

REARRANGEMENT OF 2-ARYLSULFONYL- Δ^3 -1,3,4-THIADIAZOLINE-1-OXIDES BY A NEW 1,3-MIGRATION REACTION¹

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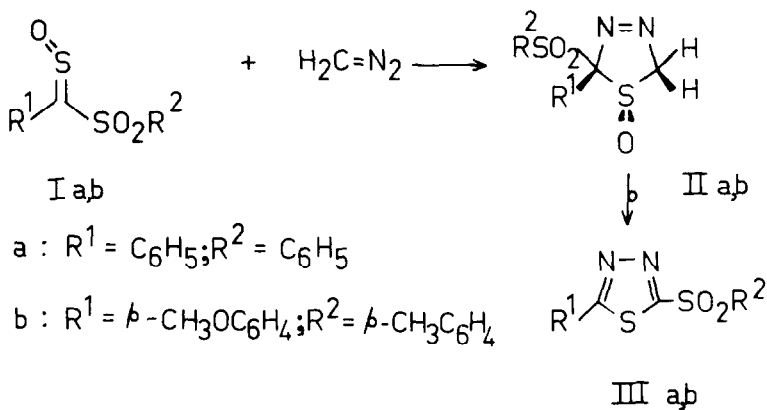
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In recent reports^{2,3,4} on the chemistry of sulfines we described the reaction of different types of sulfines with 2-diazopropane which gave Δ^3 -1,3,4-thiadiazoline-1-oxides in a regio- and stereospecific cyclo-addition reaction. In the course of this study the reaction of the arylsulfonyl substituted sulfine⁵ Ia with diazomethane was investigated.

Admixture of 0.2 mmole of sulfine Ia in 0.5 ml of CDCl_3 and a slight excess of diazomethane in ether at 0° gave a rapid discharge of the yellow colour. The NMR spectrum of this reaction mixture showed besides aromatic absorptions the methylene AB quartet of the anticipated Δ^3 -1,3,4-thiadiazoline-1-oxide IIa (Scheme I) at δ 6.08 and 6.40 ppm with $J_{AB} = 18$ Hz. However, after standing overnight at

Scheme I



0° the spectrum of the slightly turbid solution had changed significantly, *viz.* the signal of the methylene group was no longer present.

By performing the reaction on a 5 mmole scale (solvent benzene/ether 4:1, temperature 0°, reaction time 2 days) a product which analyzed correctly for $C_{14}H_{10}N_2O_2S_2$, could be isolated in 53% yield by chromatography on neutral alumina and subsequent crystallization from ethanol (m.p. 161.5-162.5°).

Structure IIIa (Scheme I) was assigned to this product on the basis of the spectral features (NMR in $CDCl_3$: two broad multiplets of aromatic protons at δ 7.35-7.8 and 7.8-8.3 ppm with a peak ratio of 6:4; IR (KBr), ν_{SO_2} 1165, 1340 cm^{-1} , no typical sulfoxide absorption), but particularly on the comparison with a sample which was synthesized by an independent route as follows: Reaction of phenyl chlorodithioformate ($ClC(=S)SC_6H_5$) with phenyldiazomethane in ether in the presence of one equivalent of triethylamine gave 2-phenyl-5-phenylthio-1,3,4-thiadiazole (yield 50%) in analogy with the formation of phenyl-1,3,4-thiadiazole from thiobenzoyl chloride and diazomethane⁶. Oxidation of the thus obtained thiadiazole derivative with *m*-chloroperbenzoic acid in dichloromethane/ether at 0° for 3 days gave the corresponding sulfone in 77% yield. However, the regioselectivity of the cyclo-addition reaction of diazo compounds and thiocarbonyl compounds must be considered with some reserve⁷. Therefore, 2-phenyl-5-phenylthio-1,3,4-thiadiazole was also synthesized by a longer, but unambiguous, route, *viz.* by reaction of thiosemicarbazide with benzoylchloride followed by ring closure with sulfuric acid to 2-amino-5-phenyl-1,3,4-thiadiazole⁸, conversion of the amino group into a chlorine *via* a Sandmeyer-type reaction⁹ and subsequent nucleophilic displacement of the halogen by thiophenolate⁹. These independent syntheses not only prove structure IIIa, but also confirm the regioselectivity of the cyclo-addition reaction of the phenylsulfonyl sulfine Ia and diazomethane.

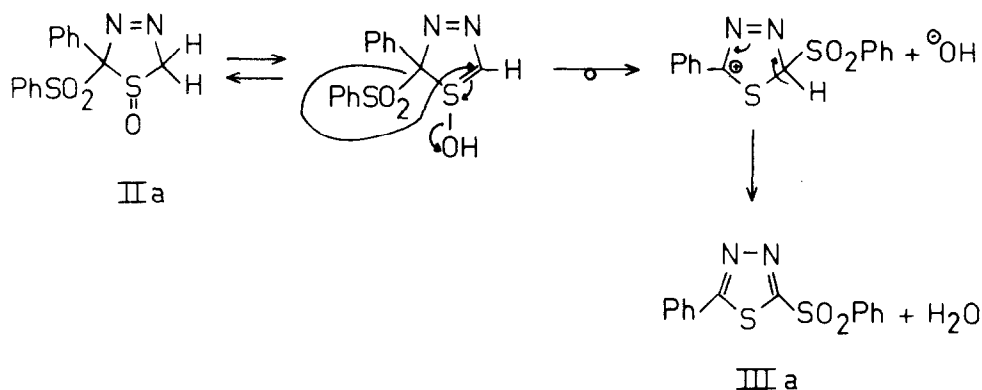
Treatment of the sulfone sulfine¹⁰ Ib dissolved in benzene/ether 1:2 with a slight excess of diazomethane gave after standing at -20° for 24 h, the separation of a crystalline product, which appeared to be the thiadiazoline-1-oxide IIb (yield 60%; m.p. 95° dec.; correct C,H,N,S analysis for $C_{16}H_{16}N_2O_4S_2$; NMR in $CDCl_3$ at -20°: AB qu at δ 6.42 + 6.14 ppm, J_{AB} 18 Hz for the methylene protons, s at δ 3.87 ppm for CH_3O , s at δ 2.49 ppm for $CH_3C_6H_4-$, AB qu at δ 6.96 + 7.70 ppm, J_{AB} 9 Hz for $CH_3OC_6H_4-$, s at δ 7.30 ppm for $CH_3C_6H_4-$; IR_{Nujol}: $\nu_{N=N}$ 1565, $\nu_{S=O}$ 1050 cm^{-1}). From the mother liquor the thiadiazole IIIb (yield 13%) was isolated by chromatography on neutral alumina (m.p. 126-127°, NMR in $CDCl_3$: δ 3.86, s, CH_3O ; δ 2.42, s, $CH_3C_6H_4-$; δ 6.99 + 8.01, AB qu, J_{AB} 9 Hz, $CH_3OC_6H_4-$; δ 7.40 + 7.87 ppm, AB qu, J_{AB} 8.5 Hz, $CH_3C_6H_4-$; IR_{KBr}: ν_{SO_2} 1155, 1340 cm^{-1} , no $\nu_{S=O}$).

When the thiadiazoline-1-oxide IIb was chromatographed on silica with ether as eluent, smooth conversion into the thiadiazole IIIb took place (yield 65%). Also upon standing in solution IIb rearranges slowly to IIIb.

The results described above reveal that the thiadiazoles IIIa and IIIb do a-

rise from the thiadiazoline-1-oxides IIa and IIb, respectively. Two mechanisms can be envisaged to rationalize this rearrangement. Firstly, an intramolecular 1,3-shift of an arylsulfonyl group with a simultaneous loss of water as depicted in Scheme II would explain¹¹ the conversion of II to III.

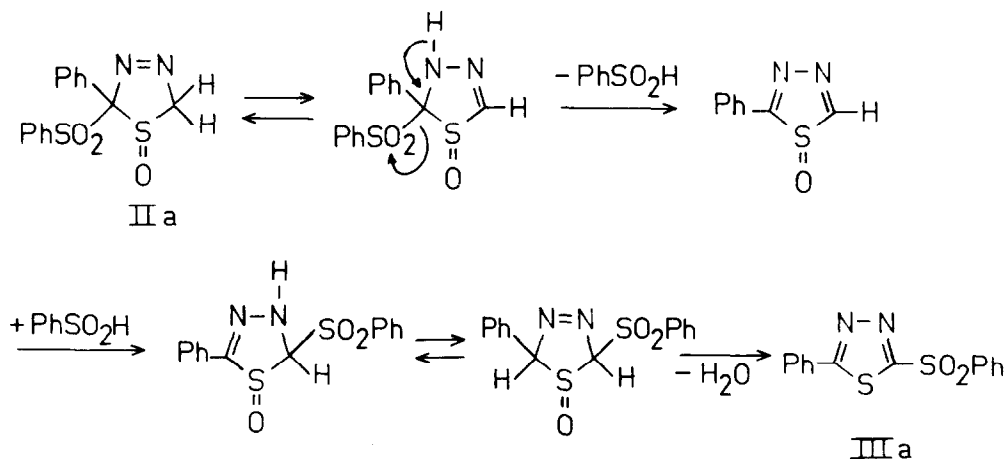
Scheme II
Intramolecular Mechanism



Secondly, an elimination-addition mechanism (Scheme III) *via* an initial isomerization of the Δ^3 - to the Δ^2 -thiadiazoline-oxide with a subsequent elimination¹² and re-addition of sulfonic acid, followed by a spontaneous loss of water in a Pummerer-type aromatization reaction, can account for the observed product transformation.

Scheme III

Elimination – Addition Mechanism



In order to differentiate between these two possibilities the following experiment was designed: A 1:1 mixture of the sulfines Ia and Ib dissolved in dichloromethane was treated with a 10% excess of diazomethane in ether at -5° and allowed to react for 2 days at room temperature. After removal of the solvents the product mixture was chromatographed on neutral alumina. The respective fractions were analyzed by means of glc and NMR. It was found that the main products were 2-phenyl-5-phenylsulfonyl-1,3,4-thiadiazole and 2-anisyl-5-tolylsulfonyl-1,3,4-thiadiazole, but in addition 2-phenyl-5-tolylsulfonyl-1,3,4-thiadiazole and 2-anisyl-5-phenylsulfonyl-1,3,4-thiadiazole were present, each in about 6% of the total amount of thiadiazole formed. This result shows that there is some "crossing-over" of sulfinic acid and thus provides evidence for the elimination-addition mechanism as given in Scheme III.

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11. Phenyl migration is unlikely because it would give an unfavourable electron deficiency adjacent to the sulfone function; moreover, the migratory aptitude of the phenyl-sulfonyl group is larger than that of the phenyl group.
12. This easy elimination of sulfinic acid from an α -aminosulfone resembles the facile dissociation, particularly in slightly acidic media, of hydroxymethyl aryl sulfones¹³ into arylsulfinic acid and formaldehyde.
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