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THE STEREOCHEMISTRY OF THE FORMATION OF Δ^3 -1,3,4-THIADIAZOLINE-1-OXIDES AND EPISULFOXIDES FROM SULFINES AND 2-DIAZOPROPANE[1]

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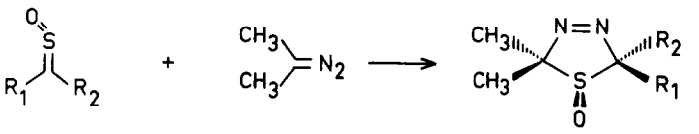
Recently it was shown[4,5] that sulfines react readily with diazoalkanes to Δ^3-1,3,4-thiadiazoline-1-oxides in a regiospecific cyclo-addition process. In one case[5] an aliphatic sulfine gave with diazomethane an episulfoxide instead of a five-membered ring product. Although we were inclined to believe 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 *E*-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 sulfone sulfines 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-

TABLE



	R_1	R_2	m.p.*	%	δCH_3	other NMR signals
Ia(*E*)	phenyl	*o*-tolyl	70°	83	1.27;2.00; 2.41	6.58-7.74(m)
Ib(*Z*)	*o*-tolyl	phenyl	75°	88	1.47;1.90; 2.19	6.99-7.72(m)
IIa(*E*)	phenyl	α-naphthyl	85°	87	1.60;2.41	arom. H
IIb(*Z*)	α-naphthyl	phenyl	89°	91	1.63;1.93	arom. H
IIIa(*E*)	*p*-tolyl	*p*-chlorophenyl	80°	88	1.05;1.94; 2.29	6.85-7.68(m)
IIIb(*Z*)	*p*-chloro-phenyl	*p*-tolyl	76-77°	67	1.14;2.02; 2.40	6.83-7.63(m)
IVa(*E*)	phenyl	chloro	72-80°	56	1.80;1.93	7.52
IVb(*Z*)	chloro	phenyl	84°	81	1.19;1.92	7.47
Va(*E*)	phenyl	phenylthio	65-67°	82	1.62;1.80	6.93-7.62(m)
Vb(*Z*)	phenylthio	phenyl	75-77°	68	1.09;1.89	6.85-7.67(m)
VIa(*E*)	anisyl	*p*-tolylthio	80°	83	1.54;1.78; 2.30;3.78	6.90+7.46(AB,J 9Hz) 7.02+7.28(AB,J 7Hz)
VIIa(*E*)	phenyl	phenylsulfonyl	97°	75	1.72;2.03	7.20-7.67(m)
VIIIa(*E*)	anisyl	*p*-tolylsulfonyl	dec.	75	1.66;2.00; 2.36;3.78	6.83+7.44(AB,J 9Hz) 7.14+7.39(AB,J 9Hz)
IX	phenylthio	phenylthio	55°	58	1.37;1.54 (-30°)	6.74-7.81(m)
X	chloro	chloro	70°	44	1.66;1.85 (CCl_4)	

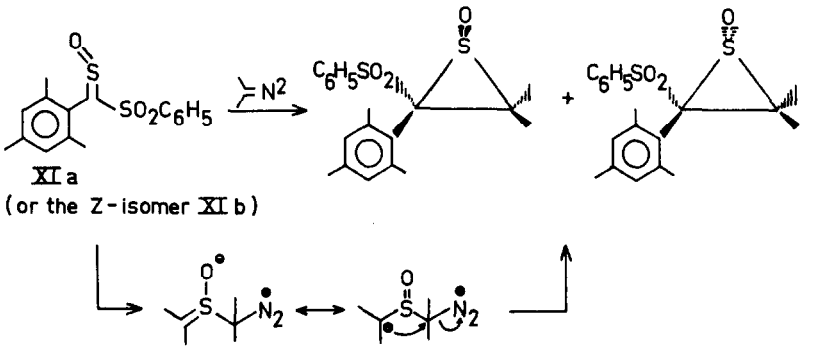
* All compounds show vigorous decomposition during melting.
(Characteristic i.r. absorptions for these compounds were observed at 1060-1080 ($\nu_{S=O}$) and 1560-1575 cm^{-1} ($\nu_{N=N}$))

pound could not withstand extensive chromatography.

The episulfoxide structure was assigned on the following grounds:a correct elemental analysis for $C_{19}H_{22}O_3S_2$, i.r. absorptions (in CS_2) at 1050 cm^{-1} ($\nu_{S=O}$), 1150 and 1325 cm^{-1} (ν_{SO_2}) and signals in the NMR spectrum ($CDCl_3$) at δ 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 thiadiazoline-oxide derived from VIIa), at δ 2.21 and 2.47 ppm for the methyls at C-2', at δ 2.16 and 2.34

ppm for those at C-4', at δ 6.62 and 6.96 ppm for the protons at C-3' and at δ 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 SO_2).

SCHEME



Bonini and Maccagnani[7] 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.

To explain this remarkable difference in stereochemistry in the formation of thiadiazoline-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 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[9] 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 Δ^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

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9. The *Z*-isomers were formed when the *E*-isomers were allowed to stand in the refrigerator for several months.