Quinizarin Boroacetate and 1,4-Diaminoanthraquinone Diboroacetate as Dienophiles

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Summary Quinizarin boroacetate undergoes a Diels-Alder reaction with cyclopentadiene to give (after hydrolysis) a mixture of *exo*- and *endo*-leuco isomers (III) in the ratio 1 : 2·6 which can be oxidised to a bridged 2,3-cycloquinizarin derivative (IV; X=OH); cycloaddition with acyclic dienes is accompanied by aromatisation.

In view of the current interest in anti-cancer agents such as daunorubicin and its analogues, and in particular the promising syntheses involving quinizarin quinone,[1] the reaction of quinizarin boroacetate with a number of dienes has been investigated.

Quinizarin and 1,4-diaminoanthraquinone are known to have the 9,10-dione structure (I; X=OH or NH_2, respectively). The reactions shown by the boric esters of these compounds suggest that these derivatives have 1,4-quinonoid or 1,4-quinonedi-imine structures, respectively.[2] An examination of the ^{13}C n.m.r. spectra of the anthraquinones and their boroacetate derivatives (II) based on the chemical shifts of the 1-, 4-, 9-, and 10-carbons has been carried out and the Table summarises the data obtained.

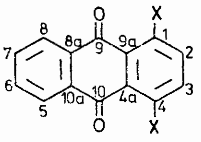
When 1,4-diaminoanthraquinone is converted into its boroacetate, the C-9 or C-10 resonance is shifted upfield from the normal quinone position of 181·2 to 157·0 or

Table. Chemical shifts in ^{13}C n.m.r. spectra of anthraquinones[a]

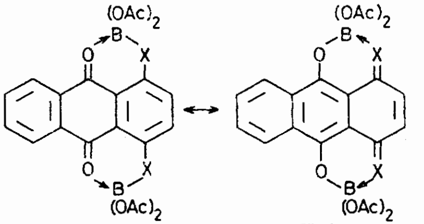
	Chemical shifts								
Compound	C-1 and -4	C-2 and -3	C-5 and -8	C-6 and -7	C-9 and -10	C-8a and 10a	C-9a and -4a	Acetate CO	CH_3
(I; X= NH_2)[b]	146·8	128·9	125·8	132·2	181·2	134·2	107·7	—	—
(II; X = NH)[b]	155·7[d]	132·0	125·4	135·1	157·0[d]	129·4	102·5	171·1	22·9
(I; X = OH)[c]	157·8	129·4	127·0	134·5	186·9	133·4	112·7	—	—
(II; X = O)[c]	167·0	138·8	129·5	136·7	173·7	130·8	108·5	172·2	22·5

[a] Natural abundance ^{13}C Fourier transform n.m.r. spectra were recorded on a Bruker WH90 spectrometer at 22·6 MHz. Chemical shifts are quoted in p.p.m. from Me_4Si. Assignments were made using ^1H-noise and single peak off-resonance decoupling techniques together with fully ^1H-coupled spectra. [b] $(CD_3)_2SO$ solution. [c] $CDCl_3$ solution. [d] These assignments are interchangeable.

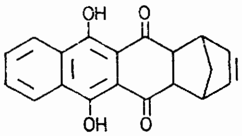
155·7 p.p.m., characteristic of phenolic carbon.[3] At the same time the C-1 or C-4 resonances are shifted downfield from 146·8 (aromatic amine) to 155·7 or 157·0 p.p.m. (imine). These results suggest that 1,4-diaminoanthraquinone diboroacetate is best represented by the 1,4-diimine structure (IIb; X=NH). In contrast the conversion of quinizarin into its diboroacetate shows less substantial shifts. Thus the C-9 or C-10 resonance in quinizarin (I) shifts from 186·9 to 173·7 p.p.m. in the boroacetate (II; X=O). This implies that quinizarin diboroacetate is a hybrid with approximately equal contributions from both canonical forms (IIa; X=O) and (IIb; X=O). Similar results have been observed for the ^{13}C n.m.r. spectrum of naphthazarin.[4]



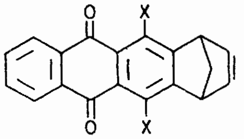
(I)



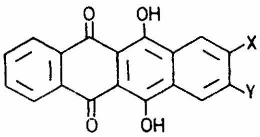
(IIa) (IIb)



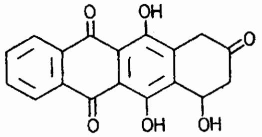
(III)



(IV)



(V)



(VI)

One chemical consequence of the structure suggested for the boroacetates (II; X=O or NH) is that the compounds should undergo the Diels–Alder cycloaddition reaction with reactive dienes, the addition taking place at the 2,3-positions, in contrast to the observed inactivity of quinizarin itself with 2,3-dimethylbutadiene under vigorous conditions.[5] This has been confirmed and quinizarin boroacetate reacts with cyclopentadiene to give (after hydrolysis) a mixture of *exo*- and *endo*-leuco isomers (m.p. 173—174 °C and 143—144 °C, respectively) of the methanonaphthacene (III)† in the ratio of *exo*:*endo* 1:2·6. The isomers, which were assigned their respective configurations by ^{1}H n.m.r. spectroscopy have been separated by preparative t.l.c. (Merck HF254, 0·2 mm, eluant 1:1 v/v toluene–cyclohexane) and fully characterised. *p*-Benzoquinone[6,7] and 1,4-naphthoquinone[6,8] have both been observed to give adducts with cyclopentadiene but in each case only the *cis-endo* isomer has been produced. Oxidation of either adduct (III) using nitrobenzene and a catalytic amount of piperidine led to (IV; X=OH), m.p. 225—227 °C.

The reaction of cyclopentadiene with diaminoanthraquinone diboroacetate (II; X=NH) is more complicated. The initial green Diels–Alder adduct is formed but attempts to hydrolyse this material led to several products of which the retro-products are dominant. The adduct could however be oxidised directly by nitrobenzene–piperidine to give, after hydrolysis of the boro-ester, the 1,6-diamino-methanonaphthacene (IV; X=NH_2), m.p. 270—272 °C.

The reaction of quinizarin boroacetate with a number of acyclic dienes has been investigated in the hope of avoiding the problem of addition at the two possible 'internal' and 'external' ene centres observed in quinizarin quinone.[1b] Diels–Alder addition occurs as expected only at the 2,3-positions but problems of subsequent aromatisation have been encountered. Thus 2,3-dimethylbutadiene reacts to give 2,3-dimethylbenzoquinizarin (V; X=Y=Me) and 1-methoxybutadiene gives benzoquinizarin (V; X=Y=H); similarly 1-methoxy-3-trimethylsilyloxybutadiene[10] gives 2-hydroxybenzoquinizarin (V; X=OH, Y=H) instead of the required ketone (VI). Methods of preventing aromatisation are being examined.

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† All new compounds reported here have satisfactory chemical analyses and supporting spectroscopic data. Leuco-quinizarin has been shown to have the 1,4-dione structure (S. M. Bloom and R. F. Hutton, *Tetrahedron Letters*, 1963, 1993) and a similar arrangement has been assumed for the leuco-adducts here.

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