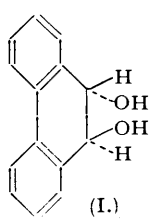
244. *The Reduction of* o-*Quinones with Lithium Aluminium Hydride.*

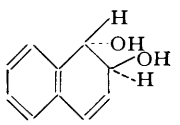
By J. Booth, E. Boyland, and E. E. Turner.

The *o*-quinones of naphthalene, anthracene, and phenanthrene are reduced by lithium aluminium hydride to give *trans*-dihydroxydihydro-derivatives, identical with the metabolites produced from the corresponding hydrocarbons in animals. The (±)-*trans*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene was partly resolved by crystallisation of the (−)-menthoxyacetate. The *cis*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene, in contrast to the *trans*-derivative, formed an *iso*propylidene derivative.

When aromatic hydrocarbons are injected into animals they are converted into glycols by addition of the elements of hydrogen peroxide to the 9 : 10-positions of phenanthrene (I) and

to the 1 : 2-positions of naphthalene (II), anthracene (III), and phenanthrene (IV) (Booth and Boyland, *Biochem. J.*, 1947, **41**, xxix; 1949, **44**, 361; Boyland and Wolf, *ibid.*, 1948, **42**, xxxii; 1950, **46**, in press; Young, *ibid.*, 1947, **41**, **417**). The hydroxyl groups so obtained have the *trans*-configuration. The chief evidence for the *trans*-configuration of the biologically produced 9 : 10-dihydroxy-9 : 10-dihydrophenanthrene was the fact that it differed from the *cis*-9 : 10-


(I.)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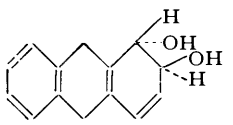
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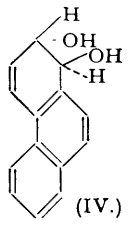
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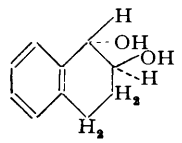
(V.)

dihydroxy-9 : 10-dihydrophenanthrene prepared by oxidation of phenanthrene with osmium tetroxide, by Criegee, Marchand, and Wannowius (*Annalen*, 1942, **550**, 99). The preparation of *trans*-9 : 10-dihydroxy-9: 10-dihydrophenanthrene by catalytic reduction of phenanthraquinone was claimed by Skita (*Ber.*, 1925, **58**, 2685), but no physical description of the product was given and its acetate is described as melting at 184°, whereas the corresponding product now described melts at 174°. Attempts to repeat this catalytic reduction of phenanthraquinone were unsuccessful.

The configuration of the hydroxyl groups of the phenanthrene derivatives is of interest as the *trans*-compound is oxidised more rapidly ($k_{20} = 130$) than the *cis*-compound ($k_{20} = 13{\cdot}8$) by lead tetra-acetate (Boyland and Wolf, *loc. cit.*). This is unusual as the *cis*-glycols are generally oxidised more rapidly than the corresponding *trans*-isomers (Criegee, Kraft, and Rank, *Annalen*, 1933, **507**, 161). Another similar anomaly is the oxidation of the *trans*-9 : 10-dihydroxy-9 : 10-dimethylphenanthrene which Criegee (personal communication) has found to react with lead tetra-acetate more rapidly than does the corresponding *cis*-derivative.

The reduction of phenanthraquinone to 9 : 10-dihydroxyphenanthrene with lithium aluminium hydride has been described by Nystrom and Brown (*J. Amer. Chem. Soc.*, 1948, **70**, 3738), but the present experiments show that the reduction yields only traces of this product, which is soluble in sodium hydroxide, and over 80% of *trans*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene. The corresponding reduction of 1 : 2-naphthaquinone appears to give about equal amounts of alkali-soluble material which may be 1 : 2-dihydroxynaphthalene and 1 : 2-dihydroxy-1 : 2-dihydronaphthalene, but the reduction of *o*-benzoquinone under these conditions yields almost entirely pyrocatechol.

Owing to the small amount of 1 : 2-anthraquinone obtained from anthraquinone-2-sulphonic acid by the synthesis described by Lagodzinski (*Annalen*, 1905, **342**, 59, 67, 80), the 1 : 2-dihydroxy-1 : 2-dihydroanthracene was not isolated in a pure form. It was, however, characterised as the diacetate. Experience with the metabolic diols had shown that acetates were more suitable derivatives for characterisation by melting point than the free alcohols. The amount of the diacetate obtained was not sufficient to allow the preparation of the dihydroxy-compound by hydrolysis.

The configuration of the hydroxyl groups in the natural dihydroxydihydro-derivative of naphthalene (II) was shown to be *trans*- (Booth and Boyland *loc. cit.*, 1949) by converting it into the known *trans*-1 : 2-dihydroxy-1 : 2 : 3 : 4-tetrahydronaphthalene (V) previously prepared by Criegee (*Annalen*, 1930, **481**, 263). This compound differs in many ways from the *cis*-compound described by Straus and Rohrbacher (*Ber.*, 1921, **54**, 40). The 1 : 2-dihydroxy-1 : 2-dihydronaphthalene obtained by reduction of 1 : 2-naphthaquinone was identical with the racemic form of 1 : 2-dihydroxy-1 : 2-dihydronaphthalene isolated from the urine of rats and rabbits dosed with naphthalene.

The synthetic *trans*-1 : 2-glycols from naphthalene, anthracene, and phenanthrene do not give the colour reaction with potassium triacetylosmate (Criegee, Marchand, and Wannowius, *loc. cit.*), which is given by the synthetic *cis*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene and other *cis*-glycols. The configuration of the hydroxyl groups of these phenanthrene derivatives is confirmed by the isolation of an *O-iso*propylidene derivative from the *cis*-compound which was not formed when the *trans*-compound was treated with acetone under the same conditions.

The 1 : 2-dihydroxy-1 : 2-dihydro-naphthalene and -anthracene are asymmetrical about the hydroxylated carbon atoms, so both the *cis*- and the *trans*-forms could be optically active. The

(+)- and the (−)-forms of the *trans*-compounds of naphthalene and anthracene have been isolated as metabolites. On the other hand, 9 : 10-dihydroxy-9 : 10-dihydrophenanthrene is symmetrical about the 9 : 10-carbon atoms and the *cis*-form is thus a *meso*-compound. The *trans*-form must be dissymmetrical and although the 9 : 10-dihydroxy-9 : 10-dihydrophenanthrene isolated as a phenanthrene metabolite was inactive, the synthetic compound has been partly resolved by crystallisation of the (−)-menthoxyacetate. This partial resolution, which is under investigation, is further evidence of the *trans*-configuration of this compound.

Experimental.

Reduction of 1 : 2-*Naphthaquinone.*—1 : 2-Naphthaquinone (4 g.), dried *in vacuo* over phosphoric oxide, was placed in the thimble of a Soxhlet apparatus. Ether (200 ml.; dried over sodium) was placed in the flask of the apparatus with lithium aluminium hydride (in amounts shown in the table) and refluxed

$LiAlH_4$ used, g.	0·5	1·0	2·0	4·0
Yield of 1 : 2-dihydroxydihydronaphthalene	1·0	1·80	1·52	1·9
Yield of alkali-soluble material	0·42	1·36	1·54	1·35

until all naphthaquinone appeared to be extracted. The ethereal solution was cooled, and water (5 ml.) and 2N-sulphuric acid (30 ml.) were added slowly to decompose the excess of lithium aluminium hydride. The ethereal layer was separated by centrifugation, and the residue extracted with ether. The combined ethereal extracts were extracted with 2N-sodium hydroxide and evaporated under reduced pressure. The residue which had an odour of naphthalene was crystallised from benzene and then from *cyclo*hexane and then had m. p. 103° [alone and mixed with (±)-1 : 2-dihydroxy-1 : 2-dihydronaphthalene isolated from the urine of rabbits dosed with naphthalene] (Found : C, 73·9; H, 6·4. Calc. for $C_{10}H_{10}O_2$: C, 74·0; H, 6·2%). The alkaline extracts were acidified and extracted with ether to yield a dark solution the contents of which were not fully characterised.

Reduction of 1 : 2-*Anthraquinone.*—1 : 2-Anthraquinone (0·2 g.), prepared from 9:10-anthraquinone-2-sulphonic acid, was treated with lithium aluminium hydride (0·5 g.) in ether (50 ml., as described above). The reaction mixture was treated with water (5 ml.) and 2N-sulphuric acid. The ethereal layer was extracted with 2N-sodium hydroxide and evaporated, yielding 1 : 2-dihydroxy-1 : 2-dihydroanthracene (0·05 g.), m. p. 170° [the m. p. of (±)-*trans*-1 : 2-dihydroxy-1 : 2-dihydroanthracene isolated from urine of rabbits dosed with anthracene is 184°]. This product was acetylated in pyridine with acetic anhydride and yielded an acetate, m. p. 121° (alone and mixed with an authentic specimen prepared from the natural metabolite) (Found : C, 72·5; H, 5·5. Calc. for $C_{18}H_{16}O_2$: C, 73·0; H, 5·4%).

Reduction of 9 : 10-*Phenanthraquinone.*—9 : 10-Phenanthraquinone (4 g.), dried over phosphoric oxide, was extracted for 3 hours in a Soxhlet apparatus with ether (200 ml.; dried over sodium) containing lithium aluminium hydride (1 g.). To the cooled ethereal solution water (5 ml.) and 2N-sulphuric acid (40 ml.) were added. The ethereal layer and the ethereal extract of the aqueous layer were extracted with 2N-sodium hydroxide, dried (NaOH), and evaporated to dryness. The crude 9 : 10-dihydroxy-9 : 10-dihydrophenanthrene (3·35 g.) was isolated and recrystallised from benzene and then from *cyclo*hexane; it had m. p. 185° [alone or when mixed with (±)-*trans*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene] (Found : C, 79·0; H, 5·5. Calc. for $C_{14}H_{12}O_2$: C, 79·3; H, 5·7%).

The alkaline extract was acidified with 5N-sulphuric acid and extracted with ether. The extract gave 0·25 g. of crude material from which phenanthraquinone (m. p. 205—208° alone and mixed with an authentic specimen) was isolated.

Preparation of cis-9 : 10-iso*Propylidenedioxy*-9 : 10-*dihydrophenanthrene.*—Phenanthrene was oxidised with osmic acid to give *cis*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene (Criegee, Marchand, and Wannowius, *loc. cit.*). (*a*) This *cis*-derivative (0·5 g.) was dissolved in dry acetone (100 ml.) and shaken for 24 hours with anhydrous copper sulphate (1·0 g.). The copper sulphate was filtered off, and the unchanged dihydroxy-compound recovered from the acetone. (*b*) This *cis*-derivative (0·5 g. was dissolved in acetone (25 ml.; dried over potassium carbonate) containing concentrated hydrochloric acid (0·05 ml.). After being kept for 16 hours in a desiccator, the acetone and hydrochloric acid were removed under reduced pressure. The residue was dissolved in dry ether and cooled. Crystals separated which consisted of the unchanged *cis*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene. The filtrate was evaporated to dryness, and the residue crystallised from methyl alcohol containing 20% (v/v) of water. The iso*propylidene* derivative, recrystallised from 80% methyl alcohol, yielded 0·096 g. of white plates, m. p. 61—62° (Found : C, 80·7; H, 6·5. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%).

Failure of trans-9 : 10-*Dihydroxy*-9 : 10-*dihydrophenanthrene to form an* iso*Propylidene Derivative.*—Under precisely the same conditions as above, the *trans*-compound was recovered unchanged.

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