

AROMATIC SULFINES WITH NITRILIMINES.^{1,2}

A regiospecific, non-stereospecific cyclo-addition reaction.

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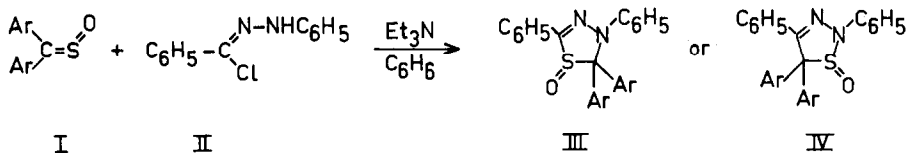
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Sulfines represent a class of sulfur containing heterocumulenes which may serve as potential dipolarophiles in 1,3-dipolar cyclo-addition reactions. In a previous paper we reported^{3,4} the cyclo-addition reaction of aromatic sulfines with diazoalkanes which leads to a five-membered heterocyclic system, *i.e.* Δ^3 -1,3,4-thiadiazoline-S-oxides. In this communication we wish to describe the cyclo-addition of aromatic sulfines with nitrilimines and to discuss the direction of the addition as well as the stereochemistry of the reaction.

When the sulfines I were allowed to react with diphenylnitrilimine, generated⁵ *in situ* by the action of triethylamine on N-(α -chlorobenzylidene)-N'-phenyl-hydrazine (II), in boiling benzene for one hour, 1:1-adducts were obtained in good yields (Scheme 1). The adducts which were single compounds according to TLC, gave correct combustion analyses for C, H, N and S. The IR spectra of all of these compounds showed a strong S=O band at 1070 cm^{-1} and a C=N absorption at 1535 cm^{-1} . The NMR spectrum of the adduct derived from the sulfine

Scheme 1

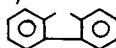


a : Ar = C₆H₅

b : Ar = C₆H₄OCH₃-~~A~~

c : Ar = C₆H₄CH₃-~~A~~

d : Ar-Ar=



a : m.p. 167-8°; yield : 68.5 %

b : m.p. 137-8°; yield : 58 %

c : m.p. 152-3°; yield : 85.5 %

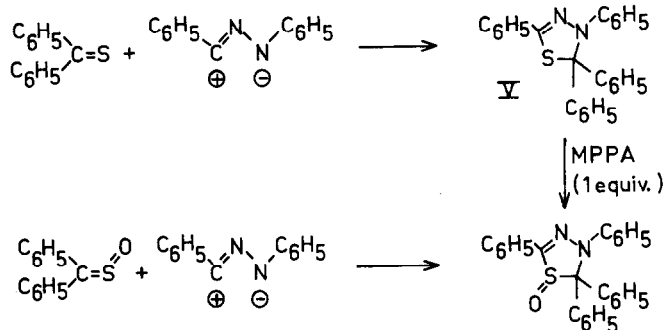
d : m.p. 173-4°; yield : 92 %

Ib as well as from Ic exhibits two non-equivalent methyl signals (δ 3.81 and 3.86 ppm for the former, δ 2.30 and 2.36 ppm for the latter) indicative of the presence of the asymmetric pyramidal sulfoxide function.

On the basis of the information presented so far, two possible structures for the 1:1-adducts can be envisaged, *viz.* III and IV (Scheme 1). In order to elucidate the orientation of the cyclo-addition, the product isolated from the sulfine Ia was compared with that obtained by oxidation of the adduct V prepared⁶ from thiobenzophenone and diphenylnitrilimine (Scheme 2). The structure of V was proven beyond any doubt by Huisgen *et al.*⁶, hence the structure III should be assigned to the sulfine-nitrilimine adducts.

It is interesting to note that the regioselectivity of the cyclo-addition with the thioketone and its S-oxide is the same, although the charge distribution in both substrates is considerably different⁷.

Scheme 2

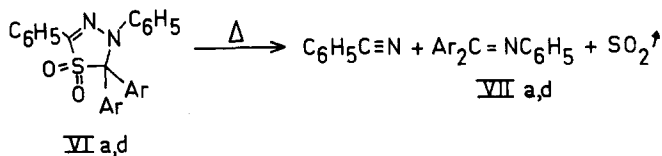


All these Δ^2 -1,3,4-thiadiazoline-S-oxides III could easily be oxidized to the corresponding sulfones VIa-d by means of excess of mono-perphthalic acid (MPPA) at 20°. As may be expected the sulfones VIb and VIc show only one methyl signal in their NMR spectra.

An interesting independent proof of the structure of the adducts was provided by the thermolysis of the sulfones VIa and d (Scheme 3). When heated in refluxing benzene for 15-20 min. SO₂ was liberated quantitatively and benzonitrile together with the anils VIIa and VIId, respectively, were isolated in high yields. This thermal two-fold extrusion process⁸, demonstrates which bonds were formed during the cyclo-addition reaction.

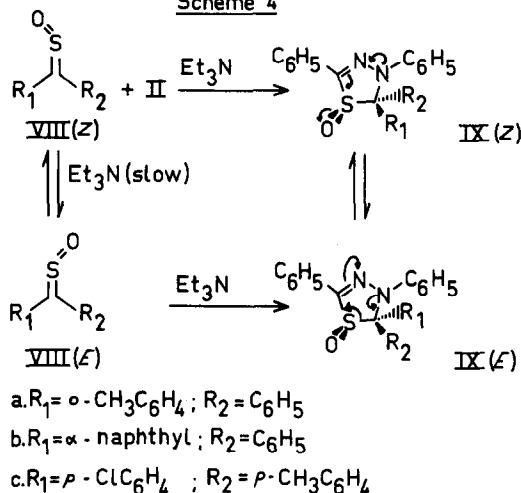
The bent nature of the CSD-system⁹ offers the possibility to study the stereochemistry of the cyclo-addition reaction. The geometrical isomers of VIIIa (Scheme 4) were treated with diphenylnitrilimine in benzene at reflux temperature (6 h). In the resulting coloured reaction mixture only starting material and 1:1-adduct could be detected by NMR and TLC, in either case (ratio sulfine: adduct 3:4 for both isomers). By careful thick-layer chromatography unreacted sulfine (which had its original geometry) and cyclo-adduct could be separated. In contrast to our expectation both geometrical isomers of VIIIa gave the same ad-

Scheme 3



duct¹⁰ (m.p. 130-132°, dec. from methanol). An attempt was made to prepare the epimeric sulfoxides IXa *E* and IXa *Z* by oxidation of the parent ringsystem (obtained by cyclo-addition of 2-methyl thiobenzophenone and diphenylnitrilimine in 57% yield) with *m*-chloroperbenzoic acid. However, this oxidation resulted in the formation of only one isomer (m.p. 130-132°) in 52% yield, which was identical with that obtained from the cyclo-addition of the sulfoxines VIIIIa *E* and VIIIIa *Z*. The isomeric sulfoxines VIIIIb *E* and VIIIIb *Z* gave with diphenylnitrilimine also only one 1:1-adduct (m.p. 154-155°; yield on recrystallized material 57 and 64%, respectively).

Scheme 4



Since steric effects could have influence on the product formation from the sulfoxines VIIIIa and VIIIIb, the *E*- and *Z*-isomers of VIIIIc were subjected to cyclo-addition. In both cases a mixture of diastereomeric thiadiazoline-S-oxides IXc was obtained as an oil (yield 90%, reaction for 3 days at 20°, δ_{Me} 2.29 ppm for IXc *E*, δ_{Me} 2.36 ppm for IXc *Z*). The *Z*-sulfoxine (m.p. 72-74°) gave a product ratio *E*:*Z* = 2:3, the *E*-isomer (m.p. 102-104°) gave an *E* to *Z* ratio of 1:1 for IXc. Oxidation of the parent thiadiazoline (R₁ = *p*-ClC₆H₄, R₂ = *p*-CH₃C₆H₄) with *m*-chloroperbenzoic acid yielded after 12 h. at 20° in 90% the S-oxide IXc with *E*:*Z* = 1:2. This *E*/*Z* ratio as also that of 1:1, changed to 2:3 upon standing or gentle warming of the mixture in chloroform. Partly separation by means of thick-layer chromatography gave *E*/*Z* = 3:2, which on standing equilibrated to *E*/*Z* = 2:3.

The presented data show that the cyclo-addition of sulfoxines with diphenyl-

nitrilimine results in a non-stereospecific formation of Δ^2 -1,3,4-thiadiazoline-S-oxides. In principle three possible explanations for this non-stereospecificity can be envisaged: *i.* isomerization of the sulfine prior to the cyclo-addition, *ii.* product equilibration afterwards, *iii.* loss of stereochemistry during the adduct formation. In a blank experiment sulfine isomerization was indeed observed for VIIIa E and VIIIa Z in the presence of triethylamine, however, at a much lower rate than the formation of the cyclo-adduct. The experiments with VIIIc and IXc clearly reveal that product equilibration afterwards takes place. Although loss of stereochemistry during the cyclization cannot completely be excluded, the most likely explanation for this non-stereospecific 1,3-dipolar cyclo-addition is an initial stereospecific product formation followed by a product equilibration, leading to one isomer of IXa and IXb, and an E/Z-ratio of 2:3 for IXc.

Sulfoxides are usually quite stable towards stereomutation¹¹, but conjugative participation of the lone pair of electrons at N-4 (see Scheme 4, formula IX (Z)) could possibly lower¹² the barrier of pyramidal inversion of the S=O in the present case. Alternatively, a ring opening-ring closure mechanism, for instance as indicated by arrows in formula IX (E) (Scheme 4), could cause the thermodynamic isomerization.

References and notes

1. Sulfines, Part VI (Italian group), Part V, B.F. Bonini and G. Maccagnani, Tetrahedron Lett. 1973, in press.
2. Also Part XXI in the series "Chemistry of Sulfines" by the Dutch group (Part XX, B. Zwanenburg and W.A.J. Janssen, Synthesis, 1973, in press).
3. B.F. Bonini, G. Maccagnani, A. Wagenaar, L. Thijs and B. Zwanenburg, J.C.S. Perkin I, 1972, 2490.
4. See also: C.G. Venier and C.G. Gibbs, Tetrahedron Lett. 1972, 2293, and B. Zwanenburg, A. Wagenaar, L. Thijs and J. Strating, J.C.S. Perkin I, 1973, 73.
5. R. Huisgen, M. Seidel, G. Wallbillich and H. Knupfer, Tetrahedron, 17, 3 (1962).
6. R. Huisgen, R. Grashey, M. Seidel, H. Knupfer and R. Schmidt, Lieb. Ann. Chem. 658, 169 (1962).
7. B. Zwanenburg, L. Thijs and J. Strating, Rec. Trav. Chim. 86, 577 (1967).
8. Cf. Olefin formation by two-fold extrusion processes: D.H.R. Barton and B.J. Willis, J.C.S. Perkin I, 1972, 305.
9. B. Zwanenburg and J. Strating, Quart. Reports Sulfur Chem. 5, 79 (1970).
10. The NMR data did not allow an unequivocal assignment of the geometry in this adduct, tentatively the structure IXa E having the least steric congestion is proposed.
11. P.H. Laur, "Steric aspects of sulfur chemistry" in "Sulfur in organic and inorganic chemistry" (A. Senning, ed.), Vol. 3, Marcel Dekker, Inc., 1972.
12. A. Rauk, L.C. Allen and K. Mislow, Angew. Chem. 82, 453 (1970).