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PYROLYSIS OF 2-AZIDOARYL THIOKETONES: A NOVEL ROUTE TO 2,1-BENZISOTHIAZOLES

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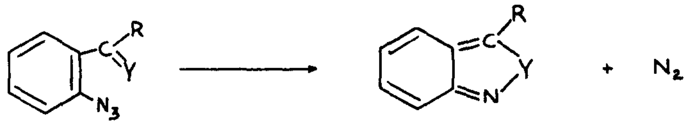
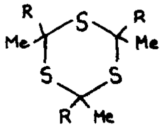
The thermolysis of o-substituted arylazides constitutes a practicable synthesis for various N-heterocyclic systems by intramolecular cyclisation and loss of nitrogen[1]. For instance, the azido-group reacts readily on heating with an ortho-positioned carbonyl group to form isoxazoles with evolution of nitrogen (e.g. R = Ph, Y = O 1→2a). Intramolecular interaction of an azido with a thiocarbonyl group (C=S) has, however, not been reported so far. On the other hand aryl azides react intermolecularly with thiones such as thiobenzophenone[2] to produce the appropriate Schiff base as shown: $ArN_3 + Ph_2CS \rightarrow N_2 + S + Ar\text{-}N{:}CPh_2$.

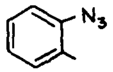


1 2

a) R = Ph; Y = O
b) R = Me; Y = S
c) R = Ph; Y = S
d) R = H; Y = S



3

R =


We now wish to report on the interaction of aromatic azides with an ortho-positioned thione group. Ethanolic o-azidoacetophenone with hydrogen chloride and hydrogen sulphide gases at -10° gave the tri-(o-azidothioacetophenone) (3) (m.p. 147°; 44%). Its mass spectrum did not show a molecular ion but had a base peak m/e 149 corresponding to the isothiazole (2b). At its melting point the trimer (3) turned purple owing to formation of the monomeric thione and this was followed by evolution of nitrogen. When compound (3) was added to boiling t-butyl benzene, nitrogen was evolved and chromatography of the residue (alumina/benzene) gave 3-methyl-2,1-benzisothiazole (2b) as a colourless solid m.p. 55° (54%)[3].

Treatment of ethanolic o-azidobenzophenone at -30° as described above gave a blue solution from which o-azidothiobenzophenone separated as deep blue needles after 4 hr. The dry crystals decomposed explosively when allowed to warm to room temperature leaving a residue of 3-phenyl-2,1-benzisothiazole (2c). Upon keeping the blue filtrate from the above reaction at 0° overnight the colour was discharged with formation of a further yield of 2c. Chromatographic purification of the combined portions gave 2c as a colourless solid m.p. 56°, (75%). As crystallization of the unstable thione from the reaction mixture did not occur above -15° the reaction could be conducted safely at -10° followed by addition of the blue solution to t-butyl benzene at 100°. The spontaneous decomposition of o-azidothiobenzophenone at room temperature makes a nitrene mechanism unlikely since the usual fragmentation temperature of aryl azides with ortho-side chains is considerably higher. We thus consider this cyclisation to be an extreme example of assisted loss of nitrogen due to a nucleophilic attack of the thione group on the azide function. Apart from analysis and spectral data the isothiazole structures (2b and 2c) were confirmed by desulphurization with Raney nickel which produced the expected o-substituted anilines. A small amount (ca. 5%) of o-aminobenzophenone was also isolated presumably the result of proton abstraction by an intermediate nitrene which is a side reaction followed by conversion of the thione to a carbonyl group on the alumina.

There are few references to 2,1-benzisothiazoles[4a] although the parent ring system (2d) was first produced over 70 years ago by reduction of o-nitrobenzylmercaptan[4b].

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References

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2. A. Schönberg and W. Urban, J. Chem. Soc., 1935, 530.
3. M. Davis and A.W. White J. Org. Chem. 34, 2985 (1969) report this compound as having m.p. 103°. We are grateful to the referee for pointing out that according to personal communication with the authors their substance is not 2b.

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