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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$^4,5$ 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 $-20^\circ$ to $-30^\circ$ 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 benzenene/ether (1:1) at $-10^\circ$. 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$^\circ$) was obtained, thus, indicating a non-stereospecific process (see Scheme). The mixture could not be separated because the com-
TABLE

\[
\begin{array}{cccccc}
R_1 & R_2 & \text{m.p.°} & \delta\text{CH}_3 & \text{other NMR signals} \\
\text{Ia(8)} & \text{phenyl} & \text{o-tolyl} & 70^\circ & 1.27; 2.00; 2.41 & 6.58-7.74(m) \\
\text{Ib(8)} & \text{o-tolyl} & \text{phenyl} & 75^\circ & 1.47; 1.90; 2.19 & 6.99-7.72(m) \\
\text{IIa(8)} & \text{phenyl} & \text{a-naphthyl} & 85^\circ & 1.60; 2.41 & \text{arom. H} \\
\text{IIb(8)} & \text{a-naphthyl} & \text{phenyl} & 89^\circ & 1.63; 1.93 & \text{arom. H} \\
\text{IIIC(8)} & \text{p-tolyl} & \text{p-chlorophenyl} & 80^\circ & 1.05; 1.94; 2.28 & 6.65-7.68(m) \\
\text{IIIC(8)} & \text{p-chloro-} & \text{p-tolyl} & 76-77^\circ & 1.14; 2.02; 2.40 & 6.83-7.63(m) \\
\text{IVA(8)} & \text{phenyl} & \text{chloro} & 72-80^\circ & 1.80; 1.93 & 7.52 \\
\text{IVB(8)} & \text{chloro} & \text{phenyl} & 84^\circ & 1.19; 1.92 & 7.47 \\
\text{VA(8)} & \text{phenyl} & \text{phenylthio} & 85-67^\circ & 1.62; 1.80 & 6.93-7.62(m) \\
\text{Vb(8)} & \text{phenylthio} & \text{phenyl} & 75-77^\circ & 1.09; 1.89 & 6.85-7.67(m) \\
\text{VIa(8)} & \text{anisyl} & \text{p-tolythio} & 80^\circ & 1.54; 1.78; 2.30; 3.78 & 6.90+7.46(AB, J 9Hz) \\
\text{VIIa(8)} & \text{phenyl} & \text{phenylsulfonyl} & 97^\circ & 1.72; 2.03 & 7.20-7.67(m) \\
\text{VIIIa(8)} & \text{anisyl} & \text{p-toly sulfonyl} & \text{dec.} & 1.66; 2.00; 2.36; 3.78 & 6.83+7.44(AB, J 9Hz) \\
\text{IX} & \text{phenylthio} & \text{phenylthio} & 55^\circ & 1.37; 1.54 & 6.74-7.81(m) \\
\text{X} & \text{chloro} & \text{chloro} & 70^\circ & 1.65; 1.85 & 6.18\text{CCl}_4 & 1.65; 1.85
\end{array}
\]

* All compounds show vigorous decomposition during melting.

(Characteristic i.r. absorptions for these compounds were observed at 1060-1080 (\(\nu_{S=0}\)) and 1560-1575 cm\(^{-1}\) (\(\nu_{N=N}\)).

The episulfoxide structure was assigned on the following grounds: a correct elemental analysis for \(\text{C}_{19}\text{H}_{22}\text{O}_{3}\text{S}_{2}\), i.r. absorptions (in CS\(_2\)) at 1050 cm\(^{-1}\) (\(\nu_{S=0}\)), 1150 and 1325 cm\(^{-1}\) (\(\nu_{SO_2}\)) and signals in the NMR spectrum (CDCl\(_3\)) at \(\delta\) 1.01, 1.40, 1.70 and 1.78 ppm for the methyl protons at C-2 (note the distinct different position of the methyl protons at C-2 in the thiadiazolone-oxide derived from VIIa), at \(\delta\) 2.21 and 2.47 ppm for the methyls at C-2', at \(\delta\) 2.16 and 2.34
ppm for those at C-4', at $\delta$ 6.62 and 6.96 ppm for the protons at C-3' and at $\delta$ 7.18-7.80 ppm for the phenyl protons. Furthermore, oxidation of the product with m-chloroperbenzoic acid in ether at 20°C gave 1-mesityl-2-methyl-1-phenylsulfonyl-1-propene (m.p. 120-122°C) in 46% yield (oxidation to episulfone with subsequent extrusion of SO$_2$).

**SCHEME**

Bonini and Maccagnani$^7$ found that aromatic sulfines such as diphenylsulfine and thiofluorenone-S-oxide react with phenylazomethane to give a triaryl substituted episulfioxide 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 thiadiazolinedioxides 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 episulfioxide. 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 thiadiazolinedioxides. 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°C or at 25°C in benzene/pentane, containing some silicagel, 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.$^8$
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 diazocalkanes will be the concerted cyclo-addition to $\Delta^3$-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.