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# THE SYNTHESIS OF SULFUROUS DIAMIDE HETEROCYCLES THROUGH THE CYCLOADDITION REACTION OF N-SULFINYLANILINES WITH BENZALANILINES

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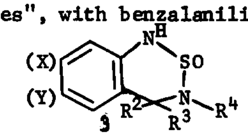
Summary: The cycloaddition reaction of N-sulfinylanilines - serving as "dienes" - with aromatic Schiff bases provides a convenient access to the thiadiazine oxide system (3).

The cycloaddition reactions of aromatic N-sulfynilanilines (1) with a variety of 1,3 - dipolar systems to afford six- and five-membered heterocyclic sulfinamides have been well documented[1-4]. Also, reactions in which N-sulfynilanilines undergo 1,2-cycloaddition with special-type carbon-carbon double bonds have been reported[5-6]. In all cases, the reaction with 1 takes place across the -N=S- bond. Only in the case of norbornenes, N-sulfinylanilines underwent cycloaddition reaction as the "diene" counterpart[7]. It turns out, that the former are unique in that no other cyclic or acyclic olefins tried would react with N-sulfinylanilines.

We report here the successful synthesis of the six-membered heterocyclic 1-thia-2,6-diazine-1-oxide system 3, containing the sulfurous diamide array -N-SO-N-, through the cycloaddition reaction of N-sulfinylanilines 1, which participate as "dienes", with benzalanilines 2.

$$\underset{\mathbf{1}}{R^1 - N = S = 0} + \underset{\mathbf{2}}{R^2R^3C = N - R^4} \longrightarrow$$



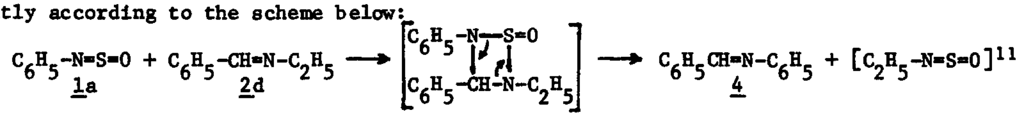
3

| | 1 | | 2 | | | | 3 |
|---|---|---|---|---|---|---|---|
| a. | $R^1=C_6H_6$ | a. | $R^4=C_6H_5$; | $R^2=C_6H_5$; | $R^3=H$ | a. | X=Y=H; $R^4=C_6H_5$ |
| b. | $R^1=m\text{-}CH_3C_6H_4$ | b. | $R^4=m\text{-}CH_3C_6H_4$ | $R^2=C_6H_5$; | $R^3=H$ | b. | $X=CH_3$; Y=H; $R^4=m\text{-}CH_3C_6H_4$ |
| c. | $R^1=p\text{-}CH_3C_6H_4$ | c. | $R^4=p\text{-}CH_3C_6H_4$ | $R^2=C_6H_5$; | $R^3=H$ | c. | X=H; $Y=CH_3$; $R^4=p\text{-}CH_3C_6H_4$ |

The said cycloaddition was realized by a thorough mixing of equimolar amounts of 1 and 2, without a solvent and allowing the reaction mixture to stand at room temperature for 7-10 days. Recrystalization of the mass obtained, from either water or wet ethanol afforded pure 3x2$H_2O$ in practically quantitative yield[8], mp of 3a-c being 122, 108-109, and 117-118°C respectively. The formation of 3b rather than its isomer in the cycloaddition of 1b and 2b is probably due to steric effects.

In contrast to the case of the five-membered 1,2,5-thia-diazole 1-oxides[2,3,9] the literature contains very little about the analogous 1-thia 2,6-diazine-1-oxide systems 3[10].

Neither six- nor four-membered ring products could be obtained when N-alkyl- rather than N-aryl-substituted Schiff bases (i.e. 2, $R^4$=alkyl) were used. Thus, the product isolated from the reaction of equimolar amounts of 1a and 2d in refluxing THF was banzalaniline (4), apparently according to the scheme below:



We note that: a) Except for intramolecular cycloadditions[12], only aromatic, but not aliphatic

N-sulfinylamines have been shown thus far to undergo either reversible cycloadditions as dienophiles with dienes[1,2,13] or in a 2+2 fashion with special carbon-carbon double bonds[5,6]. b) Only in the cycloadditions with norbornenes do N-sulfinylanilines participate as the "diene" counterpart. c) Any mode of 2+2 reopening of possibly formed four-membered ring intermediates in the cycloaddition of either of the pairs 1+2 will lead to the starting reactants.

We, therefore, assign the successful formation of 3a-c to the following factors: a) The relative stability of the aromatic - compared with that of the aliphatic-N-sulfinylamines. b) The relatively enhanced nucleophilicity of the carbon-nitrogen double bond of Schiff bases 2 compared with that of ordinary carbon-carbon double bonds. c) The non-reversibility of the 4+2 cycloaddition reaction, once its final cycloadduct (i.e. 3) has been formed.

The reaction of 3a -c in pyridine with access of either acetic anhydride or mesyl chloride afforded the corresponding acetanilides (i.e. $R^4NHCOCH_3$) and mesylates ($R^4NHSO_2CH_3$) respectively in the expected stochiometric yields. In contrast to the easy "clean" oxidation and reduction of 1,2-thiazine 1-oxides to the corresponding thiazine-dioxides and thiazines respectively[6,7,14], oxidation of 3 with either hydrogen peroxide or m-chloraperbenzoic acid, or its reduction with lithium aluminium hydride afforded mixtures of ill-defined oily products.

In summary, we have demonstrated the feasibility of the formation of six-membered ring sulfurous diamide heterocycles through the cycloaddition reaction of N-sulfinylanilines with benzalanilines. The scope and generality of this reaction as well as the chemistry of the thiadiazine oxide system 3 is currently under investigation.

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8. All the new compounds reported here gave satisfactory spectral and analytical data, which for the parent heterocycle 3a is as follows: IR (KBr): 3315 (NH), 1595, 1490, 1155, 1022 (SO), 743, 697 $cm^{-1}$; $H^1$ NMR (DMSO-$d_6$): δ 8.03-7.64 (m.,2H,arom.), 7.59-7.24 (m.,3H,arom.), 7.33-6.97 (m.,5H,arom.), 6.93 (S.,1H,CH), 6.87-6.37 (m.,4H,arom.), 5.20-3.77(broad S., 5H, NH+$2H_2O$, readily exchangeable with $D_2O$). The two methyl substituents of 3b and 3c appear in each as two separated singlets at 2.37, 2.24; and 2.33, 2.27 respectively.
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