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THE ABSOLUTE CONFIGURATIONS OF THE METABOLITES OF NAPHTHALENE AND PHENANTHRENE IN MAMMALIAN SYSTEMS.

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Among various metabolic pathways[1] opened to condensed aromatic hydrocarbons, the one to yield optically active vicinal dihydrodihydroxy derivatives goes stereoselectively, and the role of oxygenase[2] in this process has been studied intensively.

(-)-9,10-Dihydro-9,10-dihydroxyphenanthrene (Ia) was isolated from the urines of rats or rabbits[3] dosed with phenanthrene by intraperitoneal injection. The fate of naphthalene in their bodies showed very interesting species specificity, e.g., (+)-1,2-dihydro-1,2-dihydroxynaphthalene (III) was found in rabbit urine and its enantiomeric modification was isolated from rat urine[4),5)].

For the studies of the reaction mechanism of oxygenase as well as for the understanding of the relation between metabolic pathways and carcinogenic properties of condensed aromatic hydrocarbons, elucidation of the absolute configurations of these metabolites which will be reported in this communication seems to be crucial.

Absolute Configuration of (-)-trans-9,10-Dihydro-9,10-dihydroxyphenanthrene (Ia).

(-)-(Ia), m.p. 159-161°, $[\alpha]_D^{23}$ -138° (c, 0.355 in $CHCl_3$) obtained by the optical resolution via dimenthoxyacetate following Booth, Boyland and Turner's procedure[6], was acetylated with acetic anhydride and pyridine to afford the diacetate (Ib), m.p. 120-121°, $[\alpha]_D^{24}$ +339° (c, 0.208 in acetone).

After exhaustive ozonolysis of (+)-(Ib) in acetic acid, the reaction product was worked up according to the method of Barton and Miller[7] to give di-O-

* M. Nakazaki, K. Naemura and S. Honmaru, and M. Nakazaki, K. Naemura and R. Miura, Abstracts III, 21st National Meeting of the Chemical Society of Japan, Osaka, Japan, March 1968, p 2189 and 2190.

acetyl-di-p-bromophenacyl tartrate (II), m.p. 155-159°, $[\alpha]_D^{27}$ -10.9° (c, 1.15 in $CHCl_3$) which was identified as the derivative of (+)-tartaric acid by the comparison with an authentic specimen (m.p. 158-159.5°, $[\alpha]_D^{28}$ -9.4° (c, 1.49 in $CHCl_3$)).

This fact indicates the (9S,10S)-configuration of the original glycol (Ia) which is further supported by analyses of the ORD and CD curves of the glycol and its diacetate (Ib) (Fig. 1 and Fig. 2).

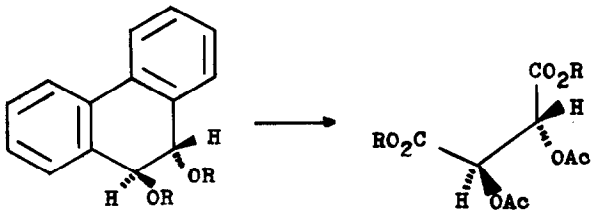
Comparison of the ORD curves with other optically active 1,1'-bridged biphenyls which have known absolute configurations and have been studied extensively by Mislow and his collaborators[8] shows that the (-)-glycol (Ia) has the (S), and the (+)-diacetate (Ib) has the (R) axial chirality of biphenyl series.

OH-π electron bondings[9] appear to be responsible for confining the molecule (Ia) in a rather uncomfortable conformation (Fig. 1).

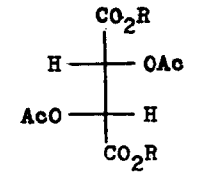
Absolute Configuration of (+)-trans-1,2-dihydro-1,2-dihydroxynaphthalene (III).

(-)-1,2-Dihydroxytetralin (IVa), m.p. 112-113°, $[\alpha]_D^{25}$ -111° (c, 1.05 in $CHCl_3$) which was reported to be derived from (+)-(III) by catalytic hydrogenation, was prepared by optical resolution[10] of racemic (IVa) via the dimenthoxyacetate. Hydrogenolysis of the (+)-diacetate (IVb) obtained by acetylation of (-)-(IVa) with acetic anhydride and pyridine gave (-)-(Vb), m.p. 41-43° $[\alpha]_D^{25}$ -67.2° (c, 1.03 in $CHCl_3$). Comparison with an authentic specimen (m.p. 47.5-48° $[\alpha]_D$ -67° (in $CHCl_3$)) established its identification as (-)-β-tetralol acetate, and this was further confirmed by the conversion into (-)-diphenylcarbamate (Vc)[11], m.p. 115-117°, $[\alpha]_D^{25}$ -22.2° (c, 1.77 in $CHCl_3$).

Since the R-configuration of (+)-β-tetralol (the enantiomer of (-)-(Vb)) has been deduced by the study of the solvolysis of (+)-(R)-indanylcarbinol tosylate[12], the (1S,2S) configuration can be assigned to (-)-(IVa)[13]. And consequently (+)-(III) from rabbit urine is shown to have the (1S,2S) configuration. Detailed analyses of the ORD and CD curves of (III), (IV) and (V) derivatives together with stereochemical features of oxygenase activity toward condensed aromatic hydrocarbons should be the subject of a subsequent communication.

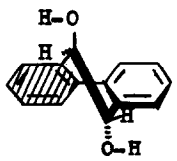


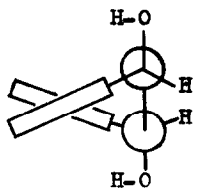
(-)-(Ia) R = H
(+)-(Ib) R = Ac

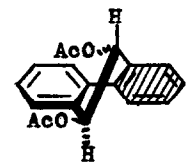


(II)

R = CH_2CO  Br







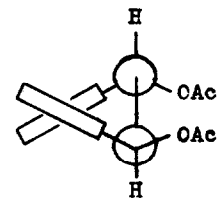
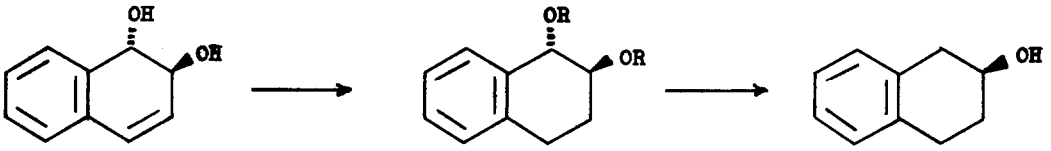


Fig. 1

Fig. 2



(+)-(III)

(-)-(IVa) R = H
(+)-(IVb) R = Ac

(-)-(Va) R = Ac
(-)-(Vb) R = OH
(-)-(Vc) R = OCONHØ

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