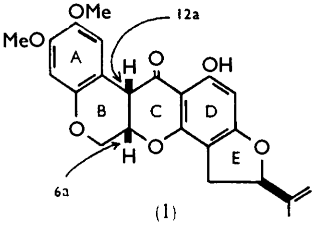
1072. *Structure and Stereochemistry of Sumatrol and Malaccol.*

By L. Crombie and R. Peace.

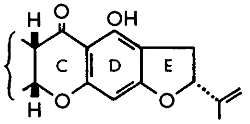
The angular orientation of the D/E rings of natural malaccol and natural sumatrol is established. (±)-Malaccol, however, is of the linear D/E form, and the two reported 6a,12a-dehydromalaccols, both of m. p. 257°, are linear and angularly fused forms. Optical rotatory dispersion correlations with natural rotenone indicate the stereochemistry shown in (I) for sumatrol and in (III) for malaccol.

Degradative study of the natural rotenoids, (—)-sumatrol[1,2] and (+)-malaccol[3,4] [sign of rotation refers to benzene solution], has led to the alternatives (I) or (II) for the former and (III) or (IV) for the latter [without the stereochemical designation]. The angularly fused forms (I) and (III) were preferred by earlier workers mainly because of analogy with the very limited number of known natural rotenoids. Later discovery of pachyrrhizone[5] (V), with a linear D/E system, weakened the inference and makes experimental decision desirable.

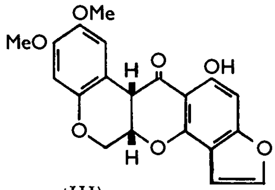
The linear or angular fusion of 11-unsubstituted rotenoids is easily decided as the 10,11-hydrogen atoms are spin coupled and give rise to a quartet in the nuclear magnetic resonance spectra of angular forms.[6] This test is not available for the 11-hydroxyrotenoids, but indophenol formation[7] (Gibbs reaction) provides suitable evidence. As a qualitative test for the presence of a free position *para* to an aromatic hydroxyl group, the reaction can be capricious and we have employed spectrophotometric control.[8] The data have been used more restrictively than usual in that (*a*) the validity of the method was first tested on a pair of established linear and angularly fused D/E 11-hydroxyrotenoids, and (*b*) decision on the two unknown rotenoids is reached by comparison of their linear and angularly fused forms.



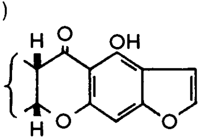
(I)



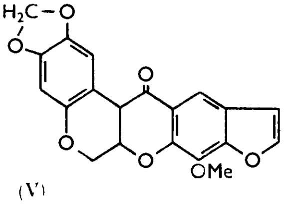
(II)



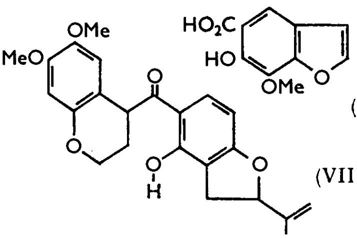
(III)



(IV)



(V)



(VI)

(VII)

The angular D/E fusion of natural (—)- and (±)-α-toxicarol (VIII) and the linear

---

[1] Robertson and Rusby, *J.*, 1937, 497.

[2] Kenny, Robertson, and George, *J.*, 1939, 1601.

[3] Harper, *J.*, 1940, 309.

[4] Harper, *J.*, 1942, 593.

[5] Bickel and Schmid, *Helv. Chim. Acta*, 1953, **36**, 664.

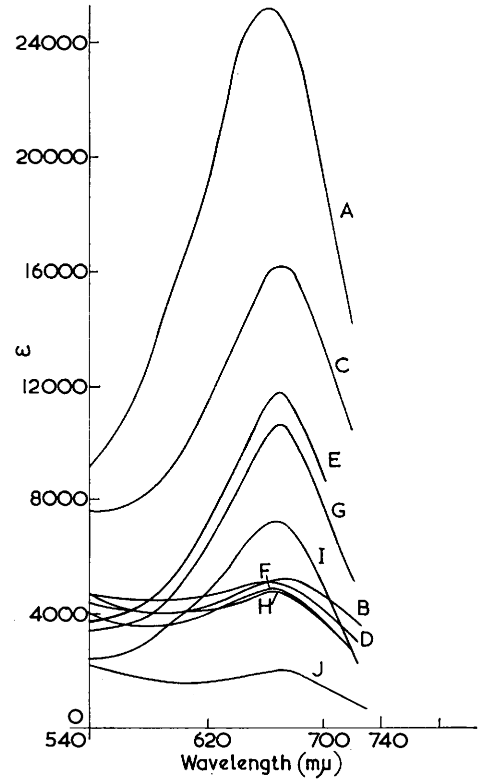
[6] Crombie and Lown, unpublished work.

[7] Gibbs, *J. Biol. Chem.*, 1927, **72**, 649.

[8] King, King, and Manning, *J.*, 1957, 563.

fusion of (±)-β-toxicarol (IX) are rigorously established [9,10] and as expected the infrared spectra of solutions of the first two are identical and differ considerably from that of the last. The figure shows the spectra of the Gibbs reaction products from (±)-β-toxicarol (curve E) with a free position *para* to the hydroxyl group, and from (—)- or (±)-α-toxicarol with a blocked *para*-position (curve F).* Clear differentiation between the two types of fusion is obviously possible.

Natural (+)-malaccol, when boiled with ethanolic sodium acetate, is racemised, and the (±)-product, m. p. 244°, has been accepted as having an unaltered skeleton.[3] We find, however, that the infrared spectrum of its solution differs from that of the (—)-form, and one compound must have the linear and the other the angular fusion, the D/E arrangement being altered because of the two possible ways of re-closing the ion from (X) which results from treatment with base. Natural (+)-malaccol (α-malaccol) is the angular form (III) (curve D) whereas (±)-malaccol, m. p. 244° [now referred to as (±)-β-malaccol], is the linear form (IV) (curve C). This result throws new light on the 6a,12a-dehydromalaccols, the status of which has been obscure.[3] If natural (+)-malaccol is first refluxed with alcoholic sodium acetate and is then treated with iodine and finally zinc, a dehydromalaccol, m. p. 257°, is obtained; (±)-β-malaccol gives a similar product. If, however,



(A) 6a,12a-Dehydro-β-malaccol.
(B) 6a,12a-Dehydro-α-malaccol.
(C) (±)-β-Malaccol.
(D) (+)-α-Malaccol.
(E) (±)-β-Toxicarol.
(F) (—) or (±)-α-Toxicarol.
(G) Natural sumatrol after treatment with sodium acetate (see Experimental).
(H) (—)-α-Sumatrol.
(I) Rotenol.
(J) " Acid P."

---

* The structure of pachyrrhizone and its degradation product " acid P " (VI) seem securely founded.[5] The " acid P," however, is reported to give a positive blue-violet Gibbs reaction [5] which would support an alternative structure. When examined by the technique used here " acid P " gave curve J, consistent with formulation (VI). For comparison, rotenol (VII),[11] with a free *para*-position, gave curve I. The specimen of " acid P " was provided by Professor H. Schmid, to whom we express our thanks.

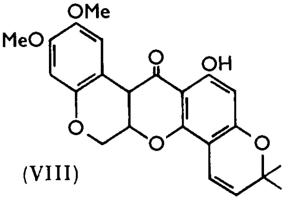
[9] George and Robertson, *J.*, 1937, 1535.

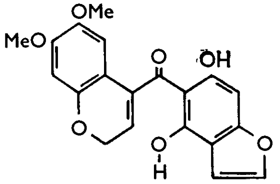
[10] Cahn, Phipers, and Boam, *J.*, 1938, 513.

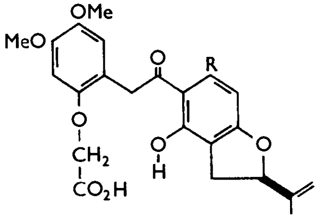
[11] Crombie, Godin, Whiting, and Siddalingaiah, *J.*, 1961, 2876.

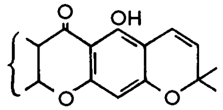
(+)-malaccol is treated with sodium acetate and the iodine is added rapidly, a dehydromalaccol also having m. p. 257°, but giving a large m. p. depression with the former, is isolated.[3] The infrared spectra of their solutions are different. Curve A shows that the first method gives, as expected, a linearly D/E-fused 6a,12a-dehydro-compound (cf. IV) whilst the second procedure gives the corresponding angular α-form (cf. III) (curve B).

Curve H shows that natural (—)-sumatrol belongs to the angularly fused D/E class (I). Treatment of this with mild base can theoretically give a mixture of four linear and four angular D/E stereoisomers, but if compounds having the thermodynamically unstable B/C fusion are discounted, this is reduced to four. Curve G shows the spectrum of the indophenols derived from the product isolated from such treatment with base. The product is largely, if not entirely, linearly D/E-fused, though separation of the individual diastereoisomers has not been undertaken because of the small supply of (—)-sumatrol available.

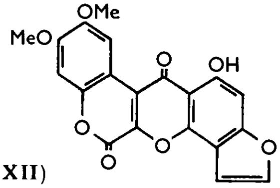

(VIII)


(X)


(XI)


(IX)

Professor W. Klyne has kindly compared the optical rotatory dispersion of sumatrolic acid[1] (XI; R = OH) with derrisic acid (XI; R = H) derived from natural rotenone. Both have the same type of negative plain curve, indicating that the 5′ centre of sumatrol has the same absolute configuration as in rotenone. This result has recently been confirmed by Professor C. Djerassi and Dr. W. D. Ollis who have also shown that 11-acetylsumatrol[12] and sumatrol[13] have a positive Cotton effect superimposed on the above negative plain curve. Rotenone also shows a positive Cotton effect[12] so that the stereochemistry of sumatrol appears to be the same as that of rotenone,[14] *i.e.*, 6aβ, 12aβ,5′β (I). Malaccol has recently been examined for us by Professor Djerassi and also has a positive Cotton effect: it too must therefore be 6aβ, 12aβ (III).


(XII)

EXPERIMENTAL

Materials Used.—Natural malaccol had m. p. 244—246°, $[\alpha]_D^{20}$ +190° (*c* 1·2 in chloroform) {lit.,[3] m. p. 225°, remelting as (±)-malaccol (racemisation) at 244°, $[\alpha]_D^{18}$ +190° (1·02 in chloroform)}. Natural sumatrol had m. p. 196—198° $[\alpha]_D^{20}$ −182° (*c* 2·84 in benzene) when freshly recrystallised: the m. p. was unaltered after storage for some days; {lit.,[1] m. p. 192—194°, 195—196° after storage for 3 days: $[\alpha]_D$ −184° (*c* 1·335 in benzene)}. Natural toxicarol had m. p. 104° (from ethyl acetate–ethanol), $[\alpha]_D^{19}$ −67·5° (*c* 2·25 in benzene) {lit.,[13] m. p. 103°, $[\alpha]_D^{20}$ −67° (benzene)}. (±)-α-Toxicarol had m. p. 218—219°, and (±)-β-toxicarol m. p. 166—167° [lit.,[10] m. p. 219° and 165—167°, respectively].

Procedure for Gibbs's Reaction.—The weighed sample (approx. 2 mg.) in " AnalaR " pyridine (1 ml.) was treated with a fresh solution of 2,6,*N*-trichloro-*p*-benzoquinoneimine in pyridine (5 ml. of 0·2% solution) and diluted to 125 ml. with sodium borate buffer (pH 9·2). Spectral

---

[12] Djerassi, Ollis, and Russell, *J.*, 1961, 1448.

[13] Djerassi and Ollis, personal communication.

[14] Büchi, Crombie, Godin, Kaltenbronn, Siddalingaiah, and Whiting, *J.*, 1961, 2843.

curves were measured by a Unicam S.P. 600 instrument against a cell containing the reagent system without the sample. The curves shown in the Figure were all measured at 20 min. as $\varepsilon_{\text{max.}}$ values change with time. This was investigated for most of the samples and is illustrated as follows:

	20 min.	40 min.	60 min.	80 min.
α-Toxicarol	4900	5200	5400	—
β-Toxicarol	11,900	12,500	12,600	12,800

There was little change in $\lambda_{\text{max.}}$, 670—675 mμ.

Besides the compounds in the Table, compounds of the rotenonone type derived from malaccol [m. p. 301° (decomp.)] (*i.e.*, XII) and α-toxicarol [m. p. 284—285° (decomp.)] were examined. These gave no maximum in the Gibbs reaction curve, but the rotenonone type of compound from β-toxicarol had $\lambda_{\text{max.}}$ 710 mμ. The compounds were made by oxidation of the parent rotenoids by active manganese dioxide [11] and we thank Dr. P. J. Godin for these measurements.

(±)-β-*Malaccol.*—(+)-α-Malaccol (50 mg.) was refluxed in acetone (2 ml.), containing potassium carbonate (100 mg.), for 2 hr. The mixture was poured into water, and just acidified, and the product was crystallised from chloroform–ethanol to give pale yellow needles, m. p. and mixed m. p. with an authentic specimen of "(±)-malaccol" 249°.[3] (±)-β-Malaccol had $\lambda_{\text{max.}}$ (in ethanol) 248i, 253, 288, and 357 mμ (ε 30,300, 36,100, 15,100, and 1800), $\nu_{\text{max.}}$ (in chloroform) 1653, 1629, and 1590 cm.$^{-1}$. (+)-α-Malaccol had $\lambda_{\text{max.}}$ (in ethanol) 246, 253·5, 264i, 287, and 362 mμ (ε 29,200, 34,100, 13,600, 12,000, and 2500), $\nu_{\text{max.}}$ (chloroform) 1645, 1623i, and 1605 cm.$^{-1}$.

6a,12a-Dehydro-α-malaccol.—Natural α-malaccol (100 mg.), suspended in boiling alcohol (10 ml.) containing iodine (200 mg.), was refluxed for 1 hr. with sodium acetate (200 mg.) in ethanol (4 ml.). The yellow product (105 mg.) was refluxed with zinc dust (100 mg.) in acetic acid (2 ml.) for 2 hr., more zinc (50 mg.) being added during the reaction. The mixture was filtered and, on cooling, deposited 6a,12a-dehydro-α-malaccol, m. p. 246—250° (from chloroform–ethanol), m. p. 258° (after sublimation), $\lambda_{\text{max.}}$ (in ethanol) 233, 240i, 257, and 315 mμ (ε 28,300, 27,900, 27,000, and 14,700), $\nu_{\text{max.}}$ (in chloroform) 1656, 1613, and 1592 cm.$^{-1}$. Harper gives m. p. 257°.[3] The compound depressed to 236° the m. p. of 6a,12a-dehydro-β-malaccol [3] (m. p. 257°), $\lambda_{\text{max.}}$ (in ethanol) 235i, 260, 275, and 312 mμ (ε 22,000, 32,000, 32,000, and 16,800), $\nu_{\text{max.}}$ (in chloroform) 1658, 1626, and 1600 cm.$^{-1}$.

Treatment of (—)-Sumatrol with Sodium Acetate.—Natural sumatrol (50 mg.) was refluxed with ethanol (10 ml.) containing sodium acetate (100 mg.) for 2 hr. The product (50 mg.) had m. p. 160—170° and crystallised from chloroform–ethanol (1 : 3) to give a stereoisomeric mixture (15 mg.), m. p. 183—190°, which was used to obtain curve (G).

We are grateful to Professor S. H. Harper for gifts of natural malaccol and its derivatives, and to Professor W. Klyne, Professor C. Djerassi, and Dr. W. D. Ollis for optical rotatory dispersion information. One of us (R. P.) is grateful to the Department of Scientific and Industrial Research for a postgraduate award.

Department of Chemistry, University of London, King's College,
Strand, W.C.2.
[*Received, June 22nd,* 1961.]