Journal of Sciences, Islamic Republic of Iran 13(2): 131-139 (2002)
National Center For Scientific Research, ISSN 1016-1104

OXIDATIVE DEHYDROGENATION OF 1-TETRALONES: SYNTHESIS OF JUGLONE, NAPHTHAZARIN, AND α-HYDROXYANTHRAQUINONES

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Abstract

Treatment of 5,8-dihydroxy-1-tetralone (9) with either 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing benzene or silver (I) oxide in refluxing 1,4-dioxane afforded juglone (5-hydroxy-1,4-naphthoquinone) (1) in good yield. With manganese dioxide in dioxane the tetralone gave a mixture of juglone and naphthazarin (5,8-dihydroxy-1,4-naphthoquinone) (3), the proportion of naphthazarin being increased by the presence of water. Silver (I) oxide in 1,4-dioxane converted 9,10-dihydroxy-1-oxo (14),9,10-dihydroxy-1,5-dioxo (15), and 1,8-dioxo-1,2,3,4,5,6,7,8-octahydro anthracene (16) into, respectively, 1-hydroxy-5,6,7,8-tetrahydro (23), 1,5-dihydroxy (6), and 1,8-dihydroxy-9,10-anthraquinone (4), in high yield. Mechanisms for these transformations are discussed.

Keywords: Oxidative dehydrogenation; 1-Tetralones; Juglone; Naphthazarin; α-Hydroxyanthraquinones; DDQ; Silver(I) oxide; Manganese dioxide

Introduction

Juglone, 5-hydroxy-1,4-naphthoqinone, (1) occurs naturally, shows allelopathic activity [2,3], and is a useful precursor for the synthesis of perylenequinones [4]. However, methods for its synthesis often give low yields, or require starting materials which are not readily available [5-9]. Thus oxidation of 1,5-dihydroxynaphthalene with chromic acid [5,10] affords only a 10% yield, whilst oxidation with peroxyacetic acid affords [11] a mixture of juglone and 5-hydroxy-1,2-naphthoquinone (2). Photosensitised aerial oxidation of 1-naphthol gives juglone in 70% yield, but, although the reactants are readily available, requires the use of a dilute solution [12].

Naphthazarin, 5,8-dihydroxy-1,4-naphthoquinone, (3) also occurs naturally [1], and can be prepared by condensation of 1,4-dimethoxybenzene with 2,3-dichloromaleic anhydride followed by reductive dechlorination and reoxidation [13], and *via* treatment of 1,5-dinitronaphthalene with sulfur in 66% oleum [14], although this method is inconvenient and low-yielding.

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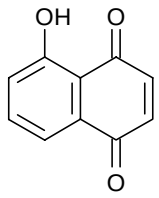

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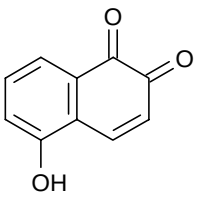

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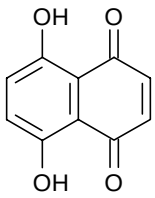

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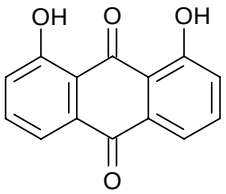

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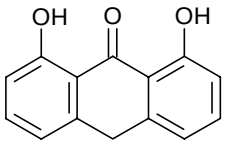

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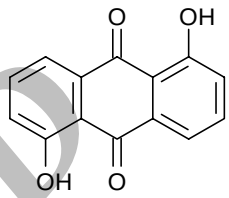

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Hydroxy-9,10-anthraquinones are important in dyestuffs chemistry [15,16], and many of them are manufactured *via* sulphonation of 9,10-anthraquinone [15-17]. The dihydroxy-9,10-anthraquinone moiety occurs widely in natural products [1], and is an important feature of the anthracycline antitumour antibiotics [18,19]. 1,8-Dihydroxy-9,10-anthraquinone (4) is the precursor for the important topical antipsoriatic drug anthralin, 1,8-dihydroxy-9-anthrone, (5) [20,21]. Intramolecular hydrogen bonding is common to quinones such as (1), (3), and (4), and is important in controlling their redox properties [22], which are vital for their roles in biochemistry.

Substituted hydroxynaphthoquinones and hydroxylanthraquinoes continue to attract attention as precursors for the preparation of biologically-active quinonoid systems [19,23], and there is therefore a need for the development of syntheses of hydroxyquinones. Herein, we describe new routes to juglone, naphthazarin, and 1-hydroxy-5,6,7,8-tetrahydro-,1,5-dihydroxy and 1,8-dihydroxy-9, 10-anthraquinone, (23), (6) and (4), respectively, based on oxidative dehydrogenation of 1-tetralones.

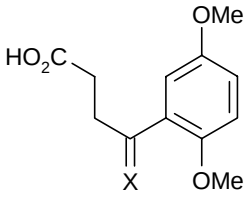
Preparation of Tetralones

4-(2,5-Dimethoxyphenyl)-4-oxobutanoic acid (7), a key starting material for the present work, was prepared [24] by Friedel-Crafts acylation [25] of 1,4-dimethoxybenzene with succinic anhydride and aluminium chloride in nitrobenzene, and subsequently reduced to give the corresponding butanoic acid (8) by treatment with triethylsilane in trifluoroacetic acid [26]. Unexpectedly, and conveniently, refluxing (8) in 48% hydrobromic acid for four hours effected both demethylation and cyclisation, affording 5,8-dihydroxy-1-tetralone (9) in 77% yield. Refluxing for a shorter period gave 4-(2,5-dihydroxyphenyl) butanoic acid (10), indicating that complete demethylation precedes cyclisation.

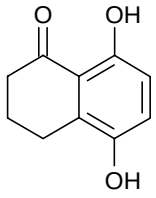
Reduction of the tetralone (11) [27] with triethylsilane afforded the tetralin (12) in 95% yield. Cyclisation with trifluoroacetic anhydride-trifluoroacetic acid then gave, almost quantitatively, the tetramethylenetetralone (13), which hydrobromic acid afforded the corresponding hydroquinone (14). The diketones (15) and (16) were available from another project [27].

Oxidative Dehydrogenation

Silver(I) oxide is a well-established oxidant for the formation of quinones from hydroquinones [28], and is useful for the preparation of some acyl-1,4-benzoquinones [29]. However, treatment of the dihydroxytetralone (9) with this reagent under standard conditions (ether, sodium sulfate, room temperature) led to recovery of the starting material, although oxidation with DDQ [28] in dichloromethane afforded the expected, but unstable, acylquinone (17) which was characterised in solution immediately after preparation by ^{1}H n.m.r spectroscopy. Its 2,3-dimethyl homologue (18) is more stable [29]. Oxidation of the tetralone (9) with DDQ in refluxing benzene (64h) eventually afforded juglone (1) in 76% yield.



(7) X = O
(8) X = H_2



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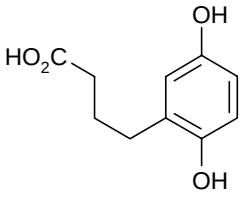

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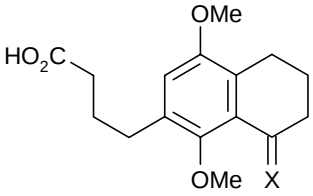
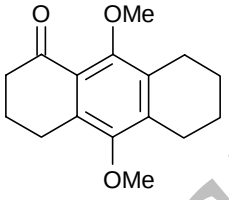


(11) X = O
(12) X = H_2



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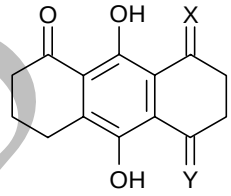
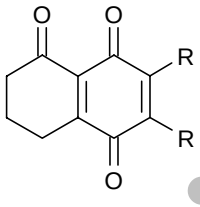
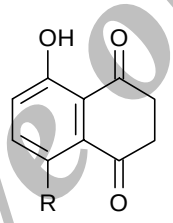


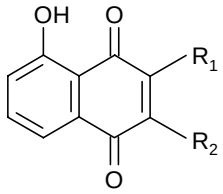
(14) X = Y = H_2
(15) X = H_2 , Y = H_2
(16) X = O , Y = H_2



(17) R = H
(18) R = Me



(19) R = OH
(20) R = H



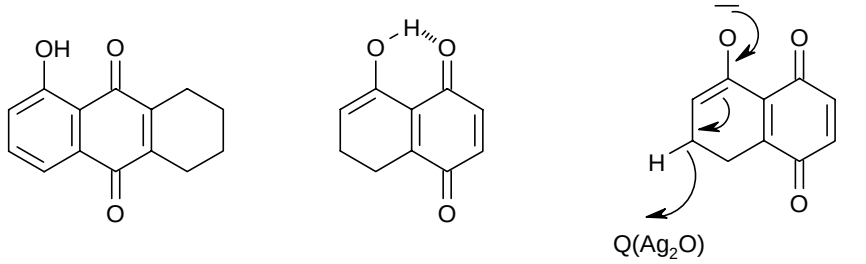
(21) R_1 = H , R_2 = OMe
(22) R_1 = OMe , R_2 = H

Oxidation of the dihydroxytetralone (9) with silver(I) oxide in 1,4-dioxane at room temperature was also unsuccessful, but at reflux afforded juglone (1) in 83% yield.

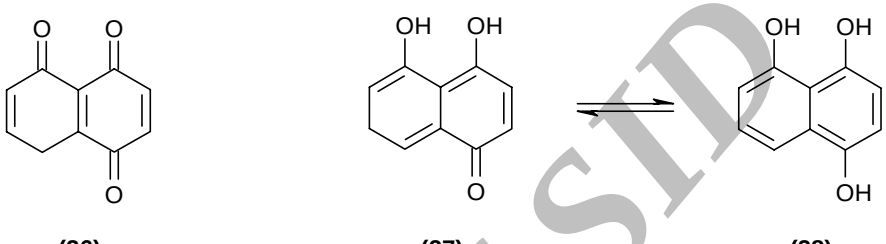
Manganese dioxide [30] is also effective for the oxidation of hydroquinones to quinines [31], and has been used for the dehydrogenation of 4a,5,8,8a-tetrahydro-1,4-naphthoquinones to naphthoquinones [32,36]. Treatment of the dihydroxytetralone (9) with reagent grade manganese dioxide in refluxing dioxane again gave juglone (1) (51%), but accompanied by naphthazarin (3) in 22% yield. The product ratio of 2.3:1; was increased to 6:1 when dry benzene was used as solvent, implicating water in the formation of naphthazarin. In agreement with this, the use of 3:1 dioxane-water afforded juglone and naphthazarin in the ratio of 1:1.8 respectively. However, conditions for the formation of naphthazarin exclusively were not found, and chromatographic separation from juglone was necessary.

Monitoring of the progress of the oxidative dehydrogenation of the tetralone (9) by thin layer chromatography revealed the formation of several intermediates, one of which, 2,3-dihydronaphthazarin (19) [33], was isolated; the corresponding dihydro-juglone (20) [34], was not identified amongst the products.

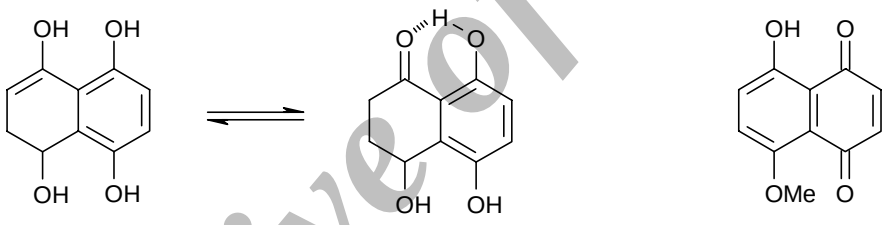
A mixture of juglone and naphthazarin (5:1) was formed when dioxane/methanol was employed as solvent; but juglone, 2-methoxyjuglone (21) [35], and 3-methoxyjuglone (22) [36] when methanol was used alone. These methoxyjuglones were also formed when juglone was refluxed with manganese dioxide in methanol.



(23) (24) (25)



(26) (27) (28)



(29) (30) (31)

Oxidation of the tetramethylenetetralone (14) with silver(I) oxide in refluxing dioxan afforded 1-hydroxy-5,6,7,8-tetrahydro-9,10-anthraquinone (23) in 78% yield. However, with manganese dioxide, the yield of tetrahydroanthraquinone (23) fell to 52%, and it was accompanied by a 10% yield of a mixture of 1-hydroxy-9,10-anthraquinone,1,4-dihydroxy-9,10-anthraquinone (quinazarin), and its 1,5-and 1,8-dihydroxy isomers (4) and (6) respectively, identified in the mixture by a combination of mass spectrometry and ^{1}H n.m.r. spectroscopic comparison with the spectra of authentic hydroxyanthraquinones. There was no evidence for further hydroxylation.

The tricyclic diketone (15) was essentially resistant to oxidation by manganese dioxide in refluxing dioxane, but was completely oxidized during 24 h when the oxidant was silver(I) oxide, affording 1,5-dihydroxy-9,10-anthraquinone (6) in 78% yield. The isomeric diketone (16) was consumed by the silver(I) oxide system in 19 h, giving 1,8-dihydroxy-9,10-anthraquinone (4) in 81% yield.

Discussion

The first intermediate in the overall oxidative dehydrogenation of 5,8-dihydroxy-1-tetralone (9) with silver(I) oxide or manganese dioxide is thought to be the corresponding quinone (17), the instability of which, noted above, is probably attributable to dipole-dipole repulsions between the adjacent carbonyl groups; analogous repulsions probably account for the non-planarity of 1,4,5,8-naphthodiquinone [37]. This repulsion can, in principle, be relieved by enolization to form the cross-conjugated system (24) which is stabilised by intramolecular hydrogen bonding [38].

Oxidation of an hydroquinone (QH_2) to the quinone (Q) by silver(I) oxide results in the generation of an alkaline medium:

$$QH_2 + Ag_2 \longrightarrow Q + 2Ag + H_2O$$

$$Ag_2O + H_2O \rightleftharpoons 2AgOH$$

Hence the enol (24) may be converted into its enolate (25) from which transfer of hydride to either preformed quinone (Q) or silver(I) oxide, affords the enone (26). Tautomerization in (26) yields juglone (1) because a particularly favourable transformation to a benzenoid system and a strong intramolecular hydrogen bond are formed.

Manganese dioxide also converts the tetralone (9) into juglone, but hydroxylation, giving naphthazarin (3), competes, suggesting the intervention of a quinone methide [28,39]. The methylene group adjacent to the quinonoid moiety in the enol (24) is vinylogously-to the 1-carbonyl group, and is activated further by the intramolecular hydrogen bond, thus facilitating proton transfer, for example to yield the orthoquinonemethide (27) [40]. This may be dehydrogenated to juglone either directly, or *via* its trihydroxynaphthalene tautomer (28). Alternatively, it may be hydrated since addition of nucleophile to quinone methides is a facile process because aromatization is concomitant [28,39], to afford the benzylic alcohol (29), which would be expected to tautomerise to the ketone (30). Manganese dioxide is well known for its ability to oxidation of benzylic alcohols to the corresponding carbonyl compounds [30,41] and thus the (observed) formation of dihydronaphthazarin (19) as an intermediate in the oxidative dehydrogenation of the tetralone (9) to naphthazarin would be accounted for.

The nature of both the surface of the manganese dioxide and the nucleophile may be critical. Thus 8-methoxyjuglone (31) was not obtained when the oxidation was performed in dioxane-methanol, although a mixture of 2-and 3-methoxyjuglone, (21) and (22) respectively, was obtained when methanol was the solvent; addition of methanol to juglone apparently predominates under these conditions.

Silver(I) oxide dehydrogenates the hydroxycarbonyl moieties of the tetramethylenetetralone (14) and the related diketones (15) and (16) cleanly to afford the corresponding hydroxyquinones (23), (6) and (4) respectively. However, manganese dioxide is not satisfactory for the quinones because it effects both dehydrogenation of the cyclohexane moiety of the tetramethylene compound (14) and further, mono hydroxylation at each of the positions-to the initial hydroquinone system, implying the involvement of all three isomeric orthoquinonemethides. It fails to oxidise the diketone (15). The mechanisms outlined above account for the formation of juglone and naphthazarin from 5,8-dihyroxy-1-tetralone (9). Analogous ones can be envisaged to explain the oxidative dehydrogenation of the related tricyclic systems (13)-(16), and the oxidative hydroxylation of the tetramethylenetetralone (14) in the presence of manganese dioxide.

Interestingly, the formation of juglone (1) from the tetralone (9) represents the reverse of the process whereby this tetralone is produced by reduction [44] of juglone with hydrogen in the presence of Raney nickel.

The methods for oxidative dehydrogenation described herein complement those based on the use of oxygen as oxidant, either in dimethylformamide [42] to parallel transformation in the anthracycline series, or in ethanolic potassium hydroxide [43] for the dehydrogenation of 2,3-dimethyl-1,4,4a,9a-tetrahydro-9,10-anthraquinone, and may be applicable where other functionality is incompatible with these conditions. The ability to effect hydroxylation, albeit incomplete, in the presence of manganese dioxide-water adds a further dimension.

Experimental

Infrared spectra were obtained using a Perkin-Elmer FT instrument. N.m.r spectra, referenced to internal tetramethylsilane, were recorded using Perkin-Elmer R 32 (22O MHz) and Varian SC 300 instruments in deuteriochloroform ($CDCl_3$). Mass spectra were determined with a Kratos MS 30 spectrometer.

4-(2,5-Dimethoxyphenyl)-4-oxobutanoic acid (7)

To a solution of 1,4-dimethoxybenzene (8 g, 58 mmol) in dry nitrobenzene (150 ml) was added over 15 min anhydrous succinic anhydride (10 g, 100 mmol). Then a solution of aluminium chloride (20 g, 150 mmol) in dry nitrobenzene (100 ml) was added, and the solution was stirred for 4 h at room temperature.

The reaction mixture was added with stirring to a mixture of 40% hydrochloric acid (400 ml) and ice (200 g). The nitrobenzene layer was separated and extracted with saturated sodium hydrogen carbonate solution (4 × 100 ml). The bicarbonate extracts were washed with ether (3 × 50 ml), acidified by slow dropwise addition of concentrated hydrochloric acid. The precipitate was filtered, washed with water and dried to give 4-(2,5-dimethoxyphenyl)-4-oxobutanoic acid (12.63 g, 91%) as white needles, m.p. 100-101°C (lit, [24] m.p. 101-102°C). (found: M = 238.0843 $C_{12}H_{14}O_5$ requires M = 238.0841).

^{1}H n.m.r (300 MHz) δ 2.75 (t, J = 6.4, 1 x CH_2), 3.35 (t, J = 6.4, 1 x CH_2), 3.80 (s, 1 x OMe), 3.90 (s, 1 x OMe), 6.92 (t, J = 9, H-3). 7.06 (dd, J_1 = 9, J_2 = 3.1, H-

4), 7.37 (d, J = 3.1, H-6), 10-12.5 (bs, CO_2H) ;υ_{max} (film) 2970 b, 1690 vs, 1658 s, 1501 vs, 1446 m, 1410 s, 1281 s, 1262 s, 1185 s, 812 s cm^{-1}; and m/z (EI) 238 (M^+, 31.4) 165 (100), 150 (10.7), 135 (6.4), 122 (18.2), 107 (32.3), 92 (15), 79 (20 .2), 77 (26.3), 58 (27), 55 (19.8), 45 (18.8), 44 (12.8), 43 (85.8), 29 (20.2), 27 (21.7).

4-(2,5-Dimethoxyphenyl) butanoic acid (8)

A solution of 4-(2,5-dimethoxyphenyl)-4-oxobutanoic acid (3.57 g, 15 mmol) in trifluoroacetic acid (40 ml) was cooled in an ice-bath. Triethylsilane (5.4 ml, 34 mmol) was then added dropwise over 45 min while the solution was stirred. The ice-bath was then removed and the reaction mixture was stirred for further an hour at room temperature. The solvent was removed and traces of trifluoroacetic acid, triethylsilane and triethylsilanol were then removed at oil-pump pressure.

The residue was extracted with saturated sodium hydrogen carbonate (200 ml). The bicarbonate extracts were washed with ether (2 × 25 ml) and acidified by slow addition of concentrated hydrochloric acid. The product was extracted with chloroform (100 ml), the organic layer was separated, washed with water, and dried (Na_2SO_4). Removal of the solvent gave 4-(2,5-dimethoxphenyl)butanoic acid (3.03 g, 90%) as colourless needles, m.p. 67-68°C (lit., [24] m.p. 68-69°C). (found: M = 224.1050 $C_{12}H_{16}O_4$ requires M = 224.1049).

^{1}H n.m.r (300 MHz) δ 1.96 (quintet, J=7.4, 1 x CH_2), 2.38 (t, J= 7.4, 1 x CH_2), 2.67 (t, J = 7.4, 1 x CH_2), 3 .76 (s, 1 x OMe), 3.77 (s, 1 x OMe), 6 .69 (dd, J_1= 9, J_2 = 3, H-4), 6.72 (bs, H-6), 6.77 (bd, J = 9, H-3), 9.5-12.5 (bs, CO_2H); υ_{max} (film) 2948 s, 2835 s, 1709 vs, 1590 s, 1499 s, 1433 vs, 1280 s, 1222 vs, 1208 vs, 1180 s, 1024 s, 933 s cm^{-1}; and m/z (EI) 225 [$(M+1)^+$, 13.7], 224 (M^+, 100), 164 (55.5), 163 (39.1), 151 (67.9), 121 (83.8), 91 (54.5), 77 (49.8), 65 (47.9), 45 (36.5), 39 (44).

5,8-Dihydroxy-1-tetralone (9)

4-(2,5-Dimethoxyphenyl)butanoic acid (1 g, 4.46 mmol) was dissolved in 48% hydrobromic acid (20 ml) by heating, and the solution was refluxed (oil-bath 120-130°C) with stirring for 4 h. The solution was cooled to room temperature, and then diluted with water (50 ml). The product was extracted with ether (2 × 50 ml), washed with water, and dried (Na_2SO_4). Removal of the solvent and recrystallization of the residue from petroleum ether (b.p 100-120) gave 5,8-dihydroxy-1-tetralone (0.61 g, 77%) as yellow needles, m.p.184°C (lit, [44] m.p. 185°C).

(Found: M = 178.0638 $C_{10}H_{10}O_3$ requires M = 178.0630).

^{1}H n.m.r (300 MHz) δ 2.11 (quintet, J = 6.4, 1 x CH_2), 2.68 (t, J = 6.4, 1 x CH_2), 2.88 (t, J = 6.4, 1 x CH_2), 5.06 (bs, 5-OH), 6.71 (d, J= 9, H-7), 7.00 (d, J = 9, H-6), 12.01 (s, 8-OH); υ_{max} (film) 3247 b, 1616 vs, 1579 vs, 1472 vs, 1406 m, 1328 s, 1278 s, 1222 s cm^{-1}; and m/z (EI) 178 (M^+, 100), 150 (64.2), 136 (9), 122 (38.5), 121 (26.2), 94 (9.3), 77 (15.9), 66 (21.9), 65 (20.7), 55 (20.4).

5-Hydroxy-1, 4-naphthoquinone (1)

(a) 5,8-Dihydroxy-1-tetralone (178 mg, 1 mmol) was dissolved in dioxane (40 ml) and silver oxide (1 g, excess) was added. The reaction mixture was stirred under reflux for 10 h. The solution was filtered and the solvent was removed to give 5-hydroxy-1,4-naphthoqlone (144 mg, 83%) as yellow needles, m.p. 162-163°C (lit, [17] m.p. 165°C). (Found: M = 174.0316 $C_{10}H_6O_3$ requires M = 174.0317). Spectroscopic data and t.1.c analysis were in accord with those of authentic 5-hydroxy-1,4-naphthoquinone.

^{1}H n.m.r (300 MHz) δ 6.96 (s, H-2 + H-3), 7.26 (m, H-6), 7.62 (m, H-7+H-8), 11.91 (s; 5-OH); υ_{max} (film) 3065 b, 1665 s, 1594 m, 1451s, 1363 s, 1290 vs, 1226 s cm^{-1}; and m/z (EI) 176[$(M + 2)^+$, 10.8], 174 (M^+, 100), 173 (21.9), 146 (15.9), 120 (29.6), 118 (48.8), 92 (31.4).

(b) 5,8-Dihydroxy-1-tetralone (178 mg, 1 mmol) was added to dry benzene (50 ml), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (500 mg, 2.2 mmol) was then added. The reaction mixture was stirred under reflux for 70 h. The solution was filtered through silica gel (10 g), and washed with chloroform (10 ml). Removal of the solvent gave 5-hydroxy-1,4-naphthoquinone (122 mg, 76%) as orange yellow needles, m.p.160-162°C (lit, [17] m.p. 165°C).

Spectroscopic data and t.1.c analyses were similar to those of authentic sample of 5-hydroxy-1,4-naphthoquinone.

^{1}H n.m.r (220 MHz) δ 6.95 (s, H-2+H-3), 7.27 (m, H-6), 7.63 (m, H-7+H-8), 11.91 (s, 5-OH).

Treatment of 5,8-Dihydroxy-1-tetralone (9) with Manganese Dioxide

(a) 5,8-Dihydroxy-1-tetralone (44.5 mg, 0.25 mmol) in dioxane (15 ml) was stirred under reflux with manganese dioxide (350 mg, excess) for 2 h. Manganese dioxide was filtered off, washed with dioxane and the filtrate was evaporated to give brown solid (39 mg). Its n.m.r spectrum showed that it was a

mixture of 5-hydroxy-1,4-naphthoquinone and 5,8-dihydroxy-1,4-naphthoquinone in the ratio of 3:1, respectively. The mixture was separated by silica gel p.l.c using 1:2 diethyl ether-petroleum ether (b.p.40-60°C).

The first band gave 5-hydroxy-1,4-naphthoquinone (23.4 mg, 51%) as orange yellow needles, m.p. 163°C (lit, [17] m.p. 165°C).

The second band gave 5,8-dihydroxy-1,4-naphthoquinone (10.3 mg, 22%) as deep red needles, m.p.228-232°C (lit, [15] m.p. 237°C). N.m.r and t.l.c were compared with those of the authentic sample. ^{1}H n.m.r (200 MHz) δ 7.16 (s, H-2 + H-3), 7.27 (s, H-6 + H-7), 12.43 (s, 5-OH + 8-OH).

(b) 5,8-Dihydroxy-1-tetralone (10 mg) in dry benzene (6 ml) was stirred under reflux with manganese dioxide (100 mg) for 8 h. Manganese dioxide was filtered off, and the solvent was removed to give a dark orange solid (7.6 mg). Its n.m.r showed to be a mixture of 5-hydroxy-1,4-naphthoquinone and 5,8-dihydroxy-1,4-naphthoquinone in the ratio of 6:1 respectively due to the integrals of the hydroxy groups.

Treatment of 5,8-Dihydroxy-1-tetralone (9) with Manganese Dioxide in Presence of Water

(a) A mixture of dioxane (4 ml), water (1 ml) and manganese dioxide (100 mg, excess) was refluxed for 30 min. 5,8-Dihydroxy-1-tetralone (12 mg, 0.067 mmol) was added and the reaction mixture was refluxed with stirring for 8 h. Manganese dioxide was filtered off, washed with dioxane and the filtrate was evaporated to give orange needles (8.9 mg). Its n.m.r showed to be a mixture of 5-hydroxy-1,4-naphthoquinone and 5,8-dihydroxy-1,4-naphthoquinone in the ratio of 2:3.5 respectively, due to the integrals of hydroxyl groups.

(b) 5,8-Dihydroxy-1-tetralone (12 mg, 0.067 mmol) in a mixture of dioxane (4 ml) and water (1 m1) was stirred under reflux with manganese dioxide (100 mg, excess) for 30 min. The solution was filtered and the solvent was removed to give sticky orange solid (9.3 mg). Its n.m.r showed to be a mixture of 5-hydroxy-1,4-naphthoquinone, 5,8-dihydroxy-1,4-naphthoquinone and 2,3-dihydro-5,8-dihydroxy-1,4-naphthoquinone (intermediate). The mixture (6 mg) was separated by silica gel p.l.c using chloroform.

The first band was separated to give a mixture of 5-hydroxy-1,4-naphtho-quinone and 5,8-dihydroxy-1,4-naphthoquinone (2.2 mg).

The second band gave 2,3-dihydro-5,8-dihydroxy-1,4-naphthoquinone (1.9 mg) as yellow needles, m.p.154-155°C (lit, [18] m.p.153-154°C). Spectroscopic data and t.l.c analysis were in accord with those of 2,3-dihydro-5,8-dihydroxy-1,4-naphthoquinone.

^{1}H n.m.r (220 MHz) δ 3.06 (s, 2×H-2+2×H-3), 7.26 (s, H-6 + H-7), 11.97 (s, 5-OH + 8-OH).

Treatment of 5,8-Dihydroxy-1-tetralone (9) with Manganese Dioxide in the Presence of Methanol

(a) 5,8-Dihydroxy-1-tetralone (12 mg, 0.067 mmol) was added to a mixture of dioxane (5 ml), dry methanol (1 ml) and manganese dioxide (100 mg, excess). The reaction mixture was refluxed for 6h. Manganese dioxide was filtered off and the filtrate was evaporated to give a brown solid (8.4 mg). Its n.m.r showed to be mainly a mixture of 5-hydroxy-1,4-naphthoquinone and 5,8-dihydroxy-1,4-naphthoquinone in the ratio of 5:1 respectively.

(b) 5,8-Dihydroxy-1-tetralone (14 mg, 0.078 mmol) was dissolved in dry methanol (6 ml) and manganese dioxide (100 mg, excess) was added. The reaction mixture was refluxed for 4 h. Manganese dioxide was filtered off and the solvent was removed to give a dark brown sticky solid (9.8 mg). Its n.m.r spectrum was very complex, and it showed three main spots on t.1.c. The mixture (6 mg) was separated by silica gel p.1.c using chloroform.

The first band gave 5-hydroxy-1,4-naphthoquinone (1.2 mg) as orange yellow needles m.p.164°C (lit, [17] m.p. 165°C).

The second band was isolated to give 5-hydroxy-2-methoxy-1,4-naphthoquinone (1.6 mg) as yellow needles, m.p. 160-161°C (lit, [19] m.p. 159-160°C).

^{1}H n.m.r (300 MHz) δ 3.93 (s, OMe), 6.12 (s, H-3), 7.28 (dd, $\underline{J}_1$ = 7.8, $\underline{J}_2$ = 1.2, H-8), 7.59 (t, J= 7.8, H-7), 7.70 (dd, $\underline{J}_1$ = 7.8, $\underline{J}_2$ = 1.2, H-6), 12.24 (s, 5-OH); and $\underline{m}/\underline{z}$ (EI) 204 ($\underline{M}^+$, 3.6); $\underline{m}/\underline{z}$ (CI/NH_3) 205 [($\underline{M}$ + H)$^+$, 34.7].

The third band was isolated to give 8-hydroxy-2-methoxy-1,4-naphthoquinone (1.3 mg) as orange yellow needles m.p. 220-222°C (lit, [36] 223-224°C).

^{1}H n.m.r (300 MHz) δ 3.93 (s, OMe), 6.17 (s, H-3), 7.24 (dd, $\underline{J}_1$ = 5.9, $\underline{J}_2$ = 3.6, H-7), 7.64 (d, $\underline{J}$ = 3.6, H-5), 7.65 (d, $\underline{J}$ = 5.9, H-6), 11.79 (s, 8-OH); and $\underline{m}/\underline{z}$ (EI) 205 [($\underline{M}$+1)$^+$, 9.3], 204 ($\underline{M}^+$, 56.9), 189 (20.5), 175 (17.2), 174 (24.1), 173 (9.8); $\underline{m}/\underline{z}$ (CI/NH_3) 205 [($\underline{M}$+H)$^+$, 100], 204 ($\underline{M}^+$, 7.5), 190(3).

Treatment of 9,10-Dihydroxy-3,4,5,6,7,8-hexahydro-1(2$\underline{H}$)-anthracenone (14) with Manganese Dioxide

9,10-Dihydroxy-3,4,5,6,7,8-hexahydro-1(2$\underline{H}$)-anthracenone [27] (20 mg, 0.086 mmol) was dissolved in dioxane (10 ml) and manganese dioxide (150 mg, excess) was added . The reaction mixture was stirred

under reflux (oil bath) for 3 h. T.l.c showed no starting material left. Filtration through celite and removal of the solvent gave an orange solid (14 mg). The p.m.r spectrum ($CDCl_3$) indicated a mixture with 1-hydroxy-5,6,7,8-tetrahydro-9,10-anthraquinone as major component. The mixture was separated by silica get p.l.c using ether/petroleum ether (b.p.40-60°C) (1:2).

The first band was isolated to give 1-hydroxy-5,6,7,8-tetrahydro-9.10-anthraquinone (10.3 mg, 52%) as orange yellow needles, m.p.108-109°C.

The second band was isolated to give orange needles (1.9 mg). Its p.m.r spectrum indicated a complex mixture of 1-hydroxy-9,10-anthraquinone, 1,4-dihydroxy-9,10-anthraquinone, 1,5-dihydroxy-9,10-anthraquinone and 1,8-dihydroxy-9, 10-anthraquinone, also mass spectroscopy had m/z 240 and 224 which would be the molecular ions for above mentioned dihydroxy and monohydroxy anthraquinones respectively.

1,5-Dihydroxy-9,10-anthraquinone (6)

1,2,3,4,5,6,7,8-Octahydro-9,10-dihydroxy-1,5-anthracenedione (24.6 mg, 0.1 mmol) was dissolved in dioxane (15 ml), and silver oxide (140 mg, excess) was added. The reaction mixture was filtered under reflux for 24 h. The solution was filtered through celite, and the solvent was removed. The residue was recrystallized from glacial acetic acid to give yellow needles (18.7 mg, 78%) m.p. 279-281°C (lit, [45] m.p. 280°C), identified as 1,5-dihydroxy-9,10-anthraquinone by comparison (t.l.c and n.m.r.) with an authentic sample.

^{1}H n.m.r (220 MHz) δ 7.34 (dd, J_1 = 8.3, J_2 = 1.5, 2H), 7.70 (dd, J_1 = 8.3, J_2 = 7.4, H-3 + H-7), 7.86 (dd, J_1 = 7.4, J_2 = 1.5, 2H), 12.66 (s, 2 × OH); υ_{max} (film) 3340 b, 1633 vs, 1600 s, 1569 m, 1448 s, 1299 s, 1238 vs, 1049 s cm^{-1}; and m/z (EI) 241 [$(M+1)^+$, 8.6], 240 (M^+, 100], 121 (13.4).

1,8-Dihydroxy-9,10-anthraquinone (4)

1,2,3,4,5,6,7,8-Octahydro-9,10-dihydroxyanthracene-1,8-dione [27] (24.6 mg, 0.1 mmol) was dissolved in dioxane (8 ml) and silver oxide (120 mg, excess) was added. The reaction mixture was stirred under reflux (oil bath) for 19 h. Filtration through celite and removal of the solvent gave 1,8-dihydroxy-9,10-anthraquinone (18.7 mg, 81%) as orange yellow needles, m.p.=189-191°C (lit [45] m.p=193°C). spectroscopic data and t.l.c analysis were in accord with those of authentic sample.

^{1}H n.m.r (220 MHz) δ 7.31 (dd, J_1 = 8.4, J_2 = 1.3, H-2 + H-7), 7.70 (t, J = 8, H-3 + H-6), 7.84 (dd, J_1 = 7.7, J_2 = 1.3, H-4 + H-5), 12.08 (s, 1-OH + 8-OH).

Treatment of 9,10-Dihydroxy-3,4,5,6,7,8-hexahydro-1(2H)-anthracenone (14) with DDQ

9,10-Dihydroxy-3,4,5,6,7,8-hexahydro-1(2H)-anthracenone [27] (20 mg, 0.086 mmol) was dissolved in dichloromethane (10 ml). DDQ (19.5 mg, 0.086 mmol) was added, and the reaction mixture was stirred at room temperature for 2 h. The solution was filtered through celite and the solvent was removed to give 3,4,5,6,7,8-hexahydro-1(2H)-9,10-anthracenetrione as pale orange needles (18.6 mg, 94%) m.p. 89-90°C.

^{1}H n.m.r (220 MHz) δ 1.68 (quintet, J = 3.2, 2 x CH_2), 2.1(quintet, J = 6.5, 1 x CH_2), 2.43 (broad m, 2 x CH_2), 2.56(t, J = 6.5, 1 x CH_2), 2.72 (t, J = 6.5, 1 x CH_2); υ_{max} (film) 1703 vs, 1641 vs, 1600 m, 1362 m, 1286 m cm^{-1}; and m/z (EI) 230 (M^+, 4.4), 229 (12.2), 228 (58.8), 202 (1.7), 200 (3.5), 199 (5).

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