

Phenol Dehydrogenation

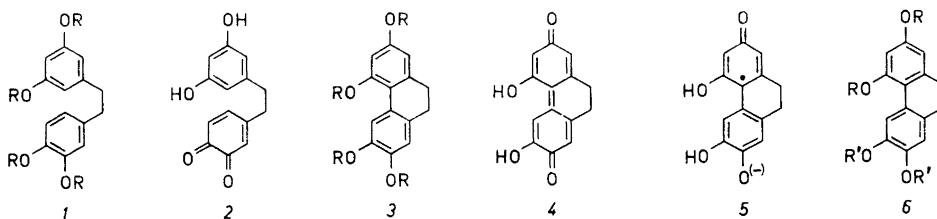
Part 11.* Intramolecular Oxidative Coupling of Dihydropiceatannol

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The intramolecular oxidative phenol coupling of 3,4,3',5'-tetrahydroxydibenzyl with formation of 9,10-dihydrophenanthrene derivatives is described and the course of the reaction is discussed.

Several years ago¹ it was found that an alkaline solution of 3,4,3',4'-tetrahydroxydibenzyl rapidly absorbed oxygen, turning deep green. On acidification a blue-violet precipitate was formed which on reductive acetylation furnished 2,3,6,7-tetraacetoxy-9,10-dihydrophenanthrene and polymeric products.



Similarly 3,4,3',5'-tetrahydroxydibenzyl, **1** (R=H), "dihydropiceatannol", gives an emerald green colour reaction. The colour is unstable and in the absence of oxygen the solution gradually turns brown. On readmission of oxygen the green colour reappears and disappears again when the oxygen is consumed. These colour changes can be repeated many times. Finally, when the solution no longer absorbs oxygen, it remains brown. On acidification of this brown solution a black precipitate is formed. No crystalline phenolic substance could be isolated from the filtrate and reductive acetylation of the black material gave a brownish, amorphous product. When a green, incompletely oxidised

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solution was acidified, a black precipitate was also formed, but the filtrate contained a mixture of phenols which on acetylation gave 3,4,3',5'-tetraacetoxydibenzyl, *1* (R=Ac), and 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene, *3* (R=Ac). Reductive acetylation of the black precipitate gave an amorphous product. The reaction was followed semiquantitatively with the results given in Table 1. As long as the solution remains green the acidified solution contains unchanged starting material as well as the coupling product *3* (R=H). The amount of crystalline products decreases and that of amorphous polymers increases with the amount of oxygen absorbed. The polymers must arise either by intermolecular coupling of the starting material or, as will be shown, more probably, from a quinonoid oxidation product of the 9,10-dihydrophenanthrene *3* (R=H) *e.g.* *4*.

On addition of ferric chloride or ammonium cerisulphate to an aqueous solution of 3,4,3',5'-tetrahydroxydibenzyl a blue-black product was immediately precipitated which was easily washed free from inorganic substances. Reductive acetylation of this material gave a mixture containing 80 % 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene, *3* (R=Ac), and 20 % of a brownish polymer. The main component of the blue-black product is obviously a quinone derived from 2,3,5,7-tetrahydroxy-9,10-dihydrophenanthrene, *e.g.* *4*, and could be formed by oxidation of 3,4,3',5'-tetrahydroxydibenzyl to the corresponding *ortho*-quinone (*2*) followed by intramolecular coupling to *3* (R=H) and oxidation to *4* or by direct radical coupling. Quinone *4* polymerised completely when heated to 90° for 2 h (*cf.* Ref. 2).

The quinone was not obtained in a pure state. It was sparingly soluble in ethyl acetate and methanol giving a reddish-violet solution [λ_{\max} (EtOAc) 290, 360 and 494 nm]. The absorption at 494 nm could be used for an approximate estimation of the amount of quinone present. The solutions were relatively unstable and spectrophotometric quinone estimations were made using fresh solutions. The quinone dissolves in alkali giving a deep green colour and the phenol *3* (R=H) gives the same colour when treated with alkali and air.

The crude quinone obtained by oxidation of 3,4,3',5'-tetrahydroxydibenzyl with ferric chloride was dissolved in alkali with exclusion of air. At intervals, samples of the solution were acidified and shaken with ethyl acetate and the extracts were examined photometrically.

The quinone was rapidly destroyed. For example, after 5 h acidification of the greenish solution and reductive acetylation of the black precipitate gave an amorphous product containing at the most only traces of 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene. The filtrate gave a product which after acetylation afforded polymeric material together with 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene (*3*, R=Ac); the sole crystalline product. Thus, in alkaline solution the quinone *4* undergoes dismutation to polymeric products and the phenol *3* (R=H). If the quinone solution was acidified a few minutes after the start of the experiment 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene could be isolated from the black precipitate after reductive acetylation. If the quinone *4* was treated with an alkaline solution of glucose the initial green colour rapidly disappeared (*cf.* Ref. 2). The solution then no longer gave a precipitate on acidification but afforded an almost

quantitative yield of 2,3,5,7-tetrahydroxy-9,10-dihydrophenanthrene (isolated as the acetate).

The ESR spectra of the fresh, green alkaline solutions showed that these contained considerable amounts of a semiquinone anion radical (*e.g.* 5) as long as the green colour persisted.

Phenol 3 (R=H) was methylated to 3 (R=CH₃) and then dehydrogenated with palladium to 2,3,5,7-tetramethoxyphenanthrene (6, R=R'=CH₃). This compound was demethylated to 6 (R=R'=H) and acetylated to 6 (R=R'=Ac).

2,3,5,7-Tetramethoxyphenanthrene was also obtained directly in 50 % yield from piceatannol tetramethyl ether by an iodine-sensitised photochemical reaction.³ No isomer, *e.g.* 1,2,5,7-tetramethoxyphenanthrene, could be detected in the reaction mixture. Similarly piceatannol tetraacetate gave the phenanthrene 6 (R=R'=Ac). Alkaline hydrolysis of the latter acetate in the presence of air gave a violet solution.

Mild treatment of 2,3,5,7-tetramethoxyphenanthrene with boron tribromide gave 2,3-dihydroxy-5,7-dimethoxyphenanthrene 6 (R=CH₃, R'=H). On complete demethylation followed by acetylation 2,3,5,7-tetraacetoxyphenanthrene was obtained. Mild treatment of piceatannol tetramethyl ether with boron tribromide led to complete demethylation.

The structures of the various phenanthrenes and 9,10-dihydrophenanthrenes follow from their NMR spectra (*cf.* Tables 2 and 3). It was not possible to hydrogenate 2,3,5,7-tetramethoxyphenanthrene catalytically to 2,3,5,7-tetramethoxy-9,10-dihydrophenanthrene and attempts to synthesise the latter compound from a diiodination product of 3,4,3',5'-tetramethoxydibenzyl by means of an intramolecular Ullmann coupling failed because both iodine atoms had entered the resorcinol nucleus. The diiodo compound gave veratric acid on oxidation with permanganate.

EXPERIMENTAL

3,4,3',5'-Tetraacetoxydibenzyl. 3,4,3',5'-Tetraacetoxy stilbene⁴ was hydrogenated (PtO₂) in ethyl acetate. Crystals from methanol, m.p. 73–74°. (Found: C 63.3; H 5.5. Calc. for C₂₂H₂₂O₈: C 63.8; H 5.3).

3,4,3',5'-Tetrahydroxydibenzyl. The tetraacetate (10 g) in 2 % methanolic sulphuric acid (200 ml) was boiled under nitrogen. The colourless phenolic product (yield 93 %) was recrystallised from benzene-acetic acid (3:1). Crystals, m.p. 159–160°. (Found: C 68.1; H 5.7. Calc. for C₁₄H₁₄O₄: C 68.3; H 5.7).

Oxidation of 3,4,3',5'-tetrahydroxydibenzyl with oxygen in alkaline solution. These experiments were done in a two-necked flask connected with a separatory funnel and a gas burette. After placing the 3,4,3',5'-tetrahydroxydibenzyl (0.5 g) in the flask, the apparatus was flushed with pure oxygen. Water (50 ml) followed by sodium hydroxide solution (5 ml, 2 N) was then sucked into the flask *via* the separatory funnel. When the required amount of oxygen had been consumed, sulphuric acid (5 ml, 2 N) was introduced *via* the funnel. The black precipitate (A) that immediately formed was isolated by filtration. (A) was subjected to reductive acetylation with zinc and acetic anhydride. The product obtained was amorphous and easily soluble in methanol. The filtrate from A was extracted with ether (3 × 50 ml) and the extracts washed with water and evaporated. The residue was acetylated and the resulting acetate mixture was triturated with a little cold methanol to remove polymers (about 5 % of the mixture). TLC on silica gel (eluent: ether-benzene, 1:1) showed the presence of 3,4,3',5'-tetraacetoxydibenzyl and 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene. The molar ratio between the two ace-

Table 1. Oxidation of 3,4,3',5'-tetrahydroxydibenzyl with oxygen in alkaline solution.

Moles O ₂ per mole of dibenzyl	Duration of oxygen uptake (minutes)	% yield of 1 (R=Ac)	% yield of 3 (R=Ac)	% yield of polymers
0.25	2.5	65	10	0
0.50	5.0	50	14	4
0.75	9.0	30	12	7
1.00	14.0	21	9	14
1.25	22.0	12	6	30

tates was determined from the integrated NMR-spectrum of the mixture (the areas corresponding to the methylene protons of the dibenzyl at 3.9 ppm and at 3.8 ppm of the dihydrophenanthrene were particularly useful). The results are given in Table 1.

Oxidation of 3,4,3',5'-tetrahydroxydibenzyl with ferric chloride. 3,4,3',5'-Tetrahydroxydibenzyl (1 g) was dissolved in distilled water (200 ml) and a solution (50 ml) containing ferric chloride (anhydrous, 2.62 g, or 4 oxidation equivalents per mole of phenol) was added over about 3 min. The black precipitate (A) was collected by centrifugation, suspended in distilled water (50 ml) and centrifuged again. This operation was repeated twice. Finally the precipitate was suspended in sulphuric acid (50 ml 2 N) and centrifuged. (The supernatant did not contain any iron ions). The precipitate was treated with zinc and acetic acid until the colour had disappeared. Acetic anhydride and pyridine were added and the acetylated product was isolated in the usual way. The yellowish crystalline product was triturated with methanol (3 × 5 ml) which dissolved about 0.2 g of amorphous material.

The yield of almost pure 2,3,5,7-tetraacetoxy-9,10-dihydrophenanthrene was 1.1 g (66 %). In a similar experiment the black precipitate A was rapidly dried and weighed (0.82 g). Assuming that the reductive acetylation gives a quantitative yield of acetate this weight indicates that the precipitate A contained 80 % of pure quinone 4. The acetate was recrystallised from acetic acid. Colourless crystals (1.0 g), m.p. 200–201°. [Found: C 63.8; H 4.9. M=412 (Mass spec.). Calc. for C₂₂H₂₀O₈: C 64.1; H 4.9; M 412]. NMR-data see Table 2.

Treatment of the quinone 4 with alkali in an inert atmosphere. 3,4,3',5'-Tetrahydroxydibenzyl (1 g) in water (200 ml) was oxidised with ferric chloride (5.24 g, anhydrous) in water (50 ml). The quinone was isolated, washed with water until free from iron and dissolved in sodium hydroxide solution (35 ml 1.15 N) care being taken to exclude air.

Table 2. Proton magnetic resonance spectra of derivatives (3) of 2,3,5,7-tetrahydroxy-9,10-dihydrophenanthrene in CDCl₃. Shifts in ppm (δ) relative TMS.

R=	H-1 singlet	H-4 singlet	H-6 doublet	H-8 doublet	Protons in positions 9 and 10	Substituents in positions 2, 3, 5, and 7
Ac	7.13	7.87	7.00 6.92 <i>J</i> =2.5 cps		2.70 (four-proton singlet)	2.18 (twelve-proton singlet)
CH ₃	6.67	7.90	6.42 (two-proton singlet)		2.86 (four-proton singlet)	Two three-proton singlets at 3.70 and 3.85, respectively, and a six-proton singlet at 3.78

The solution immediately turned intensely green. At intervals 0.1 ml samples were transferred to test tubes containing sulphuric acid (1.5 ml 2 N) and ethyl acetate (2 ml). After shaking and centrifugation the reddish-violet ethyl acetate phase separated from the colourless aqueous phase was diluted to 100 ml and its absorption at 494 nm measured. The absorptions of the different samples were related to the absorption of a sample from a similar experiment in which the alkaline solution was replaced by distilled water. Results, see Table 1.

2,3,5,7-Tetrahydroxy-9,10-dihydrophenanthrene. 2,3,5,7-Tetraacetoxy-9,10-dihydrophenanthrene (500 mg) was deacetylated as described above. The product was crystallised from benzene-acetic acid (3:1). Colourless needles, m.p. 291–292°. (Found, sublimed sample: C 68.8; H 4.9. Calc. for $C_{14}H_{12}O_4$: C 68.9; H 4.9).

2,3,5,7-Tetramethoxy-9,10-dihydrophenanthrene. 2,3,5,7-Tetrahydroxy-9,10-dihydrophenanthrene in methanol-water was methylated with diazomethane (excess) in ether. Colourless crystals from methanol, m.p. 81–82°. (Found, sublimed sample: C 72.2; H 6.8. Calc. for $C_{18}H_{20}O_4$: C 72.0; H 6.7).

2,3,5,7-Tetramethoxyphenanthrene, (a). 2,3,5,7-Tetramethoxy-9,10-dihydrophenanthrene (100 mg) was mixed with palladium on carbon (10 %, 100 mg) and the mixture heated to 300° for 10 min in a nitrogen atmosphere. Extraction with acetone gave a brown oil which was chromatographed on alumina with benzene-ether (3:1). The main fraction was a yellow oil which soon crystallised. Crystals from methanol, m.p. 141–142°, identical (IR, NMR, mix. m.p.) with 2,3,5,7-tetramethoxyphenanthrene prepared as below.

2,3,5,7-Tetramethoxyphenanthrene, (b). 2,3,5,7-Tetramethoxyphenanthrene was prepared from 3,4,3',5'-tetramethoxystilbene according to the procedure described in Ref. 3. A solution of 3,4,3',5'-tetramethoxystilbene (3 g) and iodine (0.127 g) in ethanol (1000 ml, 99 %) was irradiated for 30 h with a 75 watt medium pressure mercury lamp. The reaction was followed by measuring the ultraviolet absorption of the reaction mixture. The stilbene has a strong maximum at 330 nm ($\epsilon=55\ 000$) where the phenanthrene has $\epsilon=1400$ and the phenanthrene has a maximum at 261 nm ($\epsilon=76\ 000$) where the stilbene has $\epsilon=3500$. The reaction mixture was evaporated and the residue was dissolved in benzene (20 ml) and chromatographed on alumina (30 g) with benzene as eluent. Only one crystalline substance (m.p. 141–142°) could be isolated. The NMR spectrum (see Table 3) showed it to be 2,3,5,7-tetramethoxyphenanthrene. (Found: C 72.4; H 6.0. Calc. for $C_{18}H_{18}O_4$: C 72.5; H 6.0). Yield 50 %.

2,3,5,7-Tetraacetoxyphenanthrene. 3,4,3',5'-Tetraacetoxy-9,10-dihydrophenanthrene (4.12 g) and iodine (0.127 g) were dissolved in ethanol (1000 ml, 99 %) and irradiated for 40 h. The reaction mixture, worked up as above, yielded only one crystalline substance, m.p. 171–172°

Table 3. Proton magnetic resonance spectra of 2,3,5,7-tetrahydroxyphenanthrene derivatives.

R =	R' =	H-1 singlet	H-4 singlet	H-6 doublet	H-8 doublet	H-9 doublet	H-10 doublet	Substituents at positions 2, 3, 5, and 7
CH ₃	CH ₃	7.18	9.10	6.87	6.72 $J=2.3$ cps	7.46	7.64 $J=9.0$ cps	four three-proton singlets at 3.88, 3.95, 4.01, and 4.04, respectively
CH ₃	Ac	7.70	9.10	6.87	6.73 $J=2.3$ cps	7.59 (singlet; two protons)		Two three-proton singlets (–OCH ₃) at 3.85 and 4.00, respectively; and two three-(OAc) proton singlets at 2.30 and 2.34, respectively
Ac	Ac	7.73	9.07	7.62	7.27 $J=2.2$ cps	7.68 (singlet; two protons)		Two three-proton singlets at 2.35 and 2.49, respectively, and a six-proton singlet at 2.33

(NMR see Table 3). (Found: C 64.2; H 4.3. Calc. for $C_{22}H_{18}O_8$: C 64.4; H 4.4). Yield 48 %. Acid hydrolysis followed by methylation with diazomethane gave 2,3,5,7-tetramethoxyphenanthrene (IR, mix. m.p.).

2,3-Dimethoxy-5,7-diacetoxyphenanthrene. 2,3,5,7-Tetramethoxyphenanthrene (300 mg) was dissolved in dry benzene (10 ml) and boron tribromide (1 ml) was added at 0°. After 30 min at 0° methanol (10 ml) was added and the solvents evaporated. The residue was acetylated with acetic anhydride and pyridine and the oily reaction product triturated with ether. Recrystallisation from methanol yielded white crystals, m.p. 145–146°. (Found: C 67.6; H 5.2. Calc for $C_{20}H_{18}O_8$: C 67.8; H 5.1). The NMR and IR spectra showed the presence of two methoxyl groups and comparison with the NMR spectra (see Table 3) of 2,3,5,7-tetramethoxyphenanthrene and 2,3,5,7-tetraacetoxyphenanthrene showed that the substance, m.p. 145–46°, was 2,3-dimethoxy-5,7-diacetoxyphenanthrene. Demethylation of 2,3,5,7-tetramethoxyphenanthrene with boron tribromide in boiling benzene or by boiling with 48 % hydrogen bromide gave 2,3,5,7-tetrahydroxyphenanthrene (isolated as the tetraacetate).

Demethylation of 3,4,3',5'-tetramethoxystilbene with boron trifluoride as above or even under milder (–65° in methylene chloride) conditions gave 3,4,3',5'-tetrahydroxystilbene.

3,4,3',5'-Tetramethoxydibenzyl. 3,4,3',5'-Tetramethoxystilbene in ethyl acetate was hydrogenated over platinum oxide. Colourless crystals from methanol, m.p. 56.5–57.5°. (Found: C 71.5; H 7.3. Calc. for $C_{18}H_{22}O_4$: C 71.5; H 7.3).

3,4,3',5'-Tetramethoxy-2',6'-diiododibenzyl. 3,4,3',5'-Tetramethoxydibenzyl (3.02 g) dissolved in ethanol (35 ml) was reacted with iodine (5.6 g) and mercuric oxide (4.47 g) according to Ref. 5. The iodination product was only sparingly soluble in ethanol and precipitated during the reaction. The reaction mixture was filtered and the solid washed with ethanol and then extracted with chloroform. The combined chloroform extracts were washed twice with a saturated aqueous sodium iodate solution (20 ml) then three times with water (20 ml). Evaporation yielded 4.4 g of colourless crystals, m.p. 148–149°. (Found: I 45.9. Calc. for $C_{18}H_{20}O_4I_2$: I 45.9).

The substitution pattern of the diiodo compound was determined from its oxidation to veratric acid by potassium permanganate in acetone and from its decoupled (INDOR-method) 100 Mc NMR spectrum [H-6: Quartet around 6.95 ppm ($J_{H-6/H-5}=9$ cps and $J_{H-6/H-2}=2$ cps); H-5: Doublet around 6.80 ppm ($J_{H-5/H-6}=9$ cps); H-2: Doublet around 6.98 ppm ($J_{H-2/H-6}=2$ cps)].

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