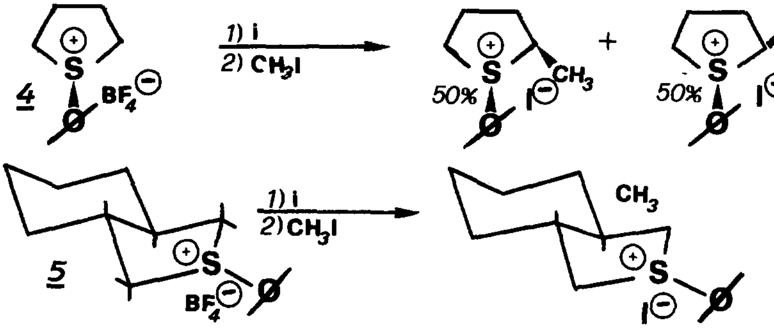
Most recently the methylation of the sulfonium ylides derived from cis- and trans-1-thioniabicyclo[4.4.0]decane has been found to be highly stereoselective(8). In relation to this work we wish to report a number of results on the methylation of S-phenyl-thianium and -thiolanium ylides generated from the corresponding salts (1-5) by treatment with $LiCHCl_2$ or $LiN(i\text{-}Pr)_2$ in dimethoxyethane at low temperature(9). The salts were obtained either from α,ω-thiophenoxybromides(10),or from the corresponding cyclic sulfides by direct phenylation with $Ø_2IBF_4$(11). All new products have been identified by ^1H and ^{13}C NMR,on the basis of established criteria(12). The results are summarized in Schemes I and II below.

Scheme I



i) $LiCHCl_2$ (1.2 eq.) in DME, temperature kept at -70°C for 1 h. before quenching

Scheme II



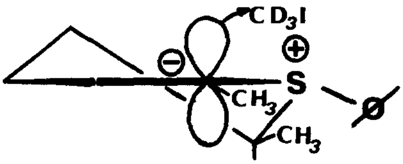
all four monomethylated products are formed in comparable amounts

i) LDA (1.2 eq.) in DME, temperature kept at -78°C for 8' (comp.4) or 15' (comp.5) before quenching

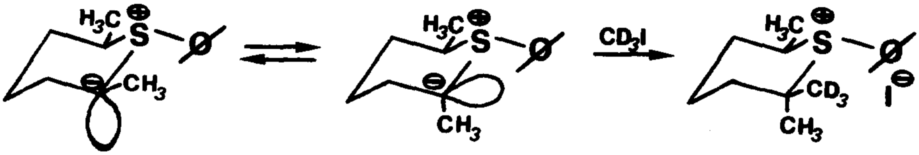
As far as the thianium cations are concerned all three successive methylations occur with a high degree of stereoselectivity and a trans arrangement of the entering methyl and the S-phenyl groups is always obtained. This behaviour closely matches that observed with the corresponding thiane-1-oxides(13); though in the case at hand the stereochemistry cannot be governed by those carbanionic carbon-lithium cation-sulfoxide oxigen interactions, that appear to be dominant with the α-lithiosulfoxides(14).

The overall result, trans methylation, does not provide any evidence about the stereochemistry of the individual steps involved in going from the starting sulfonium salt to the methylated product. This question could be answered, in fact, only if both i) the identity of the proton(s) removed and ii) the structure of the intermediate ylide(s) were experimentally determined. Consider, for instance, the result obtained with substrate 3. An axial proton is removed and "replaced" by an equatorial CD_3 group. Two possible explanations can be envisioned:

1) the intermediate ylide is planar at the carbanionic carbon,and methylation occurs at the least hindered diastereotopic face,i.e. trans to the phenyl group



2) the intermediate ylide is pyramidal at carbon,the initially formed "axial" ylide inverts its configuration giving the "equatorial"one,which then reacts preferentially in the subsequent step



The first explanation is at odds with the results of theoretical investigations on the structure of unstabilized model sulfonium ylides(7). The second explanation demands that pyramidal inversion at the carbanionic carbon occurs rapidly at -70° C This conclusion,however,contradicts the finding that the ylide derived from cis--1-thioniabicyclo [4.4.0] decane undergoes stereomutation at carbon at -23° C,but is stable for at least 1.5 h. at -72° C(8). Thus a clear cut choise between the two possibilities cannot be madė at the present time and we are currently investigating the structure of the ylides by low temperature ^1H and ^{13}C NMR.

Concerning the thiolanium ylides derived from 4 and 5,both appear to react without any significant stereoselectivity;moreover 4 undergoes extensive decomposition even at very short reaction times.

The comparison between the thianium and the thiolanium ylides is striking insofar as the behaviour of the two systems is precisely opposite to that which is observed in H/D base-catalyzed exchange in water,where high stereoselectivity is found in the thiolanium and little or no selectivity in the thianium system(4,15). A definite elucidation of this point has to be delayed until the detailed mechanism of the methylation will be known.Nevertheless it may be pointed out that, although the ylide is the intermediate both in H/D exchange and in methylation, there is no a priori reason to expect that reprotonation and alkylation of the ylide may have the same stereochemistry. They are in fact different reactions occuring in different media,and may well have different or even opposite stereochemical requirements.

Acknowledgement.I am indebted to Prof.A.Fava for many helpful discussions

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(Received in UK 6 December 1979)