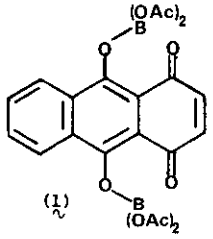
THE USE OF QUINIZARIN DIBOROACETATE AS A DIPOLAROPHILE IN THE SYNTHESIS OF FUSED TETRACYCLIC ISOXAZOLES AND PYRAZOLES

Alan M. Birch and Anthony J.H. Mercer *
School of Chemical and Physical Sciences, Kingston Polytechnic, Penrhyn Road, Kingston upon Thames, Surrey KT1 2EE, U.K.
and Colin W. Greenhalgh
Imperial Chemical Industries Limited, Organics Division, Blackley, Manchester M9 3DA, U.K.

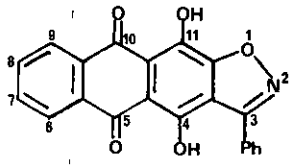
Abstract - Quinizarin diboroacetate undergoes [3 + 2] cycloaddition reactions with benzonitrile oxide to give an anthra[2,3-d]isoxazole (2) and with diphenyldiazomethane to form an anthra[2,3-c]pyrazole (4) which decomposes at 250° to a 13H-indenoanthracene (8); the diphenyldiazomethane dihydro-adduct (9; R=B(OAc)$_2$) undergoes thermal decomposition at room temperature to give 2-(diphenylmethyl)quinizarin (11).

We have recently shown that quinizarin diboroacetate exists as a hybrid structure in which the ene-1,4-dione (1) predominates and that as a consequence Diels-Alder [4 + 2] cyclo-additions with reactive dienes have been observed.[1] We now wish to report that quinizarin diboro-acetate also reacts as a dipolarophile with 1,3-dipolar compounds to give 4-ring heterocycles. Benzonitrile oxide[2] was liberated from α-chlorobenzaldoxime by stirring with aqueous sodium carbonate and then extracted into ether.[3] The dried ethereal solution of the nitrile oxide reacted with quinizarin diboroacetate to give, on aqueous workup, the anthra[2,3-d]isoxazole (2),[4] m.p. 230-231°, in 20% yield after preparative thin layer chromatography on Merck Kieselgel H (Type 60) (0.3 mm) eluted with toluene/chloroform (1:1), the initially formed leuco-adduct having spontaneously aromatised. The ^{1}H n.m.r. spectrum showed the expected AA'BB' pattern for the 6,9- and 7,8-protons at δ8.44 and 7.87; the phenyl group appeared as two multiplets at δ8.13 and 7.58 p.p.m.. The mass spectrum showed a molecular ion at m/e 357 and a fragmentation ion at m/e 329 (loss of CO). This and the lack of an AB pair of doublets expected for the 3a,11a-protons demonstrated that the product could not be the dihydro-adduct. Spontaneous aromatisation has also been observed in the naphthoquinone-benzonitrile oxide adduct.[5]

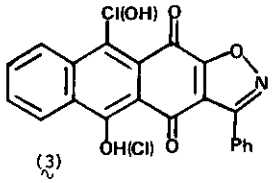
In an attempt to improve the yield of the isoxazole (2), an alternative synthesis was undertaken. Benzonitrile oxide reacted with 9-chloro-10-hydroxy-1,4-anthraquinone (Green's compound)[6] to give a 24% yield of an adduct (3), presumably as a mixture of isomers although this could not be demonstrated by n.m.r. The mass spectrum of the adduct (3) had molecular ions at m/e 375/377 (ratio 3:1 typical of a monochlorinated product) and a M^+-CO ion at m/e 347/349. The low and wide melting range of the adduct (212-220°) suggested that a mixture of isomers was present. Conversion of the adduct (3) to its dihydroxy-analogue (2) was achieved in high yield by heating in sulphuric acid (75% w/v) for several hours.



(1)



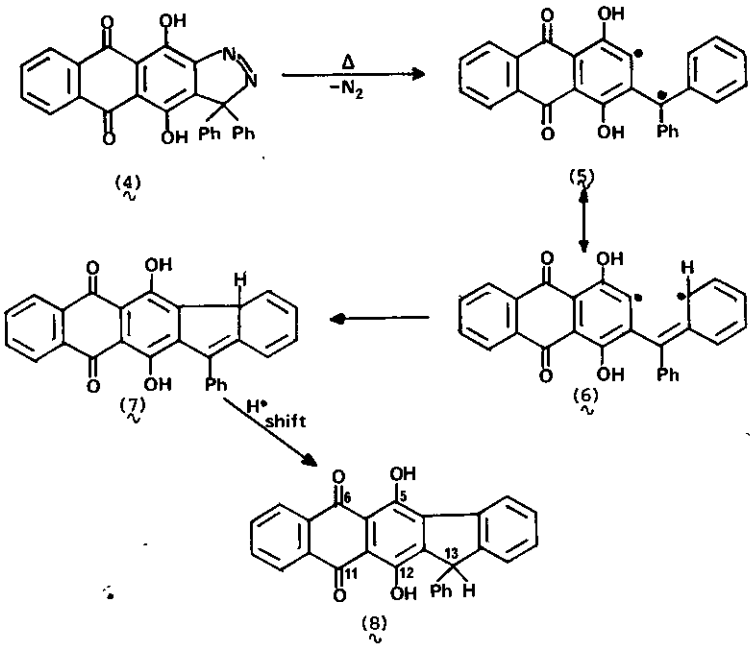
(2)



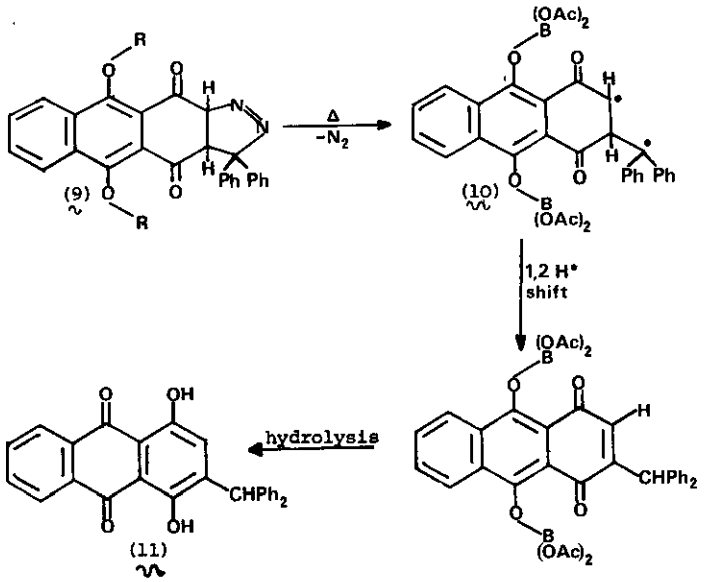
(3)

Quinizarin diboroacetate also gave a [3 + 2] cycloaddition with diphenyldiazomethane to form on aqueous workup an anthra[2,3-c]pyrazole (4), m.p. 230° (dec.), in 49% yield, after dry column chromatography. Once again the dihydro-adduct (9; R=H) could not be isolated but underwent aromatisation to the pyrazole (4) during work up of the reaction mixture. However, a study of the thermal decomposition of the adducts under different conditions provided some evidence of the intermediacy of the dihydro-adduct (9) in the reaction. Thus the isolated anthrapyrazole (4) decomposed on heating at 250° under vacuum for 1 minute to give the indenoanthracene-6,11-dione (8), m.p. 252-255°, in 40% yield in a reaction reminiscent of the thermal decomposition of 3,3-diphenyl-3H-benz[f]indazole-4,9-diol.[7] The structure of the indenoanthracene was confirmed by ^{1}H n.m.r. which showed singlets each 1H at δ5.28 (13-H), and δ13.11 and 13.69 p.p.m. (5- and 12-OH).

In contrast if the boroacetate derivative of the dihydroadduct (9; R=B(OAc)$_2$) after initial formation (but not isolation) from quinizarin diboroacetate and diphenyldiazomethane was allowed to stand in degassed tetahydrofuran solution at room temperature under nitrogen for 4 hours, the product isolated after aqueous work up was 2-(diphenylmethyl)quinizarin (11), m.p. 225-227°, in 20% yield.[8] The formation of both decomposition products can be rationalised by postulating initial loss of nitrogen with formation of biradical intermediates (5) and (10). In the case of



Scheme 1



Scheme 2

the aromatised adduct (4) the reaction is via a biradical, the ortho-resonance form (6) of which is stabilised by extended conjugation with the aromatic anthraquinone system. The 4a*H*-indenoanthracene (7) is formed and subsequently rearranges by a hydrogen shift to the fully aromatic 13*H*-indenoanthracene (8) (Scheme 1). On the other hand the biradical (10) from the dihydropyrazole (9) is able to undergo a direct hydrogen radical 1,2-shift to the substituted quinizarin (11) after hydrolysis of the boroester intermediate (Scheme 2).

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References and Notes

1. A.M. Birch, A.J.H. Mercer, A.M. Chippendale, and C.W. Greenhalgh, J.C.S. Chem. Comm., 1977, 745.
2. A. Quilico, G.S. d'Alcontres, P. Grünager, Gazz. Chim. Ital., 1950, 80, 479.
3. The more convenient method of generating the nitrile oxide in situ by dropwise addition of triethylamine to an ethereal solution of the chloroxime and the dipolarophile which suppresses the dimerisation of the N-oxide could not be used since quinizarin diboroacetate reacts with triethylamine to give a nitrogen-boron adduct which prevents further reaction taking place.
4. All new compounds reported here have satisfactory chemical analyses and supporting spectroscopic data.
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6. C.W. Greenhalgh, Endeavour, 1976, 35, 134.
7. P.G. Jones, J.C.S. Chem. Comm., 1966, 894.
8. For a similar decomposition in the naphthoquinone analogues see
   A.R. Bader and M.G. Ettlinger, J.Amer. Chem. Soc., 1953, 75, 730;
   L.F. Fieser and M.A. Peters, J. Amer. Chem. Soc., 1931, 53, 4080.

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