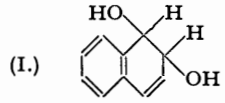
642. *Ultra-violet Absorption Spectra of Some Metabolites of Naphthalene, Anthracene, and Phenanthrene.*

By R. N. Beale and E. M. F. Roe.

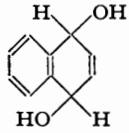
The ultra-violet absorption spectra of metabolites of naphthalene, anthracene, and phenanthrene in rabbit and rat have been measured. Comparison with relevant reference compounds confirms the structure of the naphthalene metabolite to be 1 : 2-dihydro-1 : 2-dihydroxynaphthalene, that of the anthracene metabolite from rat and rabbit to be 1 : 2-dihydro-1 : 2-dihydroxyanthracene, and those of the phenanthrene metabolites from the rabbit to be 9 : 10-dihydro-9 : 10- and 1 : 2-dihydro-1 : 2-dihydroxyphenanthrene and from the rat 9 : 10-dihydro-9 : 10-dihydroxyphenanthrene.

In order to assist in the elucidation of the chemical structures of dihydrodihydroxy-derivatives produced during the metabolism of the hydrocarbons naphthalene, anthracene, and phenanthrene by rabbits and rats (Boyland and Levi, *Biochem. J.*, 1935, **29**, 2679; Booth and Boyland, *ibid.*, 1949, **44**, 361; Boyland and Wolf, *ibid.*, 1950, **47**, 64) the spectra of these substances have been measured and compared with those of relevant reference compounds. The compounds were examined in alcoholic solutions, both spectrographic and spectrophotometric techniques being used.

Naphthalene Metabolites.—Optically active and inactive *trans*-stereo-isomers were isolated as metabolic products of naphthalene from the rat and the rabbit, and these compounds give spectra of the same general shape (Fig. 1 and Table I). There are clearly two most probable structures for these metabolites, *i.e.*, (I) and (II). These should be easily distinguishable spectroscopically, for (I) should have a spectrum resembling that of 1 : 2-dihydronaphthalene,



(I.) and



(II.)

i.e., of the styrene type, while the spectrum of (II) would resemble that of 1 : 4-dihydronaphthalene or of tetralin, *i.e.*, of the *o*-xylene type. The data for these compounds are compared in Table I and indicate structure (I) as the correct formula for the metabolite, in accordance with the chemical evidence (Booth and Boyland, *loc. cit.*). Further, a synthetic specimen of the racemic 1 : 2-dihydro-1 : 2-dihydroxynaphthalene (Booth, Boyland, and Turner, *J.*, 1950, 1188) has a spectrum (Fig. 1; Table I) of the same type as that of the racemic

Table I.

Compound	$\lambda_{max.}$, mμ.	$\varepsilon_{max.}$ (mol.)
Styrene	244	11,000 [1]
1-Propenylbenzene	248	14,900 [2]
Indene	246	10,000 [3]
1 : 2-Dihydronaphthalene	262	10,230 [3]
o-Xylene	263	270 [4]
Tetralin	~267	740 [3]
1 : 4-Dihydronaphthalene	~267	800 [3]
1 : 2-Dihydro-1 : 2-dihydroxynaphthalene (synthetic racemate, m. p. 103°)	263	6,830
,, ,, ,, (rabbit, racemate, m. p. 100°) ...	263	7,850
,, ,, ,, (rabbit, optically active, m. p. 126°)	265	8,410
,, ,, ,, (rat, racemate, m. p. 101°)	264·5	7,790
,, ,, ,, (rat, optically active, m. p. 126°)	265	8,100

[1] Arends, *Ber.*, 1931, **64**, 1936. [2] Koch, *J.*, 1948, 1123. [3] Morton and de Gouveia, *J.*, 1934, 911. [4] Wolf and Herold, *Z. physikal. Chem.*, 1931, *B*, **13**, 201.

rabbit metabolite; the discrepancy in extinction values must be due to impurity in one or both of the compounds. The spectrum confirms structure (I) as the formula for the metabolic 1 : 2-dihydro-1 : 2-dihydroxynaphthalenes.

It is of interest to note the spectral changes in these compounds caused by cyclisation involving the double bond conjugated to the benzene chromophore. Thus, from Table I it is seen that styrene and 1-propenylbenzene have similar spectral characteristics, while in 1 : 2-dihydronaphthalene a considerable bathochromic shift occurs with little change in maximum extinction. This wave-length shift is not found in the spectrum of indene, where cyclisation involves a five-membered ring.

In the early work on the chemistry and spatial configuration of the naphthalene metabolites (Booth and Boyland, *loc. cit.*) these compounds were hydrogenated to the corresponding 1 : 2 : 3 : 4-tetrahydro-1 : 2-dihydroxy-derivatives, and the spectrum of one of them (hydrogenated racemate, m. p. 111°, from rabbit; Fig. 2) was examined, together with those

FIG. 1.

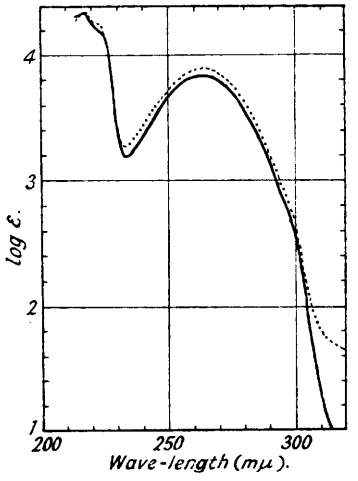


FIG. 2.

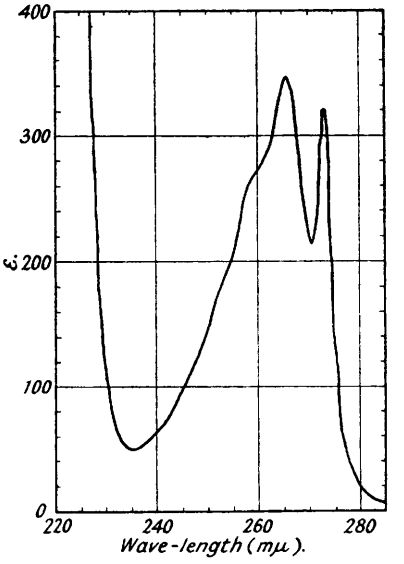


FIG. 1.

1 : 2-*Dihydro*-1 : 2-*dihydroxynaphthalenes* : ——— *synthetic* trans-(*racemate*); – – – *metabolite* (*racemate*) *from rabbit.*

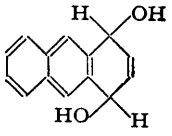
FIG. 2.

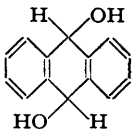
Hydrogenated naphthalene metabolite (*racemate*) *from rabbit.*

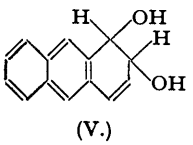
of the hydrogenated synthetic *cis*- and *trans*-racemates. The reduction in extinction which occurs when the ($\Delta^{3:4}$)-conjugated double bond is saturated is as expected, the resulting spectrum resembling that of an alkylbenzene, cf. *o*-xylene (Table I). The spectra are almost the same for the three racemates although there is somewhat closer agreement between those of the synthetic *trans*-isomer and the hydrogenated metabolite than between the latter and the synthetic *cis*-compound. The differences in $\varepsilon_{max.}$ (of the order of 3%) are probably not significant, but the closer agreement between the values of $\lambda_{max.}$ for the synthetic *trans*-compound and the hydrogenated metabolite may be significant (hydrogenated metabolite 272·8 and 265·4 mμ.; *trans*-compound, 272·8 and 265·5 mμ.; *cis*-compound, 272·3 and 265·3 mμ.). Unequivocal spectroscopic differentiation between the *cis*- and the *trans*-derivatives is not possible.

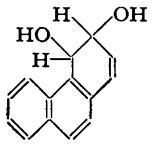
Anthracene and Phenanthrene Metabolites.—One anthracene and two phenanthrene diols were isolated by metabolism of the corresponding hydrocarbons. In the case of the anthracene diol three structures may be postulated, namely, (III)—(V). Chemical evidence (Boyland and Levi, *loc. cit.*) and spectroscopic evidence also (see below) show that (III) and (IV) are impossible structures for this diol. For the phenanthrene diols there are four possible structures, namely, (VI)—(IX). Of these, chemical evidence (Boyland and Wolf, *loc. cit.*) shows that (VI) and (VII) are impossible and that (IX) is the sole product from the rat and

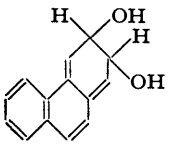
(VIII) and (IX) both result from metabolism in the rabbit. Spectroscopic evidence (see below) supports these conclusions.

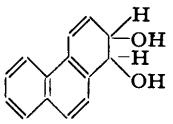

(III.)

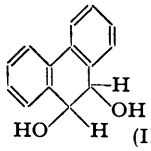

(IV.)


(V.)


(VI.)


(VII.)


(VIII.)


(IX.)

(a) *Phenanthrene metabolite from the rat and rabbit.* This compound was early shown to be the 9 : 10-diol (IX) by comparing its spectrum with that of 9 : 10-dihydrophenanthrene (Fig. 3 and Table II). Comparison with the more recently synthesised *cis*- and *trans*-9 : 10-dihydro-9 : 10-dihydroxyphenanthrenes demonstrated the identity of the metabolites with the *trans*-compound (Fig. 3 and Table II). From an examination of these spectra there

TABLE II.

Phenanthrene deriv.	$\lambda_{max.}$, mμ.	log $\varepsilon_{max.}$
9 : 10-Dihydro-	262	4·20 *
	~289	~3·60
cis-9 : 10-Dihydro-9 : 10-dihydroxy- (synthetic)	269	4·21
	(281)	(4·04)
trans-9 : 10-Dihydro-9 : 10-dihydroxy- (synthetic)	268	4·20
	(300)	(3·41)
,, ,, ,, (metabolite, rat)	267	4·19
	(300)	(3·44)

* Askew, *J.*, 1935, 512.

appears to be interaction of the hydroxyl groups with the aromatic rings in spite of the intervening saturated carbon atoms, since introduction of these groups in 9 : 10-dihydrophenanthrene causes a bathochromic shift in the spectrum of 50—70 A. (Fig. 3). Further, in the case of the synthetic *cis*- and *trans*-diols, there are small but distinct differences between the spectra; *i.e.*, the pronounced shoulder at 300 mμ. in the *trans*-spectrum is missing in the *cis*-spectrum, where a new shoulder is apparent at 281 mμ.; and the minimum at 240 mμ. in the *cis*-spectrum is considerably reduced in extinction compared with that of the *trans*-diol. Consideration of atom models of the isomers shows that in the *cis*-diol there is steric interference between one or other hydroxyl group and its neighbouring hydrogen atom on the aromatic ring, and that this hindrance is dependent on the configuration of the asymmetric carbon atoms. In the *trans*-diol there is either free rotation or steric hindrance for *both* hydroxyl groups, so that the differences in fine structure of the two spectra may probably be attributed to the differing degree of steric hindrance to the interaction of the hydroxyl groups in these two isomers.

(b) *Further phenanthrene metabolite from rabbit and anthracene metabolite from rat and rabbit.* Since chemical evidence indicated (VIII) as the structure for this second phenanthrene metabolite and (V) as that for the anthracene metabolite from rat and from rabbit, search was made for the spectra of relevant reference compounds. No corresponding hydroaromatic derivatives were available, so it was necessary to consider the data for naphthalene derivatives with conjugated substituents at the 1- and 2-positions. Thus the spectrum of (VIII) should resemble that of 1-propenylnaphthalene and that of (V) the spectrum of 2-propenylnaphthalene, for example. The only spectra of this type already recorded were those of 2-vinylnaphthalene (Laitinen, Miller, and Parkes, *J. Amer. Chem. Soc.*, 1947, **69**, 2707; see Table III) and of 1-propenylnaphthalene (Pestemer and Manchen, *Monatsh.*, 1936, **68**, 92).

The two isomeric propenylnaphthalenes were therefore synthesised, by the courtesy of Professor G. A. R. Kon and G. W. Spickett (*J.*, 1949, 2725), and the spectral data are recorded in Fig. 4 and Table III. There was good agreement with Pestemer and Manchen's data for the 1-propenyl) derivative. The spectral details of further naphthalene derivatives listed in Table III illustrate the different effects of substitution at the 1- and 2-positions in the molecule. The differences are small for methyl and chloro-substituents but much greater for strongly interacting conjugating groups. Data for derivatives with strongly polar substituents are omitted since these have different effects. They will be discussed in a later communication.

FIG. 3.

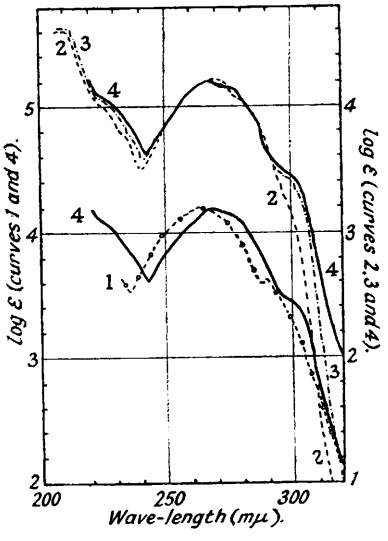


FIG. 4.

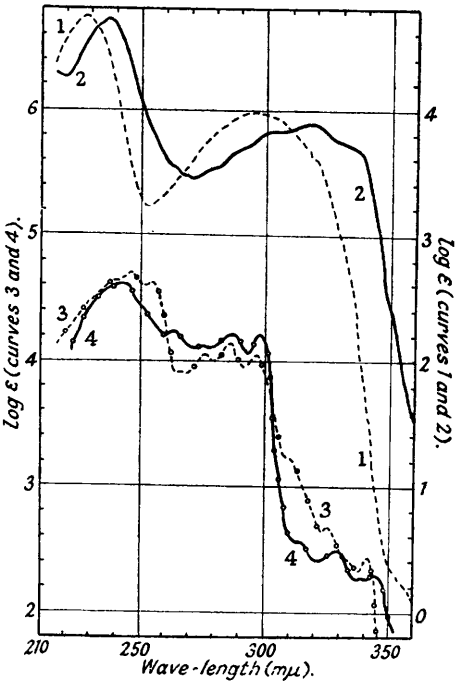


FIG. 3.

9 : 10-*Dihydrophenanthrene* – – O – – O – – (1).
9 : 10-*Dihydro*-9 : 10-*dihydroxyphenanthrene* : *synthetic* (cis) – – – – – – – – (2).
" " " *synthetic* (trans) — · — · — · — (3).
" " " *metabolite* (trans) *from rat* ———— (4).

FIG. 4.

1-*Propenylnaphthalene* – – – – – – – (1).
Phenanthrene metabolite from rabbit ———— (2).
2-*Propenylnaphthalene* – – O – – O – – (3).
Anthracene metabolite from rabbit ——O——O—— (4).

Comparison of the spectrum of the phenanthrene metabolite with those of 1-substituted naphthalenes (Table III and Fig. 4) confirms structure (VIII) for this compound. The spectrum is similar to that of 1-propenylnaphthalene but is shifted considerably to longer wave-lengths, owing in part to cyclisation involving the unsaturated side-chain and to the presence of the two hydroxy-groups (see p. 2885). Slight steric hindrance in the 1-propenylnaphthalene (expected from chemical evidence to be the *trans*-methyl compound) probably enhances this wave-length difference. The spectra of the more strongly hindered 1-phenyl- and 1-*cyclo*hexenyl-naphthalenes suffer an even larger hypsochromic shift compared with the 1-propenyl derivative, and with the phenanthrene metabolite in which the conjugated double bond is coplanar with the naphthalene residue. All of these derivatives show the changes typical of substitution of a strongly interacting group at the 1-position in naphthalene, *i.e.*, a large bathochromic shift and loss of fine structure of the middle band system at 275 mμ.

TABLE III.

Band System.

	A			B			C				
Compound	λ, mμ.	ν, cm.$^{-1}$	ε	λ, mμ.‡	ν, cm.$^{-1}$	ε	λ, mμ.§	ν, cm.$^{-1}$	ε	Solvent †	Ref.
Naphthalene	220·5	45,350	110,650	275	36,360	5,660	311	32,150	249	A	(1)
2-Methylnaphthalene	224	44,640	104,700	276	36,230	4,790	319	31,350	510	A	(2)
2-Chloronaphthalene	—*	—	—	277·5	36,050	4,000	321	31,130	400	H	(3)
2-Phenylnaphthalene	248	40,320	50,100	286	34,960	12,000	—*	—	—	A	(4)
2-Vinylnaphthalene	247	40,485	47,500	285	35,090	14,800	—*	—	—	C	(5)
2-Propenylnaphthalene	246	40,650	51,300	285	35,090	13,850	341	29,325	282	A	(6)
1 : 2-Dihydro-1 : 2-dihydroxyanthracene	244	40,985	42,650	286·5	34,905	16,600	344	29,070	195	A	(6)
1-Methylnaphthalene	—*	—	—	282·5	35,400	5,000	313·5	31,890	240	H	(7)
1-Chloronaphthalene	—*	—	—	284·5	35,160	5,150	320	31,260	200	H	(3)
1-*cyclo*Hexenylnaphthalene	225	44,450	40,000	281	35,590	6,610	—	—	—	A	(4)
1-Phenylnaphthalene	227	44,060	56,200	288	34,720	8,510	—	—	—	A	(4)
1-Propenylnaphthalene	228	43,860	53,600	296	33,785	9,340	—	—	—	A	(6) (8)
1 : 2-Dihydro-1 : 2-dihydroxyphenanthrene	238	42,015	52,300	316	31,650	7,730	—	—	—	A	(6)

(1) Mayneord and Roe, *Proc. Roy. Soc.*, 1935, *A*, **152**, 299. (2) Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127. (3) de Lazlo, *Proc. Roy. Soc.*, 1926, *A*, **111**, 355. (4) Friedel, Orchin, and Reggel, *J. Amer. Chem. Soc.*, 1948, **70**, 199. (5) Laitinen, Miller, and Parkes, *loc. cit.* (6) Present work. (7) de Lazlo, *Z. physikal. Chem.*, 1925, **118**, 369. (8) Pestemer and Manchen, *loc. cit.*

* Band not reported in literature.
† A = Ethyl alcohol; C = chloroform; H = hexane.
‡ The wave-length of maximum extinction of this band system.
§ The wave-length of maximum extinction of the strong band corresponding to the 311-mμ. band in naphthalene.

in naphthalene, so as to engulf the weak long-wave-length bands (in the region of 311 mμ. in naphthalene; Table III).

The spectrum of the anthracene metabolite is different in type from that of the phenanthrene metabolite. Comparison with the spectra of 2-phenyl-, 2-vinyl-, and 2-propenyl-naphthalenes * (Table III; Fig. 4) confirms structure (V) for this diol from anthracene. A methyl or a chloro-substituent at the 2-position in naphthalene affects the spectrum to a much smaller extent. Structure (III) is therefore eliminated for this metabolite since its spectrum would resemble that of 2-methylnaphthalene or, more closely, 2 : 3-dimethylnaphthalene. In all of these compounds, division of the spectrum into three distinct band systems remains, as in naphthalene, an effect typical of 2-substitution in this molecule. Structure (IV) is readily eliminated on spectroscopic grounds since its spectral characteristics should resemble those of *o*-xylene (Table I).

In spite of the origin of the last metabolite in anthracene, its spectrum is remarkably similar to that of phenanthrene (Mayneord and Roe, *loc. cit.*) and this is also true to a smaller extent of the 2-propenylnaphthalene. This probably indicates a marked change of symmetry in the naphthalene molecule on substitution, resulting in changes in the directions of polarisation of the electric vector of the absorbed light. The significance of this will be discussed later.

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* Atom models show the same small degree of steric hindrance in the 2-vinyl- and the *trans*-2-propenyl-naphthalenes and greater hindrance in the *cis*-2-propenylnaphthalene. The close similarity between the spectra of the first two compounds indicates the *trans*-structure for the 2-propenyl derivative.