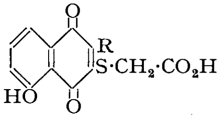
335. *The Reduction of Juglone.*

By R. H. Thomson.

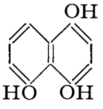
The yellow compound previously obtained by hydrogenolysis of 3-carboxymethylthiojuglone (I; R = H) with Raney nickel is shown to be 5 : 8-dihydroxy-1-tetralone (VI; R = H) arising by further reduction of α-hydrojuglone (II). Similar treatment of β-hydrojuglone gives the keto-alcohol (IV).

In the preparation of plumbagin (2-methyljuglone) by hydrogenolysis of (I; R = Me) with Raney nickel, a small amount of a yellow by-product (*A*), m. p. 164°, was isolated (*J.*, 1951, 1237). A similar yellow compound (*B*), m. p. 184°, was also obtained by hydrogenolysis of 3-carboxymethylthiojuglone (I; R = H). The unusual formation of coloured compounds by reduction of naphthaquinones seemed worthy of further investigation, and the structure of the more accessible substance (*B*) has now been established.

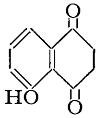
In the hydrogenolysis of (I; R = H) the quinone is very rapidly reduced to the quinol, and as (*B*) contains no sulphur it must be derived from α-hydrojuglone (II). This was confirmed when (*B*) was obtained by refluxing (II) (or juglone) with a large excess of Raney nickel in alcohol, ethyl acetate, or light petroleum. Yields were usually extremely small and consistent results could not be obtained. It was then found that (*B*) could be prepared by catalytic hydrogenation of juglone with Raney nickel at ordinary temperatures and pressures, and this method, although tedious, was reliable. After rapid uptake of 1 mol. of hydrogen, hydrogenation continued slowly, about 0·5 mol. being absorbed in 2—3 days. The reaction was even slower with Adams's catalyst and did not proceed at all in glacial acetic acid.



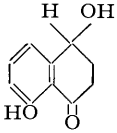
(I)



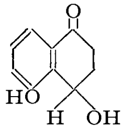
(II)



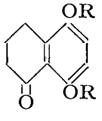
(III)



(IV)



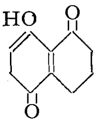
(V)



(VI)

The compound (*B*) forms a bright yellow solution in dilute sodium hydroxide solution, the colour being weaker in dilute sodium carbonate solution, and gives a transient blue-green colour with ferric chloride. It forms a diacetate, a methyl ether, a phenylurethane, and a *p*-nitrophenylhydrazone. Elementary analyses of (*B*) and its derivatives were very misleading initially and it was necessary to sublime most of the compounds in a high vacuum before satisfactory results could be obtained. The empirical formula is $C_{10}H_{10}O_3$, *i.e.* $C_{10}H_8O_3$ (II) + 2H. When juglone is refluxed with Raney nickel in alcohol the odour of acetaldehyde can be detected. It is known that Raney nickel will catalyse such oxidations in the presence of a hydrogen acceptor, usually a ketone, which is thereby reduced to a secondary alcohol, or further (Kleiderer and Kornfeld, *J. Org. Chem.*, 1948, **13**, 455). A suitable ketone could arise by isomerisation of α-hydrojuglone (II) to the β-form (III) (see *J.*, 1950, 1737). However catalytic reduction of β-hydrojuglone over Raney nickel afforded a new $C_{10}H_{10}O_3$ compound. This substance gave a red-violet ferric colour, formed a *p*-nitrophenylhydrazone, did not react with diazomethane, and on dehydration yielded 1 : 8-dihydroxynaphthalene. The keto-alcohol is therefore (IV). Small amounts of this compound were occasionally isolated after juglone had been refluxed with Raney nickel in ethyl acetate or light petroleum, and could be obtained by a similar treatment of β-hydrojuglone. Since (IV) is colourless, the isomer (V) must also be colourless. Thus (*B*) is neither (IV) nor (V) and must therefore arise by hydrogenation of the monohydroxylated ring of (II). Of the structural possibilities only (VI; R = H) could account for the properties of (*B*). Cyclisation of γ-(2 : 5-dimethoxyphenyl)butyric acid yielded 5 : 8-dimethoxy-1-tetralone (VI; R = Me) which, on demethylation, gave 5 : 8-dihydroxy-1-tetralone (VI; R = H), identical with (*B*). The compound (*A*) is consequently 5 : 8-dihydroxy-6-methyl-1-tetralone. The reduction of a naphthol to a tetralone is not new. 1-Tetralone can be obtained by hydrogenation of 1-naphthol at elevated temperatures and pressures with a nickel catalyst, and under similar conditions 1 : 5- and 1 : 8-dihydroxynaphthalene have been converted into the corresponding hydroxytetralones (Schroeter, G.P. 352,720; *Annalen*, 1922, **426**, 83). Hydroxytetralones have also been obtained by reduction of 1 : 5- and 1 : 6-dihydroxynaphthalene with Raney nickel alloy and sodium hydroxide solution (Papa, Schwenk, and Breiger, *J. Org. Chem.*, 1949, **14**, 366).

A curious feature of 5 : 8-dihydroxytetralone is its failure to undergo methylation with diazomethane. Prolonged contact in cold methanol, ether, or chloroform gave unchanged starting material contaminated with a colourless substance which, although not obtained pure, did not appear to be either the mono- or di-methyl ether, and presumably arose by reaction with the carbonyl group. Strong hydrogen bonding of the 8-hydroxyl group, demonstrated by the formation of a sparingly alkali-soluble monomethyl ether with methyl sulphate and a monophenylurethane with excess of phenyl *iso*cyanate, would prevent the formation of an 8-methyl ether, but the 5-hydroxyl group should behave in a normal manner. The possibility that the latter might exist in a keto-form such as (VII) was excluded by examination of its infra-red spectrum in the crystalline state and in chloroform solution (carbon tetrachloride could not be used at ordinary temperatures). The results are shown in the table.



(VII)

		Frequency (cm.$^{-1}$)		
		C=O		OH
Solid	1577	1619		3279
Chloroform solution	1590	1619	1644	3590

The band at 1619 cm.$^{-1}$ obtained in solution is actually a " shoulder " on the 1644 cm.$^{-1}$ band and may indicate some aggregation of the solute molecules in the dilute, but saturated, chloroform solution, or it may be due to particles of undissolved material. Both in the solid state and in solution the compound exhibits one carbonyl band and one hydroxyl band which is consistent with (VI; R = H) whereas (VII) would be expected to show two carbonyl bands with the hydroxyl band suppressed. The other bands in the 6μ region at 1577 cm.$^{-1}$ and 1590 cm.$^{-1}$ are assigned to a vibration of the benzene ring.

EXPERIMENTAL

5 : 8-*Dihydroxy*-1-*tetralone*.—(*a*) Juglone (1 g.) in ethyl acetate (100 c.c.) was hydrogenated in the presence of Raney nickel. One mol. of hydrogen was absorbed in 15 minutes and the subsequent slow absorption was allowed to proceed for 2—3 days. After filtration and extraction of the catalyst, the solvent was removed under reduced pressure and the residue extracted with boiling light petroleum (b. p. 100—120°; 1 × 100 c.c., 2 × 20 c.c.). 5 : 8-*Dihydroxy*-

1-*tetralone* separated when the solution cooled and was recrystallised from the same solvent, forming fine yellow needles (35%), m. p. 184° (Found: C, 67·25; H, 6·65. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·65%). Concentration of the original mother liquor gave a little β-hydrojuglone.

(*b*) 5 : 8-Dimethoxy-1-tetralone (0·34 g.) was added to a molten mixture of aluminium chloride (4 g.) and sodium chloride (1 g.) at 145°. The mixture was heated rapidly to 180°, maintained at that temperature for 3—4 minutes, and allowed to cool. The product was decomposed with ice and hydrochloric acid, and the suspension heated to 90° and then cooled in ice. The precipitate was collected and crystallised from light petroleum forming pale yellow needles (50%), m. p. and mixed m. p. 184°. Both products formed a *diacetate* which crystallised from dilute alcohol in blades, m. p. 177—178° (Found: C, 63·8, H, 5·4; Ac, 34·5. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·4; Ac, 32·8%). The p-*nitrophenylhydrazone* separated from aqueous alcohol in orange-brown micro-crystals, m. p. 272° (decomp.) (Found: C, 61·6; H, 5·0; N, 13·2. $C_{16}H_{15}O_4N_3$ requires C, 61·3; H, 4·8; N, 13·4%). The *phenylurethane* was obtained by refluxing a solution of the tetralone (150 mg.) in light petroleum (50 c.c.; b. p. 100—120°) with phenyl *iso*cyanate (0·3 c.c.) and 2 drops of triethylamine for 2 hours; it crystallised in leaflets, m. p. 181° (Found: C, 67·45; H, 5·3; N, 4·9. $C_{17}H_{15}O_4N$ requires C, 67·45; H, 5·15; N, 4·9%), and gave a violet-brown ferric colour.

8-*Hydroxy*-5-*methoxy*-1-*tetralone*.*—(*a*) A solution of 5 : 8-dihydroxy-1-tetralone (160 mg.) in aqueous sodium hydroxide (10 c.c.; 2N) was methylated by gradual addition of methyl sulphate (1 c.c.) with vigorous shaking. The precipitate which formed was collected, washed with water, and crystallised from dilute acetone; it formed pale yellow needles, m. p. 98°. Acidification of the filtrate gave a further quantity of less pure methyl ether. When a larger excess of methyl sulphate was used at 60° the methyl ether remained in solution but the product was less pure.

(*b*) 5 : 8-Dihydroxy-1-tetralone (100 mg.) in acetone (20 c.c.) was refluxed for 2 hours with methyl sulphate (1 c.c.) and anhydrous potassium carbonate (2 g.) and then poured into water (80 c.c.). The solution was warmed to remove most of the acetone and then cooled in ice. The crystalline precipitate was collected and recrystallised from very dilute acetone, forming fine pale yellow needles, m. p. 98° (Found: C, 68·5; H, 6·3. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%). Repetition of the process with double quantities of methyl sulphate and potassium carbonate for 4 hours did not effect any further methylation nor did methyl iodide under similar conditions. The methyl ether was only slightly soluble in cold dilute sodium hydroxide forming a yellow solution; it gave a prussian-blue colour with ferric chloride.

5 : 8-*Dimethoxy*-1-*tetralone*.—γ-(2 : 5-Dimethoxyphenyl)butyric acid (1·75 g.) (Fieser, Gates, and Kilmer, *J. Amer. Chem. Soc.*, 1940, **62**, 2966) was warmed on a water-bath for 30 minutes with sulphuric acid (3·5 c.c.; 85%), and the solution then cooled and diluted with ice water. The mixture was extracted with ether, and the extract washed with water, dilute ammonia solution, and water, and then dried ($CaSO_4$). Removal of the solvent left a semi-crystalline residue which crystallised from light petroleum (b. p. 30—40°) in micro-needles (25%), m. p. 63° (Found: C, 69·6; H, 6·7. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). The *semicarbazone* * formed small needles, m. p. 190° (from aqueous alcohol) (Found: N, 15·9. $C_{13}H_{17}O_3N_3$ requires N, 15·95%). The dimethoxytetralone is soluble in concentrated hydrochloric acid. Cyclisation of γ-(2 : 5-dimethoxyphenyl)butyric acid with anhydrous hydrofluoric acid gave a very poor yield of the tetralone.

1 : 2 : 3 : 4-*Tetrahydro*-1 : 5-*dihydroxy*-4-*ketonaphthalene*.—β-Hydrojuglone (2·21 g.) was hydrogenated in ethyl acetate in the presence of Raney nickel. One mol. of hydrogen was absorbed in 4·5 hours. The light yellow product was extracted repeatedly with boiling hexane (*ca.* 500 c.c. in all) from which the *keto-alcohol* crystallised on cooling. It separated from hexane in needles (68%), m. p. 100° (Found: C, 67·5; H, 5·65. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·65%). The p-*nitrophenylhydrazone* formed dull yellow micro-crystals (from aqueous alcohol), m. p. 222—223° (decomp.) (Found: C, 61·4; H, 4·95; N, 13·2. $C_{16}H_{15}O_4N_3$ requires C, 61·3; H, 4·8; N, 13·4%).

Dehydration of the keto-alcohol. A solution of the keto-alcohol (0·57 g.) in alcohol (10 c.c.) was refluxed for 1 hour with concentrated hydrochloric acid (10 c.c.), and then poured on ice, and the mixture extracted with ether. The extract was dried and evaporated, leaving a semi-solid residue. This was extracted with hot water (charcoal); needles of 1 : 8-dihydroxynaphthalene, m. p. 140°, separated when the extract cooled; the diacetate had m. p. and mixed m. p. with an authentic specimen, 148°.

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* Since this paper was submitted these compounds have been described by Cocker, Cross, and McCormick (*J.*, 1952, 72).

5 : 8-*Diacetoxy*-1 : 2 : 3 : 4-*tetrahydro*-1-*keto*-6-*methylnaphthalene*.—The *diacetate* crystallised from water in prismatic needles, m. p. 130° (Found : C, 65·3; H, 5·85; Ac, 32·4. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·85; Ac, 31·2%).

Analyses are by Drs. Weiler and Strauss. The author is indebted to Mr. T. S. Robinson for the infra-red spectra determinations.

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