Quinones. Part V. The Chemistry of Naphthazarin.*

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The synthesis, reduction, and addition reactions of naphthazarin and its derivatives have been investigated, and the structures of several known compounds elucidated.

At least a dozen quinones related to naphthazarin (5 : 8-dihydroxy-1 : 4-naphthaquinone) occur in Nature. In several cases the structure is not known completely, *e.g.*, of javanicin (Arnstein and Cook, *J.*, 1947, 1021), fusarubin (Ruelius and Gauhe, *Annalen*, 1950, **569**, 38), and some of the echinochromes and spinochromes (see Goodwin and Srisukh, *Biochem. J.*, 1950, **47**, 69); few of these quinones have been synthesised. As a preliminary to synthetical work in this field we have explored the methods available for the preparation of naphthazarins. Although, in principle, any substituted naphthazarin can be built up in stages starting from a suitable benzenoid compound (cf., *e.g.*, Brunner and Singule, *Monatsh.*, 1948, **79**, 81) the usual procedure is laborious and more direct methods are desirable. Again, the direct introduction of substituents into naphthazarin by the standard addition reactions would be advantageous but appears to be difficult: *e.g.*, addition of acetic anhydride requires ten days (Dimroth and Roos, *Annalen*, 1927, **456**, 191) and the addition of amines is also slow and requires a large excess (Fierz-David and Stockar, *Helv. Chim. Acta*, 1943, **26**, 92). We have therefore also examined the behaviour of naphthazarin in some common addition reactions.

Naphthazarin was first obtained by Roussin (*Compt. rend.*, 1861, **52**, 1033) by the action of sulphur and fuming sulphuric acid on 1 : 5-dinitronaphthalene. This reaction was formerly used on a commercial scale but has not been applied to the preparation of homologues of naphthazarin, indeed Kuroda and Wada (*Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1938, **34**, 1740) failed to obtain methylnaphthazarin by this method. We have,

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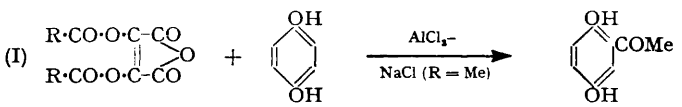
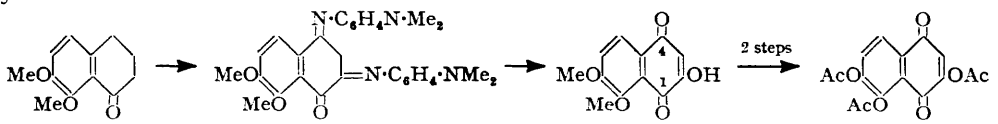
however, obtained a small yield of methylnaphthazarin from 2-methyl-1 : 5-dinitronaphthalene, and 2 : 6-dimethyl- and 2 : 6-dichloro-naphthazarin were obtained in the same way from the appropriate dinitro-compounds. Although the yields are low and the method is restricted by the inaccessibility of suitable 1 : 5-dinitronaphthalenes it is the most direct procedure for preparing 2 : 6-dialkylnaphthazarins. The formation of naphthazarin from 1 : 8-dinitronaphthalene by reaction with fuming sulphuric acid and reducing agents other than sulphur (*e.g.*, aniline, phenylhydrazine, tin) has been claimed (G.P. 79,406, 76,922) but Fierz-David and Stockar (*loc. cit.*) found the yield to be very poor and we have not investigated this route.

The most general synthesis of naphthazarins is the condensation of quinols with maleic anhydrides in fused sodium chloride–aluminium chloride (Zahn and Ochwat, *Annalen*, 1928, **462**, 72). Most known naphthazarins have been made by this means and some further examples are recorded in the Experimental section, but the method is not suitable for the synthesis of naphthazarins containing one substituent in each ring, or two substituents in one ring and one in the other, since mixtures result which are difficult to separate. Thus toluquinol and citraconic anhydride afforded a mixture of 2 : 6- and 2 : 7-dimethylnaphthazarin (Kuroda, *Proc. Imp. Acad. Tokyo*, 1939, **15**, 226). The severity of the reaction conditions is also a limiting factor as Weiss and Nord (*Arch. Biochem.*, 1950, **22**, 228) found in the attempted condensation of maleic anhydride with 2 : 5-dimethoxyphenylacetone. The most complex naphthazarin synthesised to data, echinochrome A, was obtained by Wallenfels and Gauhe (*Ber.*, 1943, **76**, 325) by condensing 2-ethyl-1 : 3 : 4-trimethoxybenzene with dibenzoyloxymaleic anhydride. The yield in this case was only 1% owing to the instability of the anhydride component. As a number of naphthazarins found in Nature contain two hydroxyl groups in the 2 : 3(or 6 : 7)-positions we attempted the similar condensation of diacetoxymaleic anhydride with quinol. No naphthazarin derivative could be detected, the principal product being 2 : 5-dihydroxyacetophenone. The corresponding condensation with dibenzoyloxymaleic anhydride gave 2 : 5-dihydroxybenzophenone. It is evident from the structure of the diesters (I) that three oxygen atoms can co-ordinate with aluminium chloride with almost equal facility and the preponderant formation of acetyl or benzoyl cations would be expected.



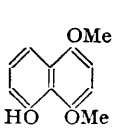
As a variety of substituted juglones (5-hydroxy-1 : 4-naphthaquinone) of known orientation are readily available (Thomson, *J. Org. Chem.*, 1948, **13**, 377, 870; 1951, **16**, 1082) methods for converting these into the corresponding naphthazarins were explored, but without success. Direct oxidation of juglone with lead tetra-acetate and with Fremy's salt yielded no naphthazarin. Oxidation by the Elbs persulphate method was also unprofitable. As juglone itself is not stable in alkaline solution the reaction was tried with 3-hydroxy-, 2-chloro-3-hydroxy-, and 2 : 6-dibromo-3-hydroxy-juglone. Oxidation products were isolated in very low yield from the first two but all the bromoquinone was recovered unchanged. The crude product obtained from 3-hydroxyjuglone gave an acetyl derivative which was not 5 : 6 : 8- or 2 : 7 : 8-triacetoxy-1 : 4-naphthaquinone : it has not been identified. A comparable persulphate oxidation of 1-hydroxyanthraquinone yielded a trace of quinizarin. 2 : 7 : 8-Triacetoxy-1 : 4-naphthaquinone was synthesised by the annexed route.



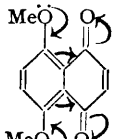
A dimethoxynaphthol, regarded as (II), was obtained by Ruelius and Gauhe (*Annalen*, 1951, **571**, 69) from juglone acetate by catalytic reduction and subsequent methylation and hydrolysis. Its conversion into naphthazarin dimethyl ether and final demethylation

would constitute a straightforward synthesis of naphthazarin from juglone. Efforts to obtain naphthazarin dimethyl ether from Ruelius and Gauhe's naphthol were fruitless and indicated that the structure (II) was incorrect (see Hayes and Thomson, *J.*, 1955, 904).

The reaction of naphthazarin with the following reagents was examined: chlorine, aniline, toluene-*p*-thiol, toluene-*p*-sulphinic acid, potassium hydrogen sulphite, hydrochloric acid, and hydrocyanic acid. In general it was found that naphthazarin was a relatively unreactive quinone. The addition of chlorine and aniline was very slow, hydrochloric acid failed to react, and no definite compound could be isolated from the crude black product resulting from the reaction with hydrocyanic acid (cf. Marschalk, *Bull. Soc. chim. Fr.*, 1935, **2**, 1809). On the other hand toluene-*p*-sulphinic acid, toluene-*p*-thiol, and potassium hydrogen sulphite reacted normally, the last two yielding diaddition products, which again suggests that these compounds add by a radical mechanism (cf. Thomson, *J. Org. Chem.*, 1951, **16**, 1082; Lyons and Thomson, *J.*, 1953, 2910). Fieser and Dunn (*J. Amer. Chem. Soc.*, 1937, **59**, 1016) observed that naphthazarin diacetate took part in Diels–Alder reactions much more rapidly than did naphthazarin itself. It has also been shown that the addition reactions of juglone are different from those of its acetate (Thomson, *loc. cit.*) and its methyl ether (McLeod and Thomson, unpublished work). Naphthazarin diacetate and dimethyl ether reacted normally with toluene-*p*-thiol. Chlorine reacted rapidly with the dimethyl ether and slowly with the diacetate (but faster than with naphthazarin itself). Both compounds failed to react with aniline. The addition of acetic anhydride to naphthazarin diacetate is very slow, as already mentioned, and the dimethyl ether did not react at all under the same conditions. An attempt to form the oxide of the dimethyl ether, by use of hydrogen peroxide, gave 2-hydroxy-5 : 8-dimethoxy-1 : 4-naphthaquinone. It is again evident that esterification and etherification of *peri*-hydroxyl groups has a marked effect on the additive powers of a naphthaquinone.



(II)



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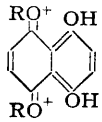

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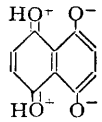
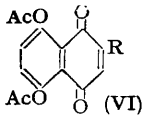


(V)

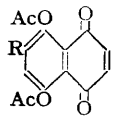
It is clear that in naphthazarin dimethyl ether (III) conjugation of the methoxyl groups with the carbonyl groups will reduce the reactivity of the 2 : 3-double bond towards nucleophilic reagents (*e.g.*, aniline) and increase the reactivity towards electrophilic reagents (*e.g.*, chlorine) and that *peri*-acetoxy-groups will have a similar, but weaker, effect. The failure of naphthazarin dimethyl ether to take part in acid-catalysed Thiele acetylation can be ascribed to salt formation, the catalyst giving rise to structures such as (IV; R = Me). (Naphthazarin dimethyl ether can be extracted from organic solvents with concentrated hydrochloric acid.) In the past, the tautomeric nature of naphthazarin has been emphasised but it is evident that its general stability, intense colour, strong hydrogen-bonding, and low chemical reactivity are due to the importance of resonance structures of the type (V) which lower the quinonoid activity of the molecule. The stability of the dianion of naphthazarin is most striking; the deep cornflower-blue solution in aqueous sodium hydroxide is stable for days and naphthazarin is recovered unchanged on acidification. This is a most unusual property for a naphthaquinone lacking a hydroxyl group in the quinonoid ring. Palacios and Salvia (*Anales Fis. Quim.*, 1934, **32**, 49) have shown by *X*-ray analysis that the naphthazarin molecule has a centre of symmetry and we did consider earlier that the hydrogen bonds might be symmetrical. This in fact has been proposed by Josien, Fuson, Lebas, and Gregory (*J. Chem. Phys.*, 1953, **21**, 331). However, a preliminary infra-red examination of dideuterated naphthazarin, kindly undertaken by Dr. T. S. Robinson, did not support this hypothesis and a fuller investigation by Hadži and Sheppard (*Trans. Faraday Soc.*, 1954, **50**, 911) has established the asymmetry of the hydrogen bonds.

Most of the new naphthazarins described in this paper have been reduced with acid

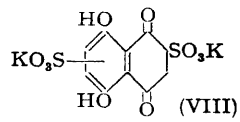
stannous chloride, to give β-hydronaphthazarin (1 : 2 : 3 : 4-tetrahydro-5 : 8-dihydroxy-1 : 4-dioxonaphthalene) and its derivatives. The only new observation (cf. Bruce and Thomson, *J.*, 1952, 2759) is that whereas chlorine atoms are normally eliminated during this reaction (see p. 1096) this is not the case with 3-chloro-2-methylnaphthazarin : a new diketone, 6-chloro-1 : 2 : 3 : 4-tetrahydro-5 : 8-dihydroxy-7-methyl-1 : 4-dioxonaphthalene, was obtained. This enabled us to establish the structure of methylnaphthazarin diacetate.



(VI)

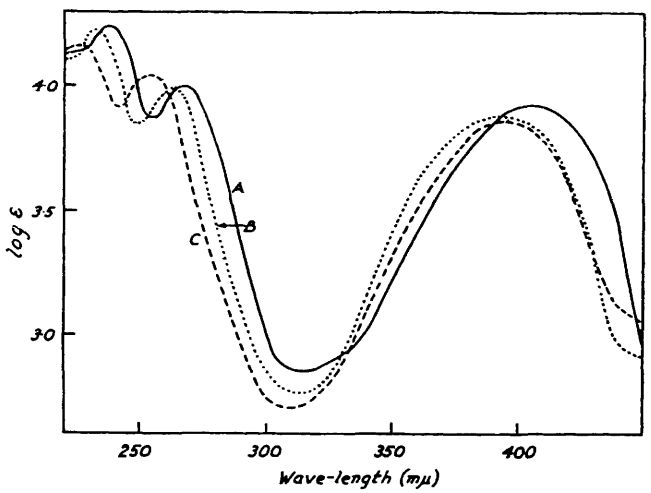


(VII)



(VIII)

There are two possible structures for the esters of substituted naphthazarins, (VI) or (VII). Fieser and Dunn (*loc. cit.*) have shown that naphthopurpurin triacetate has structure (VII; R = AcO) whereas methylnaphthazarin diacetate we find has structure (VI; R = Me). Addition of chlorine to methylnaphthazarin diacetate gave a dichloride which readily eliminated hydrochloric acid to form a chloromethylnaphthazarin diacetate. Hydrolysis



A, Naphthazarin–$KHSO_3$ *adduct.*
B, 1 : 2 : 3 : 4-*Tetrahydro*-5 : 8-*dihydroxy*-6-*methyl*-1 : 4-*dioxonaphthalene.*
C, 1 : 2 : 3 : 4-*Tetrahydro*-5 : 8-*dihydroxy*-1 : 4-*dioxonaphthalene.*

of the latter and reduction of the quinone obtained with acid stannous chloride did not eliminate the halogen atom. Since chlorine is lost by reduction of 6- and 7-chloro-2-methylnaphthazarin it follows that the chlorine atom and the methyl group must both lie in the same, *i.e.*, the quinonoid, ring of the above chloromethylnaphthazarin diacetate. Hence methylnaphthazarin diacetate must have structure (VI; R = Me). Ozonolysis of methylnaphthazarin diacetate leads to the same conclusion (Raudnitz and Behrens, *Ber.*, 1935, **68**, 1485). Chloronaphthazarin diacetate has also structure (VI; R = Cl). This is established by addition of chlorine to naphthazarin diacetate followed by elimination of hydrochloric acid from the resulting dichloride. The chloronaphthazarin diacetate obtained is identical with that produced by acetylation of chloronaphthazarin.

We have investigated the structure of the addition product of naphthazarin and potassium hydrogen sulphite (see p. 1091). A water-soluble bisulphite compound of naphthazarin, Alizarin Black S (C.I. No. 1019) was at one time used for printing. It was described as a dark brown powder (G.P. 41,518) and was apparently regarded as a normal carbonyl bisulphite compound. We find that the purified material is light yellow, and both acid and alkaline hydrolysis failed to liberate naphthazarin. The compound must therefore be formed by the usual quinonoid 1 : 4-addition. It is too stable to be a derivative of 1 : 4 : 5 : 8-tetrahydroxynaphthalene and its colour, behaviour in alkaline solution and ultra-violet absorption spectrum (see Figure) indicate structure (VIII). One objection is that, although reduction with acid stannous chloride gives a bright yellow solution,

β-hydronaphthazarin is not formed. It may be that the sulphonic acid group is eliminated only from the reduced ring, subsequent reduction and tautomerisation giving β-hydronaphthazarin-6-sulphonic acid (cf. Bruce and Thomson, *loc. cit.*).

Experimental

2-Methylnaphthazarin.—To a suspension of 2-methyl-1 : 5-dinitronaphthalene (3·5 g.) in 100% sulphuric acid (16·5 g.) was added a mixture of sulphur (1·75 g.) and fuming sulphuric acid (66% of SO_3; 26·3 g.) with constant stirring, the temperature being kept below 30°. After 1 hr. the mixture was poured on crushed ice (400 g.) with vigorous stirring, a bright blue solution being obtained. This was filtered and boiled for 1 hr. The blue colour disappeared and a reddish-brown precipitate formed. This was collected, dried, and sublimed in a high vacuum at 150°. The greenish crystalline sublimate, m. p. 167—170°, crystallised from alcohol as bright green plates, m. p. 173° not depressed on admixture with methylnaphthazarin.

2 : 6-Dimethylnaphthazarin.—To a suspension of 2 : 6-dimethyl-1 : 5-dinitronaphthalene (4 g.) in 100% sulphuric acid (67 g.) was added gradually with stirring a mixture of sulphur (1·2 g.) and fuming sulphuric acid (60% of SO_3; 20 g.) at <40°. The mixture was set aside for 1¼ hr. at room temperature and then poured on crushed ice (500 g.). The bright blue solution was filtered and boiled until the colour had changed to red. A red precipitate formed on cooling. The suspension was extracted with chloroform which in turn was repeatedly extracted with 2N-sodium hydroxide until no further blue colour appeared in the aqueous layer. The combined alkaline extracts were acidified with dilute sulphuric acid and the red precipitate thus obtained was collected, dried, and sublimed in a high vacuum at 170°, forming dark red needles with a green sheen having no m. p. (decomp. >200°) (1 g.). 2 : 6-*Dimethylnaphthazarin* crystallised from light petroleum (b. p. 100—120°) in green needles (Found : C, 65·6; H, 4·7. $C_{12}H_{10}O_4$ requires C, 66·0; H, 4·6%). Acetic anhydride and a trace of concentrated sulphuric acid in the cold afforded the *monoacetate* which crystallised from alcohol or light petroleum in orange needles, m. p. 150° (Found : C, 64·6; H, 4·7. $C_{14}H_{12}O_5$ requires C, 64·6; H, 4·65%). Acetylation in the same way, but with heating, gave the *diacetate* which formed yellow needles, m. p. 161° (from alcohol) (Found : C, 63·1; H, 4·55. $C_{16}H_{14}O_6$ requires C, 63·55; H, 4·65%).

2 : 6-Dichloronaphthazarin.—To a suspension of 2 : 6-dichloro-1 : 5-dinitronaphthalene (1·6 g.) in 100% sulphuric acid (25 g.) was added a mixture of sulphur (0·5 g.) and fuming sulphuric acid (60% of SO_3; 8 g.) at <30°. After 1½ hr. the mixture was poured on crushed ice (150 g.), forming a blue solution and a blue precipitate. The latter was filtered off and washed with concentrated hydrochloric acid, and the combined filtrate and washings were boiled until the blue colour had changed to red. The red precipitate formed on cooling was dried (0·3 g.), dissolved in chloroform, and shaken with activated alumina which rapidly became blue. The alumina was filtered off, washed with chloroform, and extracted with hot glacial acetic acid. Dilution of the extract with water gave a red *quinone* which crystallised from light petroleum (b. p. 100—120°) as almost black needles with a green sheen which had no m. p. (decomp. *ca.* 240°) (5%) (Found : C, 46·0; H, 1·5; Cl, 27·0. $C_{10}H_4O_4Cl_2$ requires C, 46·3; H, 1·55; Cl, 27·3%). The *diacetate* separated from light petroleum in yellow needles, m. p. 208° (Found : C, 49·3; H, 2·2; Cl, 20·0. $C_{14}H_8O_6Cl_2$ requires C, 49·0; H, 2·35; Cl, 20·6%).

2 : 3-Dichloronaphthazarin.—To a fused mixture of sodium chloride (20 g.) and anhydrous aluminium chloride (100 g.) at 180° was added a mixture of maleic anhydride (10 g.) and 2 : 3-dichloroquinol (18 g.) with constant stirring. The temperature was kept at 180° till evolution of hydrogen chloride had ceased and the melt then allowed to cool. After decomposition with dilute hydrochloric acid the red precipitate of *quinone* obtained was collected, dried, and crystallised from light petroleum in scarlet plates, m. p. 192° (30%) (Found : C, 46·1; H, 1·6. $C_{10}H_4O_4Cl_2$ requires C, 46·3; H, 1·55%). The *diacetate* crystallised from acetone in yellow needles, m. p. 233° (Found : C, 49·1; H, 2·3. $C_{14}H_8O_6Cl_2$ requires C, 49·0; H, 2·35%).

6- and 7-Chloro-2-methylnaphthazarin.—Chloroquinol and citraconic anhydride were condensed as above. The product crystallised from alcohol in red needles with a green sheen, melting range 155—165° indicating a mixture of two isomers (Found : C, 55·25; H, 2·7. Calc. for $C_{11}H_7O_4Cl$: C, 55·4; H, 2·95%).

Condensation of Quinol with Diacetoxymaleic Anhydride.—To a mixture of sodium chloride (4 g.) and anhydrous aluminium chloride (20 g.) at 120° was added gradually with stirring a mixture of quinol (0·8 g.) and diacetoxymaleic anhydride (1 g.). The temperature was raised to 180° for a few minutes and the mixture then allowed to cool. The product was decomposed

in the usual way with dilute hydrochloric acid and the mixture boiled for 2 min. After cooling and filtration, the residue and solution were extracted with chloroform. Evaporation of the solvent left an orange solid which crystallised from light petroleum (b. p. 100—120°) in pale yellow needles, m. p. 201° (0·5 g.) (Found: C, 63·15; H, 5·45. Calc. for $C_8H_8O_3$: C, 63·15; H, 5·3%). The compound formed a diacetate, m. p. 67·5° (Found: C, 61·0; H, 5·25. Calc. for $C_{12}H_{12}O_5$: C, 61·0; H, 5·2%). Mixed m. p.s with 2:5-dihydroxyacetophenone and its diacetate respectively showed no depression.

Condensation of quinol with dibenzoyloxymaleic anhydride in the same way provided 2:5-dihydroxybenzophenone (39%), m. p. and mixed m. p. 123°.

Persulphate Oxidation of 3-Hydroxyjuglone.—To a stirred solution of 3-hydroxyjuglone (1·9 g.) in 10% aqueous sodium hydroxide (20 c.c.) was added during 4 hr. saturated aqueous potassium persulphate (2·7 g.) so that the temperature did not exceed 20°. Next day the solution was acidified (Congo-red) with dilute sulphuric acid, and starting material recovered by filtration and ether-extraction. Concentrated hydrochloric acid (50 c.c.) was then added, and the mixture heated on the steam-bath for 30 min. and then repeatedly extracted with ether. Evaporation of the solvent left a red solid (0·1 g.) which was acetylated by warm acetic anhydride and a trace of concentrated sulphuric acid. Repeated crystallisation from alcohol afforded yellow needles of *triacetate*, m. p. 142° (Found: C, 56·8; H, 3·9. $C_{16}H_{12}O_8$ requires C, 57·8; H, 3·65%).

Persulphate Oxidation of 1-Hydroxyanthraquinone.—A solution of 1-hydroxyanthraquinone (15 g.) in 10% sodium hydroxide solution (134 c.c.) and pyridine (10 c.c.) was treated with potassium persulphate (18 g.) as before. Starting material was recovered by acidification and filtration, and the filtrate was then heated on the steam-bath for 1 hr. after the addition of more hydrochloric acid. Quinizarin was isolated by repeated extraction with ether and after crystallisation from alcohol had m. p. and mixed m. p. 195° (50 mg.). The diacetate had m. p. 208°.

1:2:3:4-*Tetrahydro*-7:8-*dimethoxy*-1-*oxonaphthalene.*—A solution of 5-chloro-1:2:3:4-tetrahydro-7:8-dimethoxy-1-oxonaphthalene (0·5 g.) (Ghosh and Robinson, *J.*, 1944, 507) in alcohol (100 c.c.) was shaken with hydrogen, 2% palladised strontium carbonate (1·5 g.), and ethanolic 10% potassium hydroxide (10 c.c.) until 48 c.c. of hydrogen had been absorbed. After filtration and evaporation to dryness, the residue was stirred with water and extracted with ether and dried (K_2CO_3). After removal of the solvent the residue was distilled at 0·001 mm. The fraction of b. p. 110° (bath) crystallised. This *ketone* recrystallised from light petroleum (b. p. 40°) in clusters of needles, m. p. 57·5° (0·35 g.) (Found: C, 69·35; H, 6·65. $C_{12}H_{14}O_3$ requires C, 69·85; H, 6·8%). The 2:4-*dinitrophenylhydrazone* formed fine orange needles, m. p. 180° (from alcohol) (Found: C, 55·75; H, 4·7; N, 14·4. $C_{18}H_{18}O_6N_4$ requires C, 55·95; H, 4·7; N, 14·5%).

3-*Hydroxy*-5:6-*dimethoxy*-1:4-*naphthaquinone.*—Aqueous 10% sodium hydroxide (5 c.c.) was added to a solution of the above ketone (2·8 g.) and *p*-nitrosodimethylaniline (5 g.) in alcohol (200 c.c.), and the mixture set aside for 18 hr. The purple crystals of the dianil which had separated were collected, dried (1·3 g.), and dissolved in water (100 c.c.) containing concentrated sulphuric acid (5 c.c.). The blood-red solution became orange and formed a brown precipitate after being boiled for 1½ hr. The solid was collected on cooling and a further quantity obtained by chloroform extraction of the filtrate. The *quinone* crystallised from light petroleum (b. p. 100—120°) in yellow needles, m. p. 205—206° (decomp.) (0·5 g.) (Found: C, 61·3; H, 4·25. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%).

3:5:6-*Triacetoxy*-1:4-*naphthaquinone.*—3-Hydroxy-5:6-dimethoxy-1:4-naphthaquinone (0·3 g.) was added with stirring to a fused mixture of sodium chloride (2·4 g.) and anhydrous aluminium chloride (12 g.) at 110°. The temperature was raised to 180° for 1 min., the mixture cooled, and the solid dissolved in dilute hydrochloric acid. The solution was raised to the boil, then cooled and the precipitate thus obtained was collected. The crude product was difficult to purify. It was obtained as brick-red microcrystals, decomp. 225—230°, after crystallisation from benzene followed by sublimation *in vacuo* and converted into the *triacetate* which formed yellow needles, m. p. 150—151° (from alcohol) (Found: C, 57·7; H, 3·6. $C_{16}H_{12}O_8$ requires C, 57·85; H, 3·65%).

Naphthazarin Dimethyl Ether (cf. Brass, Pfluger, and Honsberg, *Ber.*, 1936, **69**, 87).—A mixture of naphthazarin (2 g.), sodium carbonate (5·6 g.; dried at 150°), methyl toluene-*p*-sulphonate (8 g.), and *o*-dichlorobenzene (25 c.c.) was refluxed for 2 hr. Water which appeared in the condenser was removed. The cooled solution was filtered and the filtrate diluted with light petroleum (b. p. 100—120°; 150 c.c.). An orange-brown solid separated and more was

obtained by removing the solvent under reduced pressure. The crude product was sublimed *in vacuo* and then crystallised from light petroleum (b. p. 100—120°) forming orange needles, m. p. 157° (44%).

Addition Reactions.—With chlorine. (*a*) Excess of dry chlorine was passed into a suspension of naphthazarin (1 g.) in glacial acetic acid (100 c.c.), and the mixture left in a stoppered flask exposed to sunlight for 3 days by which time all the quinone had dissolved, the colour changing from wine-red to reddish-yellow. The solution was then poured on ice, forming a yellow precipitate; this was dissolved in glacial acetic acid (50 c.c.) along with anhydrous sodium acetate (3 g.), and the mixture was boiled for 5 min. On cooling, the red solution was diluted with water, and the precipitated chloronaphthazarin collected and crystallised from alcohol, forming needles with a green metallic sheen, m. p. 179° (76%). The diacetate had m. p. 194°. (*b*) Excess of dry chlorine was added to a suspension of naphthazarin diacetate (1 g.) in glacial acetic acid (50 c.c.), and the mixture left in a stoppered flask exposed to sunlight for 2 days. The resulting solution was then worked up as in (*a*). Chloronaphthazarin diacetate crystallised from alcohol in yellow needles, m. p. 194° (75·5%), identical with those obtained as in (*a*). (*c*) Dry chlorine (10% excess) was passed into a solution of naphthazarin dimethyl ether (1 g.) in glacial acetic acid (40 c.c.). The initially dark brown solution rapidly became yellow. The mixture was then treated as in (*a*). *2-Chloronaphthazarin dimethyl ether* crystallised from alcohol in scarlet plates, m. p. 201° (90%) (Found: C, 56·9; H, 3·5; Cl, 13·9. $C_{12}H_9O_4Cl$ requires C, 57·0; H, 3·6; Cl, 14·0%). Demethylation with sodium chloride–aluminium chloride gave chloronaphthazarin. The dimethyl ether was also obtained as follows: a mixture of chloronaphthazarin (0·35 g.), anhydrous sodium carbonate (0·4 g.), methyl toluene-*p*-sulphonate (0·8 g.), and *o*-dichlorobenzene (8 c.c.) was refluxed until the original red solution had changed to yellow (*ca.* 1 hr.). Water which separated was removed at intervals. When cool, the mixture was filtered and the filtrate diluted with light petroleum (b. p. 100—120°; 25 c.c.). The precipitate thus obtained was sublimed at 100°/0·001 mm. Crystallisation of the orange sublimate from alcohol afforded a mixture (9 : 1) of brown-yellow needles and reddish plates. The latter were separated by hand-picking and had m. p. 196° not depressed by the product obtained as in (*c*).

*With toluene-*p*-thiol.* (*a*) To a solution of naphthazarin (0·45 g.) in alcohol (50 c.c.) was added toluene-*p*-thiol (0·15 g.) in alcohol (10 c.c.). The mixture was boiled under reflux for 5 min., set aside overnight, then concentrated to 20 c.c. The dark red solid which separated was crystallised first from light petroleum (b. p. 100—120°) and then (a little red oil being discarded) from alcohol. The *tolylthioquinone* formed fine ruby needles with a slight green sheen, m. p. 156° (40·5%) (Found: S, 10·4. $C_{17}H_{12}O_4S$ requires S, 10·2%). (*b*) To a solution of naphthazarin (0·3 g.) in alcohol (50 c.c.) was added toluene-*p*-thiol (2 g.). The mixture was boiled under reflux for 5 min. and left overnight. A microcrystalline deposit was collected and crystallised from light petroleum (b. p. 100—120°). The *ditolylthioquinone* separated in dark red needles with a green sheen, m. p. 230° (44%) (Found: S, 14·4. $C_{24}H_{18}O_4S_2$ requires S, 14·7%). (*c*) To a solution of naphthazarin diacetate (0·4 g.) in alcohol (40 c.c.) was added a solution of toluene-*p*-thiol (0·15 g.) in alcohol (10 c.c.). The mixture was boiled under reflux for 5 min., and, next morning, concentrated to 20 c.c. The *product*, which separated on cooling, formed yellow plates, m. p. 184° (from alcohol) (26%) (Found: C, 63·6; H, 4·1; S, 8·9. $C_{21}H_{16}O_6S$ requires C, 63·8; H, 4·1; S, 8·1%). (*d*) To a solution of naphthazarin dimethyl ether (0·8 g.) in alcohol (6 c.c.) was added a solution of toluene-*p*-thiol (0·25 g.) in alcohol (6 c.c.). After boiling under reflux for 5 min. the mixture was allowed to cool overnight. The *product* which separated was recrystallised first from alcohol and then from benzene–light petroleum forming red-brown needles, m. p. 163·5° (32%) (Found: C, 66·8; H, 5·0; S, 8·8. $C_{19}H_{16}O_4S$ requires C, 67·0; H, 4·75; S, 9·4%).

With aniline. (*a*) (cf. Fierz-David and Stockar, *loc. cit.*) Naphthazarin (1 g.) was stirred with aniline (25 c.c.) for 24 hr. The mixture was then diluted with alcohol, and the fine crystalline precipitate washed with alcohol and crystallised from *o*-dichlorobenzene in dark green plates, m. p. 233° (61%). (*b*) A mixture of naphthazarin diacetate (0·4 g.), alcohol (40 c.c.), and aniline (0·1 g.) was boiled for 5 min., allowed to cool overnight, and then concentrated to half bulk. Unchanged starting material separated. (*c*) Naphthazarin diacetate (1 g.) was stirred with aniline (25 c.c.) for 24 hr. The mixture was then stirred with dilute hydrochloric acid, and the precipitate obtained crystallised from alcohol to give unchanged starting material. (*d*) A solution of naphthazarin dimethyl ether (0·8 g.) in alcohol (6 c.c.) containing aniline (0·2 g.) was boiled for a few minutes and left to cool. On removal of the solvent *in vacuo* and sublimation of the residue *in vacuo* unchanged naphthazarin dimethyl ether was obtained as the sole

product. (*e*) A suspension of naphthazarin dimethyl ether (1 g.) in aniline (25 c.c.) was stirred for 3 days. All the starting material was recovered.

2-Hydroxynaphthazarin Dimethyl Ether.—To a solution of naphthazarin dimethyl ether (0·5 g.) in alcohol (20 c.c.) was added a solution of sodium carbonate (0·5 g.) in water (5 c.c.) together with hydrogen peroxide (1 c.c.; 100-vol.). The original orange solution became straw-coloured and after several hours a yellow precipitate was collected and crystallised from light petroleum (b. p. 100—120°). The *hydroxyquinone* formed yellow needles, m. p. 194° (0·4 g.) (Found: C, 61·35; H, 4·3. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%). The quinone gave a dark yellow solution in aqueous sodium hydroxide and an orange solution in concentrated hydrochloric acid. Demethylation yielded naphthopurpurin.

2-Chloro-3-methylnaphthazarin.—A solution of dry chlorine (0·5 g.) in glacial acetic acid (10 c.c.) was added to a suspension of methylnaphthazarin diacetate (1 g.) in glacial acetic acid (20 c.c.) and the mixture exposed to sunlight for 2 days, by which time all the quinone had dissolved. The solution was then poured on ice, and the precipitated solid was collected, dissolved in glacial acetic acid (10 c.c.), and boiled for 5 min. with excess of sodium acetate. On cooling and dilution with water *2-chloro-3-methylnaphthazarin diacetate* separated. It crystallised from light petroleum (b. p. 100—120°) in yellow needles, m. p. 186° (0·9 g.) (Found: C, 55·6; H, 3·6; Cl, 9·9. $C_{15}H_{11}O_6Cl$ requires C, 55·85; H, 3·45; Cl, 11·0%). The diacetate (0·25 g.) was refluxed with 5N-hydrochloric acid (100 c.c.) until all dissolved and a red precipitate had appeared. This was collected after cooling and crystallised from alcohol. *2-Chloro-3-methylnaphthazarin* separated as red needles with a green metallic sheen, m. p. 189° (0·18 g.) (Found: C, 55·3; H, 3·0; Cl, 14·95. $C_{11}H_7O_4Cl$ requires C, 55·4; H, 2·95; Cl, 14·85%).

Toluene-p-sulphonylnaphthazarin.—A mixture of naphthazarin (1 g.), sodium *p*-toluenesulphinate (2·5 g.), acetone (100 c.c.), water (10 c.c.), and 2N-hydrochloric acid (10 c.c.) was shaken for 10 min. and set aside for 1 hr. with occasional shaking. The solution was filtered and oxidised by the addition of potassium dichromate (4 g.) in water (100 c.c.) containing concentrated sulphuric acid (4 c.c.). Next morning the purple *product* precipitated (0·45 g.) was collected and crystallised from benzene–light petroleum, forming dark red micro-needles, m. p. 271° (Found: C, 59·0; H, 3·6; S, 9·5. $C_{17}H_{12}O_6S$ requires C, 59·3; H, 3·5; S, 9·3%).

Dipotassium 1:2:3:4-Tetrahydro-1:4-dioxonaphthalene-(2:6?)-disulphonate.—Finely divided naphthazarin (2 g.) was added gradually to a stirred solution of potassium metabisulphite (2·6 g.) in water (15 c.c.) in 20 min. Methyl alcohol (5—10 c.c.) was then added and the mixture stirred overnight, the quinone dissolving gradually and a product then being precipitated. Saturated aqueous potassium chloride (15 c.c.) was added, stirring continued for several hours, and the precipitate then collected, dried, stirred with cold chloroform (twice), and dried (2·25 g.). This material was extracted several times with boiling alcohol and dried *in vacuo* as a yellow microcrystalline powder (Found: C, 27·7; H, 1·7; S, 14·95. $C_{10}H_6O_{10}K_2S_2$ requires C, 28·0; H, 1·4; S, 14·95%). The *sulphonate* formed a pale yellow solution in water, which on addition of sodium hydroxide rapidly changed through orange, brown, and green to blue. The salt gave a red solution in hot dilute acid and a bright yellow one when heated in acid stannous chloride solution. No coloured material was extracted from acid solutions with chloroform. Material prepared by the Colour Index recipe was similar.

Reduction of Naphthazarins with Acid Stannous Chloride.—By the procedure described before (Bruce and Thomson, *loc. cit.*), 2:3- and 2:6-dichloro-, *p*-tolylthio-, di-*p*-tolylthio-, and toluene-*p*-sulphonyl-naphthazarin all gave 1:2:3:4-tetrahydro-5:8-dihydroxy-1:4-dioxonaphthalene. The mixture of 6- and 7-chloro-2-methylnaphthazarin gave 1:2:3:4-tetrahydro-5:8-dihydroxy-6-methyl-1:4-dioxonaphthalene. 2-Chloro-3-methylnaphthazarin afforded *6-chloro-1:2:3:4-tetrahydro-5:8-dihydroxy-7-methyl-1:4-dioxonaphthalene* in yellow needles, m. p. 185° (from methanol) (Found: C, 55·2; H, 3·65. $C_{11}H_9O_4Cl$ requires C, 54·9; H, 3·8%). 2:6-Dimethylnaphthazarin yielded *1:2:3:4-tetrahydro-5:8-dihydroxy-2:6-dimethyl-1:4-dioxonaphthalene* which sublimed at 130°/0·001 mm. in orange needles, m. p. 150° (Found: C, 65·70; H, 5·5. $C_{12}H_{12}O_4$ requires C, 65·45; H, 5·5%).

[*HO*-$^2H_2$]Naphthazarin was obtained by hydrolysis of naphthazarin diacetate with a dilute solution of deuterium sulphate in deuterium oxide and purified by sublimation *in vacuo*.

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