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THERMAL REARRANGEMENT OF 3-(β-STYRYL)-2,1-BENZISOXAZOLES. A NEW SYNTHESIS OF 3-ARYL-4-QUINOLONES AND 2-ARYLIDENEINDOXYLS

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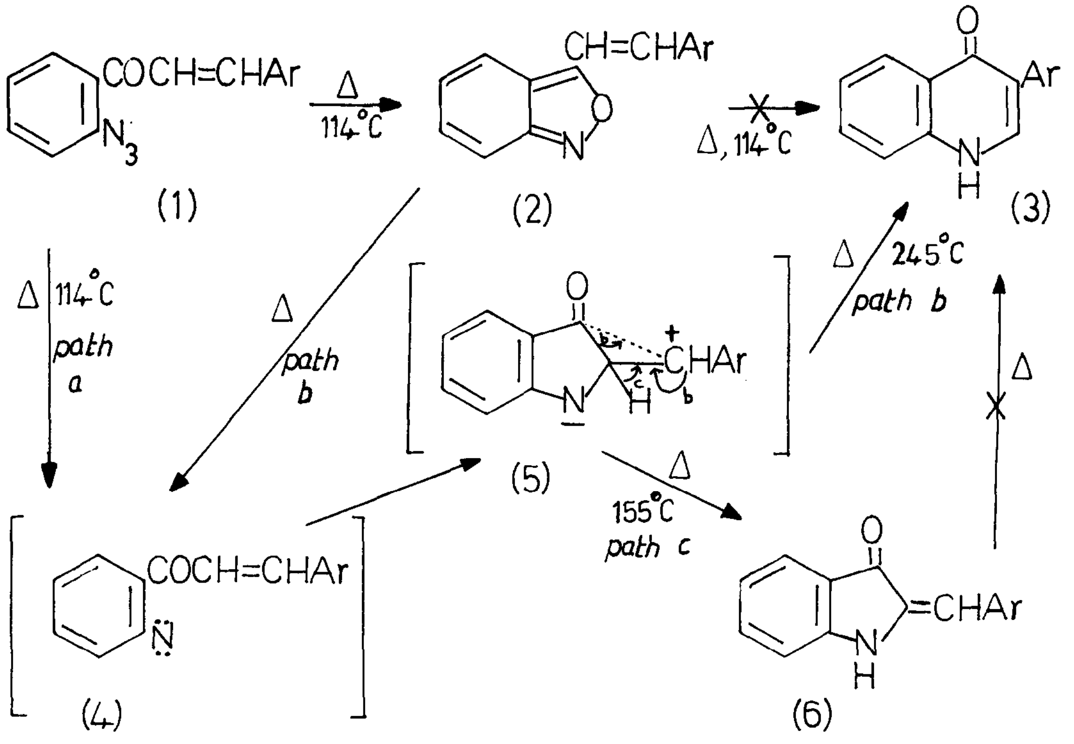
The formation of 2,1-benzisoxazoles (anthranils) by decomposition of o-azidoaryl ketones is well established[1] and involves neither a nitrene intermediate nor an assisted nitrogen loss, but rather an intramolecular 1,3-dipolar cycloaddition of the azide to the adjacent carbonyl group followed by loss of nitrogen from the cycloadduct.[2] Recently, we have become interested in the preparation of 2,1-benzisoxazoles by this method and particularly in those bearing a vinylic side-chain at the 3-position. Such compounds have been found to undergo a series of intriguing thermal transformations, preliminary details of which are reported here.

The o-azidochalcones (1; Ar = C_6H_5 and p-MeOC_6H_4), prepared by base-catalysed condensation of o-azidoacetophenone[3] with the appropriate aryl aldehyde, were thermolysed in boiling toluene (b.p. 110°C) to furnish the anticipated 3-(β-styryl)-2,1-benzisoxazoles[4] (2; Ar = C_6H_5 and p-MeOC_6H_4, respectively) in high yield (70-80%). In both cases, however, benzisoxazole formation was accompanied by a second product (5-7%), the u.v., i.r. and mass spectra of which suggested a phenyl-4-quinolone. The non-identity of the minor product from decomposition of (1; Ar = C_6H_5) with an unambiguously synthesised sample of 2-phenyl-4-quinolone[5] led us to conclude that this product must be the isomeric 3-phenyl-4-quinolone (3; Ar = C_6H_5). Identity was confirmed by comparison with an authentic sample available[6] from the thermolysis of 3-(β-styryl)-1,2,3-benzotriazin-4-one.

It appears likely that the 4-quinolone arises by direct nitrene attack on the styryl side-chain followed by rearrangement (Scheme - path a),[7] since the 2,1-benzisoxazole (2; Ar = C_6H_5) remained unchanged even after prolonged heating (24 h) in boiling toluene. Direct attack by nitrenes on ketone side-chains at the expense of anthranil formation is rare, although two examples have been reported recently.[8,9] In contrast to the above result, high temperature thermolysis (boiling 1-methylnaphthalene, b.p. 245°C) of styryl anthranil (2; Ar = C_6H_5) brought about rearrangement to 3-phenyl-4-quinolone albeit in poor (25%) yield.[10] Under these conditions 4-quinolone formation probably involves ring-opening of the 2,1-benzisoxazole to the nitreno-ketone (4; Ar = C_6H_5), followed by rearrangement of charged intermediate (5) (Scheme - path b), a process which resembles closely the production of acridones by decomposition of 3-arylanthranils.[11] In support of the proposed mechanism the (p-methoxystyryl)anthranil (2; Ar = p-$MeOC_6H_4$), for which the p-methoxy group should help stabilise the positive charge in intermediate (5), in boiling 1-methylnaphthalene, rearranges more cleanly and in much higher yield (65%) to the 3-aryl-4-quinoline (3; Ar = p-$MeOC_6H_4$).

Of particular interest in the formation of 3-aryl-4-quinolone is intermediate (5), which is the linear equivalent of the spiro-intermediates thought to be involved not only in the anthranil-acridone rearrangement,[11] but which are also invoked by Cadogan[12a,b] and others to account for various arylnitrene rearrangements.[13]



Scheme

The ease of production of 3-(p-methoxyphenyl)-4-quinolone from anthranil (2; Ar = p-MeOC_6H_4) led us to attempt the rearrangement of this anthranil at an intermediate temperature (ca. 160°C) in the presence of a dipolarophile, in the hope of trapping an intermediate of type (5) as the 1,3-dipolar cycloadduct. In the event, no adducts were obtained, but from each reaction an orange crystalline material was isolated which in solution exhibited an intense green fluorescence. Subsequent experiments showed that this product could be obtained in high yield (60%) by heating 3-(p-methoxystyryl)anthranil in boiling anisole (b.p. 155°C) for 24 h.[16] Elemental and spectral analysis suggested structure (6; Ar = p-MeOC_6H_4), i.e. a 2-arylideneindoxyl. Previously these so-called indogenides have been prepared by condensing indoxyl with aldehydes[14] or by acid hydrolysis of indican in the presence of an aldehyde.[15] The benzaldehyde and piperonal derivatives (6; Ar = C_6H_5 and 3,4-OCH_2O-C_6H_3, respectively), obtained by thermal rearrangement (155°C) of the corresponding anthranils (2) had physical constants in agreement with those reported previously.[14,15] Prolonged heating (24 h) of the 2-arylideneindoxyls in boiling 1-methylnaphthalene (b.p. 245°C) failed to bring about isomerisation to the 3-aryl-4-quinolones.

A plausible mechanistic rationale to account for indogenide formation is by a proton shift in intermediate (5) as shown in the Scheme (path c).

Further studies on the synthesis and rearrangement of 3-substituted anthranils are in progress.

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References

1. A.J. Boulton and K.-H. Wünsch, Adv. Heterocyclic Chem., 1967, **8**, 277.
2. J.H. Hall, R.E. Behr, and R.L. Reed, J. Amer. Chem. Soc., 1972, **94**, 4952.
3. J. Meisenheimer, O. Senn, and P. Zimmermann, Ber., 1927, **60**, 1736.
4. All new compounds have been characterised by elemental and spectral analysis.
5. B. Staskun and S.S. Israelstam, J. Org. Chem., 1961, **26**, 3191.
6. T. McC. Paterson and R.K. Smalley, University of Salford, unpublished results.

7. Alternatively, intermediate (5), and hence the 3-aryl-4-quinolone, may arise by a competing intramolecular 1,3-dipolar cycloaddition of the azide group to the alkene followed by loss of nitrogen from the resulting cycloadduct.

8. R.Y. Ning, J.F. Blount, P.B. Madan, and R.I. Fryer, *J. Org. Chem.*, 1977, 42, 1791.

9. R.Y. Ning, W.Y. Chen, and L.H. Sternbach, *J. Heterocyclic Chem.*, 1974, 11, 125.

10. A small amount (0.1 g) of an as yet unidentified indigo-blue semi-solid was also obtained.

11. R. Kwok and P. Pranc, *J. Org. Chem.*, 1968, 33, 2880.

12. (a) J.I.G. Cadogan, *Accounts Chem. Res.*, 1972, 5, 303;
    (b) see also references in J.I.G. Cadogan, J.N. Done, G. Lunn, and P.K.K. Lim, *J.C.S. Perkin I*, 1976, 1749.

13. An alternative mechanism involving a strained azanorcaradiene intermediate has also been proposed to account for these rearrangements (see ref. 12a).

14. A. Baeyer, *Ber.*, 1883, 16, 2188.

15. A.G. Perkin and F. Thomas, *J.C.S.*, 1909, 95, 793.

16. Latest results show that this rearrangement proceeds more quickly (10 h) and more efficiently (65%) in boiling anisole containing a catalytic amount of *p*-toluene sulphonic acid.