THE STEREOCHEMISTRY OF THE FORMATION OF $\Delta^3$-1,3,4-THIADIAZOLINE-1-OXIDES AND EPISULFOXIDES FROM SULFINES AND 2-DIAZOPROPAINE

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Recently it was shown\(^4\) that sulfines react readily with diazoalkanes to $\Delta^3$-1,3,4-thiadiazoline-1-oxides in a regiospecific cyclo-addition process. In one case\(^5\) an aliphatic sulfine gave with diazomethane an episulfoxide instead of a five-membered ring product. Although we were inclined to believe that the cyclization to thiadiazoline-oxides would be a stereospecific process, recent results with the 1,3-dipolar cyclo-addition reaction of sulfines with diphenylnitrilimine\(^6\) (a regiospecific, but non-stereospecific process) threw doubt on this anticipation. Therefore, the stereochemistry of the diazoalkane-sulfine cyclization reaction requires a closer examination.

On that account we studied the reaction of 2-diazopropane with the geometrical isomers of different types of sulfines. Treatment of these sulfines (see Table) with 2-diazopropane in ether or ether/dichloromethane at -20° - -30° resulted, after addition of pentane, in the crystallization of the desired 1:1 adducts in high yields. In all cases studied each of the geometrical isomers led to a single product which was distinctly different from that obtained from the other isomer (see Table). Particularly, the NMR spectra (CDCl\(_3\)) revealed that only one adduct was obtained from each of the isomeric sulfines. From the sulfines VI, VII and VIII only the $S$-isomer could be studied, since the $Z$-isomer was not accessible by oxidation of the corresponding dithioester. Each of these sulfines gave only one cyclo-adduct in good yield.

The data presented in the Table allow the conclusion that the spatial arrangement of the $S=O$ group and the substituents $R_1$ and $R_2$ is retained in the product. Hence, the cyclo-addition is a stereospecific process and most likely the product formation takes place in a concerted manner.

The isomeric mesityl-phenylsulfonyl-sulfines XIA and XIB reacted smoothly with 2-diazopropane in benzene/ether (1:1) at -10°. However, to our surprise an episulfoxide was isolated in 72.5% yield, instead of a five-membered ring product. From either of these isomeric sulfones the same 1:1 mixture of diastereomeric episulfoxides (m.p. 85-87°) was obtained, thus, indicating a non-stereospecific process (see Scheme). The mixture could not be separated because the com-

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All compounds show vigorous decomposition during melting.

(Characteristic i.r. absorptions for these compounds were observed at 1060-1080 \( \nu_{S=O} \) and 1560-1575 cm\(^{-1} \) \( \nu_{N=N} \))
ppm for those at C-4', at 6.62 and 6.96 ppm for the protons at C-3' and at 7.18-7.80 ppm for the phenyl protons. Furthermore, oxidation of the product with m-chloroperbenzoic acid in ether at 20° gave 1-mesityl-2-methyl-1-phenylsulfonyl-1-propene (m.p. 120-122°) in 46% yield (oxidation to episulfone with subsequent extrusion of SO₂).

and thiofluorenone-S-oxide react with phenyldiazomethane to give a triaryl substituted episulfoxide as a mixture of diastereomers (Z/E ratio ranging from 1:4 to 2:3 for the different aryl substituents). Thus, again a non-stereospecific formation of the three-membered ring.

To explain this remarkable difference in stereochemistry in the formation of thiadiazo line-oxides and episulfoxides, we suggest that the episulfoxide does not come about via an initially formed thiadiazoline-oxide, but most likely via a two step process in which firstly a nucleophilic attack of the diazocarbon at the sulfine sulfur provides a zwitter ionic diazonium compound (see Scheme). Subsequently, an internal 1,3-displacement of nitrogen produces the episulfoxide. Inspection of molecular models clearly reveals that steric crowding prevents the formation of a five-membered ring adduct and favors the less congested three-membered ring.

The mechanism in the Scheme is supported by the fact that we never found any indication of an episulfoxide formation from the thiadiazoline-oxides. However, these five-membered ring adducts are thermally rather unstable. Usually a retro-cyclo-addition reaction to starting materials as observed for the adducts derived from Va, Via and X takes place. In some cases a reverse retro-cyclo-addition reaction is observed as nicely exemplified by the adduct from IX. Warming this adduct in chloroform at 40° or at 25° in benzene/pentane, containing some silica-gel, gave besides 60% of the sulfine IX a 30% yield of tetrakis(phenylthio)-ethene arising from bis(phenylthio)diazomethane via dimerization of bis(phenylthio)carbene.

Bonini and Maccagnani found that aromatic sulfines such as diphenylsulfine and thiofluorenone-S-oxide react with phenyldiazomethane to give a triaryl substituted episulfoxide as a mixture of diastereomers (Z/E ratio ranging from 1:4 to 2:3 for the different aryl substituents). Thus, again a non-stereospecific formation of the three-membered ring.

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With other sulfines having a bulky substituent attached to the sulfine function a deviating reaction pattern was observed. Z-mesityl-phenylsulfine did not react at all with 2-diazopropane, whereas the E-isomer was isomerized quantitatively to the Z-form. Similarly, E-mesityl-phenylthio-sulfine isomerized to the Z-isomer, while the Z-form did not react. This isomerization can be rationalized by assuming the formation of a zwitter ionic intermediate (see Scheme) which then splits off 2-diazopropane to give the thermodynamically more stable sulfine isomer instead of forming the three-membered ring.

We conclude that the normal reaction of sulfines with diazoalkanes will be the concerted cyclo-addition to $\Lambda^3$-1,3,4-thiadiazoline-1-oxides. Introduction of bulky substituents in either of the reactants will sterically hamper this cyclization to five-membered rings and give rise to alternative reaction routes of which the non-stereospecific formation of episulfoxides is the most interesting one.

References and notes

3. To whom correspondence should be addressed.
6. Part XXI in this series, see ref. 1.
9. The Z-isomers were formed when the E-isomers were allowed to stand in the refrigerator for several months.