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A NEW REACTION OF BIS(o-AMINOPHENYL)DISULFIDE WITH KETONIC COMPOUNDS.

PART I. REACTION WITH CYCLOHEPTANONE

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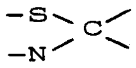
In connection with a research programme directed towards the synthesis of sulfur containing heterocyclic compounds, we have been studying, in particular, the reaction between bis(o-aminophenyl)disulfide and cycloheptanone. When the reaction was run in benzene in the presence of catalytic amounts of p-toluenesulfonic acid and under air, water was produced (1 mole per mole of cycloheptanone) and an oxygen containing compound, m.p. 107-108° (IV) was obtained as a final product.

Compound (IV) was identified as spiro[benzothiazoline-2,1'-cycloheptane-2'-one] (Found: C, 66.97 - H, 6.72 - N, 5.98 - S, 13.81 - Calcd. for $C_{13}H_{15}NOS$: C, 66.92 - H, 6.48 - N, 6.00 - S, 13.74). The infrared spectrum showed the bands of secondary amine and carbonyl groups at 3300 and 1700 cm^{-1} respectively, and the NMR spectrum ($CDCl_3$) exhibited a multiplet centered at δ =6,9(4 aromatic protons), a singlet at δ =5,35 (1 NH proton) and signals at δ =2,65 (2 protons next to carbonyl), δ =2,2 (2 protons next to  $\begin{array}{l}-S\\-N\end{array}\!\!>C<$ group) and

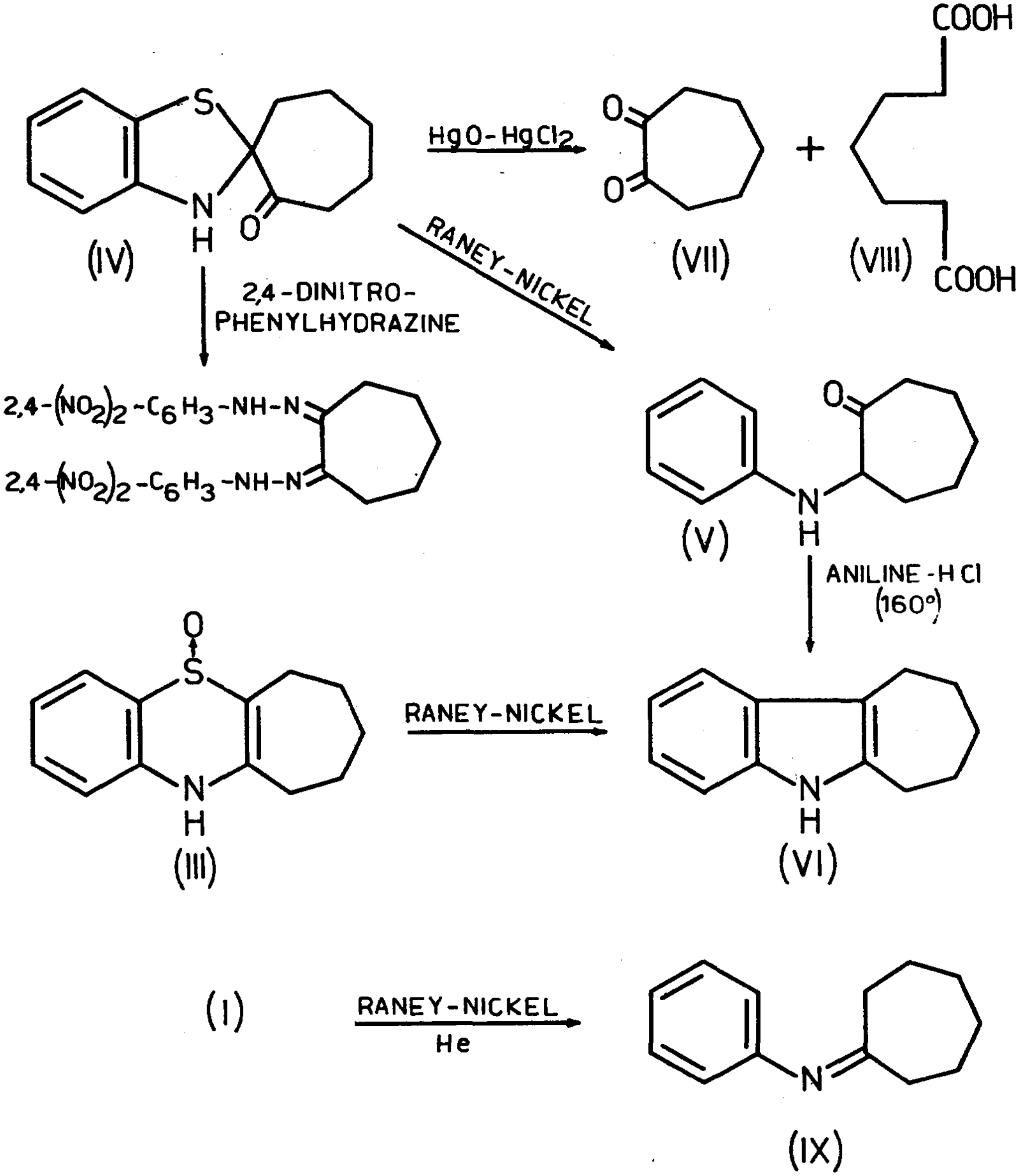
δ =1,6 (6 methylene protons). The structure (IV) was assigned on the basis of the following evidence: (IV) gave 1,2-cycloheptanedione-bis-2',4'-dinitro-phenylhydrazone by treatment with 2,4-dinitro-phenylhydrazine in acidic media: it is known that benzothiazolines are cleaved by acids to o-aminobenzenethiols and carbonyl compounds (1). The latter can be identified by treatment with 2,4-dinitro-phenylhydrazine.

Furthermore when compound (IV) was oxidized with $HgO-HgCl_2$, according to Drefahl et al.(2), two products were obtained: 1,2-cycloheptanedione (VII) and pimelic acid (VIII), as proved by comparison with authentic samples. Compound (IV) was converted by Raney-Nickel desulfurization into 2-anilino-cycloheptanone (V) m.p. 65° (Found: C, 76.87 - H, 8.73 - N, 7.20 - Calcd. for $C_{13}H_{17}NO$: C, 76.81 - H, 8.43 - N, 6.89 - I.R. ν_{max}^{Nujol} =3400 (NH) 1695 (C=O) cm^{-1}). Compound (V) by reaction with aniline hydrochloride (3) was cyclized to 5,6,7,8,9,10-hexahydro-cyclohepta[b]indole (VI), as proved by comparison with an authentic sample prepared by standard methods (4). (Chart I).

The formation of compound (IV) not being easily explicable, prompted us to a further study of the reaction, to acquire more information.

The reaction was therefore repeated under the above mentioned conditions, but with rigorous exclusion of air (Helium atmosphere). Again a rapid elimination of water (1 mole per mole of cycloheptanone) was observed and, after refluxing for a few more hours, the reaction mixture was distilled under vacuum, still in inert gas atmosphere. It was possible to isolate, in this way, a new compound (I), b.p.$_{0,02}$ 118-120°, m.p. 56°, very unstable upon exposure to air. To compound (I) we assigned the structure of bis(o-cycloheptylideneaminophenyl)-disulfide (Found: C, 71.75 - H, 7.56 - N, 6.42 - Calcd. for $C_{26}H_{32}N_2S_2$: C, 71.51 - H, 7.39 - N, 6.41); I.R. ν_{max}^{Nujol} =1620 cm^{-1} (C=N). The NMR spectrum($CDCl_3$) showed a multiplet centered at δ=7 (8 aromatic protons), and signals between δ =3,15 and

CHART I


(IV)
HgO-HgCl$_2$
(VII)
+
(VIII)
COOH
COOH
RANEY-NICKEL
2,4-DINITRO-PHENYLHYDRAZINE
2,4-(NO$_2$)$_2$-C$_6$H$_3$-NH-N
2,4-(NO$_2$)$_2$-C$_6$H$_3$-NH-N
(V)
ANILINE-HCl (160°)
(III)
RANEY-NICKEL
(VI)
(I)
RANEY-NICKEL
He
(IX)

δ=1,55 (24 protons). Compound (I) was converted by Raney-Nickel desulfurization under helium atmosphere into compound (IX), which was identical with an authentic sample of N-cycloheptylidene-aniline (Chart I).

By exposing compound (I) to air, it was rapidly converted into another compound, containing oxygen, which was proved to be a 6,7,8,9,10,11-hexahydro-cyclohepta[b][1,4]benzothiazine-5-oxide (III). Found: C, 66.78 - H, 6.69 - N, 6.26 - S, 13.71 - Calcd. for $C_{13}H_{15}NOS$: C, 66.92 - H, 6.48 - N, 6.00 - S, 13.74 - I.R. ν_{max}^{Nujol} =3200 (weak broad band, NH bonded), 1620 (strong sharp: C=C) and 990, 975, 960 cm^{-1} (three sharp peaks, S $\longrightarrow$ O; cf. 5).

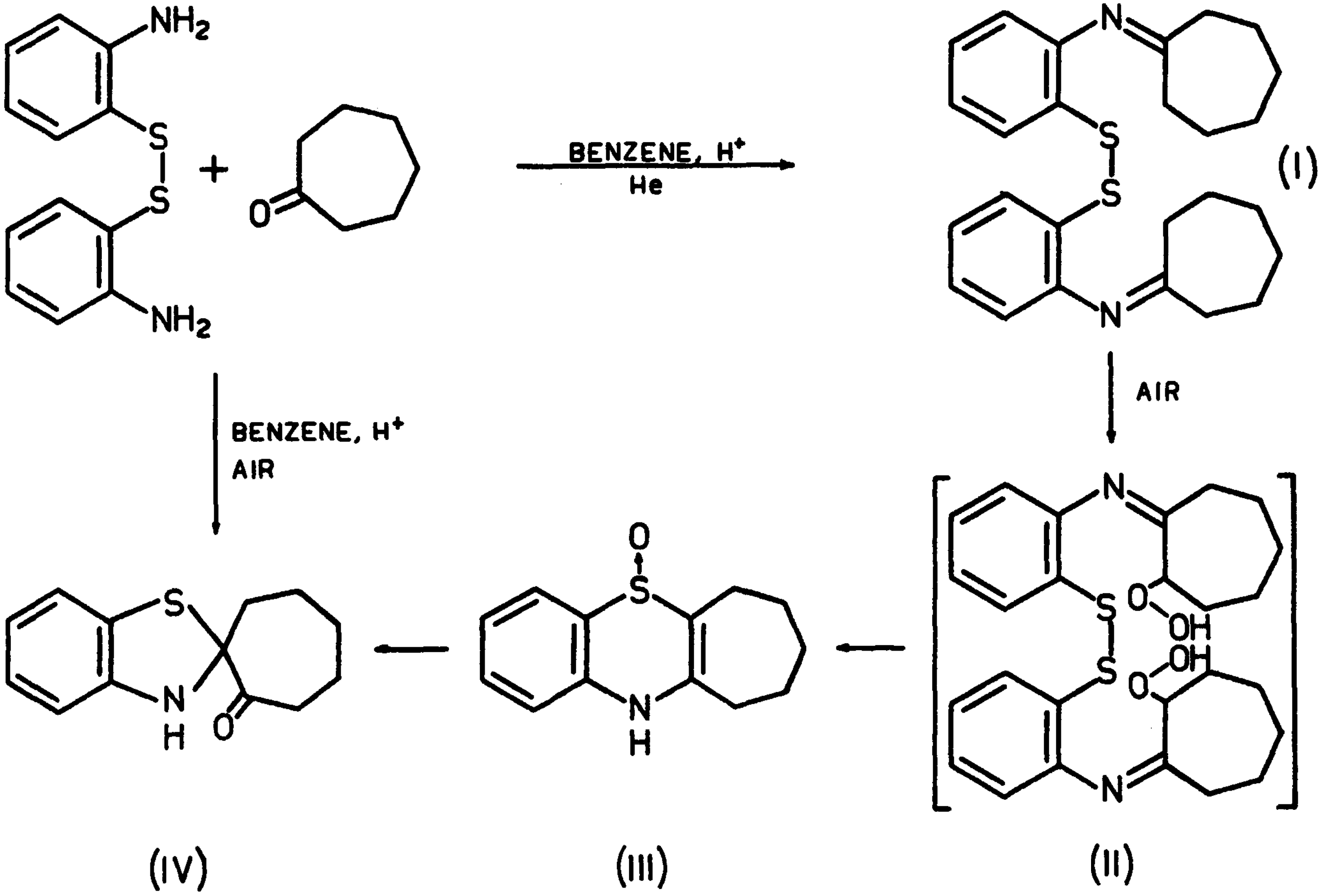
The NMR spectrum ($CDCl_3$) showed singlet at δ =10,40 (1 strongly bonded NH proton), multiplet centered at δ =7,35 (4 aromatic protons), broad signal at δ =2,8 (2 equatorial allylic protons) and multiplet centered at δ =1,7 (6 methylene protons + 2 axial allylic protons). Chemical support to the above structure was given by desulfurization with Raney-Nickel of (III) to 5,6,7,8,9,10-hexahydro-cyclohepta[b]indole (VI) as proved by comparison with an authentic sample prepared by Fisher's synthesis starting from cycloheptanone (4). (Chart I).

The sulfoxide (III) was also very reactive for it was readily transformed into spiroketone (IV) in most solvents; this reaction was faster in polar solvents and immediate in acidic media.

It is possible, at this stage, to say that the two fundamental processes leading to compound (IV), appear to be the oxidation of the bis-imine (I) to the sulfoxide (III), and the conversion of (III) to the spiroketone (IV) (Chart II).

The first step took place only on exposure to air of (I) and it is therefore reasonable to suggest an autoxidative process, probably of radical nature, especially on the grounds that the preliminary study of the oxidation rate showed an inhibitory

CHART II



effect caused by trans-stilbene; a well known inhibitor of radical reactions (6).

There are examples in the literature (7) of the formation of hydroperoxides through the radical autoxidation of Schiff's bases that, like (I), can undergo enamine ⇌ imine tautomerism.

In our case, the hydroperoxide intermediate, having a hypothetical structure (II), could yield the sulfoxide (III) by rapid decomposition. Various examples concerning the formation of sulfoxides from sulfides by autoxidation, are reported (8); furthermore it has been proved that the decomposition of peroxidic functions is considerably accelerated by anchimeric assistance of neighbouring aryl-thio or alkyl-thio groups (9).

It is premature to propose a precise mechanism to explain the rearrangement, via (III), of the disulphide (I) into the spiro-compound (IV) on the available evidence.

Further investigations of this reaction are being undertaken and will be reported later.

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