369. *The Chemistry of Fungi. Part XXXI.* The Structure of Rosenonolactone.*

By Adelaide Harris, Alexander Robertson, and W. B. Whalley.

Dehydrogenation of rosenonolactone, a metabolite of *Trichothecium roseum* Link, and of dihydro*iso*rosenonolactone gives 1 : 7-dimethyl- and 9-hydroxy-1 : 7-dimethyl-phenanthrene, a result which, in conjunction with the composition and properties of the lactones, shows that they are diterpenoid derivatives having the same nucleus. Rosenono- and *iso*rosenono-lactone and their derivatives are γ-lactones, an examination of which in conjunction with earlier work [1] enables provisional structures to be ascribed to the metabolite and its degradation products.

In continuation of the investigation on rosenonolactone,[1] a metabolite from the mycelium of *Trichothecium roseum* Link, the empirical formula $C_{20}H_{28}O_3$ has been substantiated and the compound found to exhibit infrared absorption at 1786 cm.$^{-1}$, indicating that it is a γ-lactone. Further, from the formula it appeared that this lactone was in all probability a diterpene derivative, a view now substantiated by the production of 1 : 7-dimethyl- and 9-hydroxy-1 : 7-dimethyl-phenanthrene on dehydrogenation of the lactone with selenium. The formation of the phenanthrol (I) clearly indicates the position of the keto-group. which from the infrared absorption of rosenonolactone at 1724 cm.$^{-1}$ (in CCl_4) and 1721 cm.$^{-1}$ (Nujol) together with the ultraviolet spectrum ($\lambda_{max.}$ 289 mμ, log ε 1·6) is present in a six-membered ring, whilst the fact that dihydrorosenonolactone is a saturated compound provides collateral evidence that rosenonolactone is tricyclic and may be represented by the partial formula (II). Thus rosenonolactone may be regarded, for purposes of nomenclature as a derivative of the hypothetical, fully saturated hydrocarbon, rosane.

In a re-examination of the behaviour of rosenonolactone with 2N-alcoholic acid it has been found that this reagent converts the lactone into a mixture of the unchanged compound and *iso*rosenonolactone, which from the ultraviolet ($\lambda_{max.}$ 290 mμ, log ε 1·3) and

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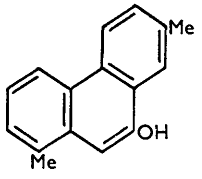
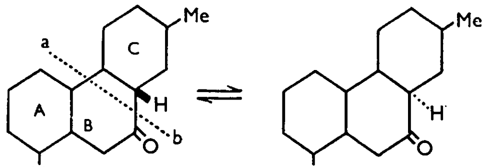
* Part XXX, *J.*, 1957, 4931.

[1] Robertson, Smithies, and Tittensor, *J.*, 1949, 879.

infrared (1712 and 1776 cm.$^{-1}$) absorption spectrum contains an isolated carbonyl group and a γ-lactone system; this reaction is reversible. The product previously designated *allo*rosenonolactone,[1] or compound (A), is not formed and the material thus described in the earlier communication [1] is a mixture difficult to separate; this has been resolved by



(I)



(II) (III)

fractional crystallisation into rosenono- and *iso*rosenono-lactone. Accompanying *iso*-rosenonolactone is a small quantity of a keto-dienoic acid, $C_{20}H_{28}O_3$, previously designated compound (B) [1] which exhibits only isolated carbonyl absorption in the ultraviolet spectrum ($\lambda_{max.}$ 286 mμ, log ε 1·89).

On reduction with potassium borohydride the carbonyl group of rosenonolactone gives rise to the corresponding secondary alcohol, rosenololactone, $C_{20}H_{30}O_3$ (infrared absorption at 3483 cm.$^{-1}$), which appears to be essentially stereochemically homogeneous, retains the γ-lactone system (infrared absorption at 1786 cm.$^{-1}$), forms an acetate, $C_{22}H_{32}O_4$, and regenerates rosenonolactone on oxidation with chromic oxide in pyridine. Similarly, on reduction *iso*rosenonolactone gives *iso*rosenololactone which retains the γ-lactone system (infrared absorption at 1783 cm.$^{-1}$) and is oxidised by chromic oxide in pyridine to *iso*-rosenonolactone. When this reduction is effected at a temperature of *ca.* 50° *iso*rosenono-lactone gives a mixture of *iso*rosenolo- and rosenolo-lactone, owing presumably to the conversion of some *iso*rosenonolactone into rosenonolactone before reduction since both rosenolo- and *iso*rosenolo-lactone are stable in the alkaline conditions which effect the interconversion of rosenono- and *iso*rosenono-lactone, a fact which clearly indicates that the keto-group is involved in the rosenono-$\rightleftharpoons$*iso*rosenono-lactone transformation. When heated with alcoholic hydrochloric acid, rosenololactone gives a high yield of an unsaturated hydroxy-acid, rosenolic acid (hydroxyrosenoic acid), $C_{20}H_{30}O_3$, by hydration of the γ-lactone system with simultaneous elimination of water, involving the liberated hydroxyl group which is probably tertiary. Similarly, *iso*rosenololactone furnishes *iso*rosenolic acid, $C_{20}H_{30}O_3$. Since on dehydrogenation with selenium both rosenono- and dihydro*iso*-rosenono-lactone give 1 : 7-dimethylphenanthrene together with 9-hydroxy-1 : 7-dimethyl-phenanthrene it seems reasonably certain that rosenono- and *iso*rosenono-lactone have the same carbon skeleton and hence the difference between the normal and the *iso* series is probably stereochemical and of the type (II) $\rightleftharpoons$ (III).

Condensation of either dihydrorosenono- or dihydro*iso*rosenono-lactone with ethane-dithiol gave the same mercaptal, $C_{22}H_{34}O_2S_2$, which cannot, at this stage, be assigned to the normal or *iso* series, and it follows that the same ambiguity applies to the derivatives of this mercaptal. On desulphurisation with Raney nickel this compound furnished *iso*(?)hydroxyrosanoic lactone, $C_{20}H_{32}O_2$, devoid of ketonic properties and having a γ-lactone system (infrared absorption at 1779 cm.$^{-1}$). This lactone, which gives only 1 : 7-dimethylphenanthrene on dehydrogenation, forms a solution in hot alcoholic sodium hydroxide which remains clear on dilution with water and from which the unchanged compound was recovered on acidification 24 hours later, a result in agreement with the hypothesis that the carbonyl group is involved in the normal $\rightleftharpoons$ *iso* series interconversion. On being heated with alcoholic hydrochloric acid or with naphthalene-2-sulphonic acid *iso*(?)hydroxyrosanoic lactone was converted in high yield into *iso*(?)rosenoic acid which, in view of its ultraviolet spectrum (log ε 3·39 at 214 mμ) and titration with perbenzoic acid (which indicates one double bond), in conjunction with its failure to be hydrogenated under the standard conditions, appears to contain a tetrasubstituted double bond. The smooth decarboxylation of *iso*(?)rosenoic acid at the melting point indicates that the double bond is in the βγ-position to the carboxyl group. Methyl *iso*(?)rosenoate, $C_{21}H_{32}O_2$, is reduced with lithium aluminium hydride to *iso*(?)rosenol, $C_{20}H_{34}O$ (infrared absorption, 3322 cm.$^{-1}$ in Nujol), and on oxidation with *tert.*-butyl chromate this primary alcohol gave the corresponding aldehyde, *iso*(?)rosenal, which was isolated as the semicarbazone, $C_{21}H_{25}ON_3$. By Wolff–Kishner reduction this derivative gave the hydrocarbon, *iso*(?)rosene, $C_{20}H_{34}$, which on dehydrogenation furnished 1 : 7-dimethylphenanthrene in high yield, thereby establishing that the carboxyl group of rosenonolactone and hence of *iso*rosenonolactone occupies a tertiary position.

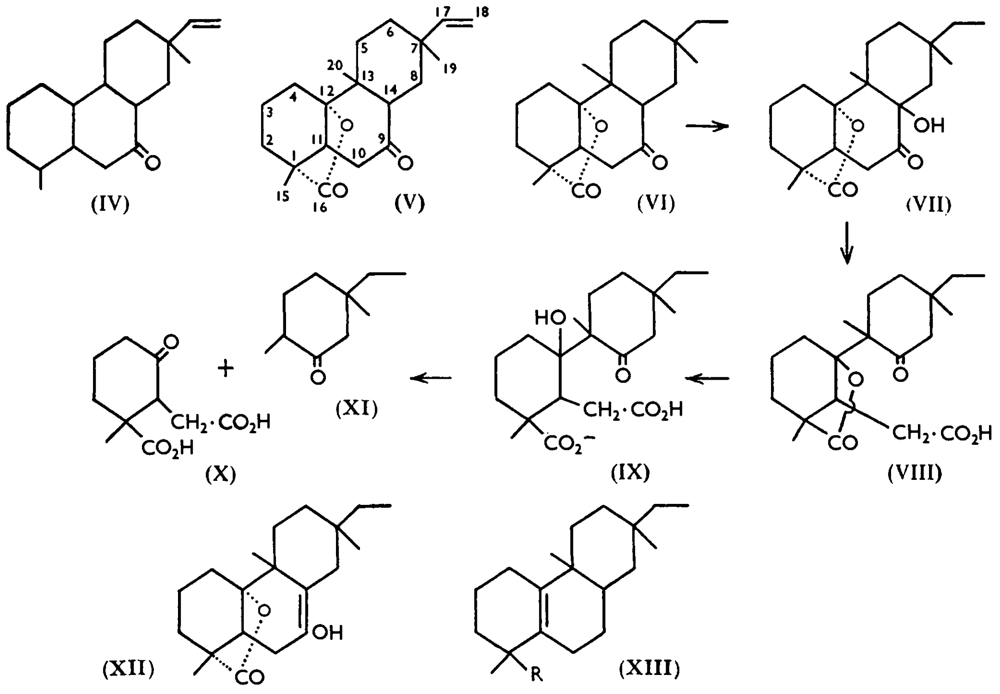
For convenience the acid, $C_{20}H_{30}O_5$, obtained by the oxidation [1] with potassium permanganate of sodium dihydro*iso*rosenonate, *i.e.*, a solution of dihydrorosenonolactone in aqueous sodium hydroxide, has been named rosoic acid. An investigation of the infrared spectrum of methyl rosoate in carbon tetrachloride indicates the presence of the following groups: γ-lactone (1783), ester (1748), and isolated ketone (1709 cm.$^{-1}$), in which the last assignment is confirmed by the ultraviolet absorption ($\lambda_{max.}$ 293—295 mμ, log ε 1·6). Reduction of methyl rosoate with potassium borohydride gives a dilactone, $C_{20}H_{30}O_4$, with infrared absorption at 1786 (γ-lactone) and 1745 cm.$^{-1}$ (ε-lactone) which is not cleaved by alkali, titrates as a dilactone, and is devoid of methoxyl and ketonic groups; methyl rosoate therefore cannot be a diketone. Rosoic acid, which is readily degraded by mild alkaline hydrolysis to a cyclic ketone $C_{10}H_{18}O$, and a dibasic keto-acid $C_{10}H_{18}O_5$,[1] is not readily decarboxylated and therefore unlikely to be a β-keto-acid. Since it appears reasonably certain that dihydro*iso*rosenonolactone contains a perhydrophenanthrene structure the combination of oxidation to rosoic acid and degradation of this with alkali must split the central ring B [as at line ab in (II)]. Further, since the Kuhn–Roth estimation shows that rosoic acid and dihydro*iso*rosenonolactone have the same *C*-methyl content it is clear that the formation of rosoic acid does not involve the conversion of a *C*-methyl group into a carboxyl group, but must occur by the scission of a carbon–carbon linkage of ring B in formula (II), and that the fission of the remaining link is effected by the alkali with the production of the two C_{10} moieties. Moreover, since rosoic acid does not appear to be a β-keto-acid or a β-diketone, fission of the carbon–carbon bond with alkali is almost certainly a retro-aldol condensation and as rosoic acid is saturated the operative residue in this condensation must be of the type $>\!C(OH)\cdot\overset{|}{\underset{|}{C}}\cdot CO\cdot$ and not $\cdot C{:}C\cdot CO\cdot$.

On oxidation with nitric acid the cyclic ketone, $C_{10}H_{18}O$, derived from rosoic acid furnished α-ethyl-α-methylsuccinic acid, the specific rotation of which could not be determined with the quantity of acid available. The acid was however identified by its infrared absorption spectrum (in Nujol) [the same as that of (±)-α-ethyl-α-methylsuccinic acid]. Consequently, contrary to earlier views,[1] the succinic acid arises from a *gem*-methylvinyl residue in the ring of rosenonolactone giving rise to the $C_{10}H_{18}O$ ketone. This result in conjunction with the conversion of rosenonolactone into formaldehyde and an acid (carboxynorrosenonolactone), $C_{19}H_{26}O_5$, with ozone serves to establish the presence of the $>\!CMe\cdot CH{=}CH_2$ system in the metabolite, and hence by analogy with the diterpenes of the dextropimaric acid series the partial structure (II) for rosenonolactone may be expanded to (IV).

The infrared absorption spectrum of the ketone $C_{10}H_{18}O$ shows the presence of a carbonyl group in a six-membered ring (1718 cm.$^{-1}$; film) consistent with the ultraviolet absorption spectrum ($\lambda_{max.}$ 283, log ε 1·6) and with the oxidation of this ketone by ozone to a monobasic keto-acid $C_{10}H_{18}O_3$.[1] In contrast with the parent C_{10} ketone this keto-acid gives an iodoform reaction, indicating the presence of a $CH_3\cdot CO\cdot$ group and hence the parent C_{10} ketone must contain the residue $\cdot CO\cdot CHMe\cdot$.

The C_{10} dibasic keto-acid,[1] derived from rosoic acid, is substantially unaffected by neutral potassium permanganate solution and alkaline hydrogen peroxide and hence must be a saturated, cyclic compound. The carbonyl group, which is ketonic and not aldehydic, exhibits absorption in the ultraviolet region at $\lambda_{max.}$ 284—286 mμ (log ε 1·39) and in the infrared region at 1710 cm.$^{-1}$ (in Nujol), is unconjugated and hence must be present in a six-atom ring.

The foregoing experimental results together with earlier work [1] may be rationalised in terms of structure (V) for rosenonolactone and (VI) for dihydrorosenonolactone. On this


(IV) (V) (VI) (VII) (VIII) (IX) (X) (XI) (XII) (XIII)

view the oxidation of sodium dihydro*iso*rosenonate probably proceeds by way of the α-ketol (VII) to rosoic acid (VIII) which in alkaline solution furnishes the anion (IX) with subsequent fission (retro-aldol condensation) of the β-hydroxy-ketone to give the C_{10} cyclic ketone (XI) and the C_{10} dibasic keto-acid (X); these structures agree with the general properties recorded for these substances in Part VI.[1] In accordance with the relative positions of the carboxyl groups in formula (X) and consequently in (IX) the acid (X) furnishes an anhydride. Formula (V) for rosenonolactone is also compatible with the rosenono–*iso*rosenono-lactone interconversion by way of the common enol (XII) (or its equivalent) but, whilst further definition of this change is required, it may be noted that the formation of enolic acetates [1] from *iso*rosenonolactone and dihydro*iso*rosenonolactone is significant in this connection. Furthermore, on the basis of the structure (VI) for dihydrorosenonolactone, *iso*(?)rosenoic acid may be represented as *iso*(?)ros-11 : 12-en-16-oic acid (XIII; R = CO_2H), *iso*(?)rosenol as *iso*(?)ros-11 : 12-en-16-ol (XIII; R = CH_2·OH) and *iso*(?)rosenal as *iso*(?)ros-11 : 12-en-16-al (XIII; R = CHO).*

The attachment of the third *C*-methyl residue to position 13 and of the carboxyl group to position 1 in formula (V) accords with the properties of rosenonolactone and its degradation products whilst the situation of the carboxyl residue is in agreement with the orientations of other natural diterpenoid acids, *e.g.*, abietic, vinhaticoic, and dextropimaric acid.

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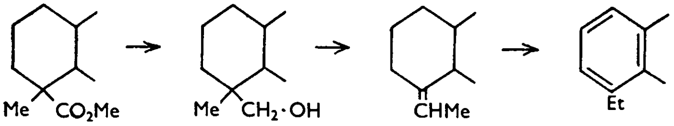
* The possibility that the double bond in these compounds occupies the 10 : 11- or (less probably) the 4 : 12-position cannot be excluded at this stage.

Moreover, from among the available tertiary locations for the carboxyl group, *viz.*, 1-, 11-, 12-, 13-, and 14-position in (V), allocation of the group to the 1-position appears to accommodate the experimental facts most satisfactorily. The divergence of formula (V) for rosenonolactone from the isoprene rule is not necessarily a valid objection since other diterpenes, *e.g.*, vouacapenic [2] and vinhaticoic acid,[3] do not conform to this principle. Attempts to substantiate the position of the carbonyl group in rosenonolactone by the following established reaction sequence [4] were unsuccessful:



Dehydration of *iso*(?)ros-11 : 12-en-16-ol furnished a conjugated heteroannular diene, $C_{20}H_{32}$ ($\lambda_{max.}$ 241, log ε 3·7), which was catalytically hydrogenated to a mono-ethenoid hydrocarbon, $C_{20}H_{34}$, in which resistance to further saturation together with the light absorption (log ε 3·66 at 216 mμ) indicate that the double bond is tetrasubstituted. On dehydrogenation this hydrocarbon, which may be a mixture, furnished a complex product from which a small quantity of 1 : 7-dimethylphenanthrene was isolated together with an aromatic polycyclic hydrocarbon having the properties and characteristic ultraviolet absorption spectrum of an anthracene.

Lactonisation of *iso*(?)ros-11 : 12-en-16-oic acid with sulphuric acid at $-5°$ furnishes a saturated γ-lactone, *allo*hydroxyrosanoic lactone, $C_{20}H_{32}O_2$ (infrared absorption at 1779 cm.$^{-1}$), together with a very small quantity of a second isomeric γ-lactone, *neo*hydroxyrosanoic lactone (see the following paper), neither of which is identical with the isomeric hydroxy*iso*(?)rosanoic lactone derived from the mercaptal of dihydrorosenonolactone. No correspondence between these three lactones and the structurally associated γ-lactones derived from dextropimaric acid [5] has been established. Whilst the stereochemistry of rosenonolactone cannot be profitably discussed at this stage it seems probable that inversion of C_{14} (formula V) occurs during the acid-catalysed lactonisation of (XIII; R = CO_2H) (cf. ref. 5) and that the 1-carboxyl and the 13-methyl group in the acid and hence in rosenonolactone are *cis*.

EXPERIMENTAL

Dehydrogenation of Rosenonolactone.—Rosenonolactone [1] separated from alcohol–chloroform or from benzene in prisms, m. p. 208°, $[\alpha]_D^{18}$ $-116°$ (*c* 2·0 in $CHCl_3$), $\lambda_{max.}$ 289 mμ (log ε 1·6; log ε 1·98 at 216 mμ) (Found: C, 75·9, 75·8; H, 9·0, 9·0. Calc. for $C_{20}H_{28}O_3$: C, 75·9; H, 8·9%). Robertson *et al.*[1] record m. p. 214°, $[\alpha]_D^{20}$ $-107·5°$. A mixture of the lactone (4 g.) and powdered selenium (8 g.) was kept at 320—330° for 48 hr., allowed to cool, and extracted with ether. The filtered ethereal solution was washed with N-sodium hydrogen carbonate (300 ml.), 2N-sodium hydroxide, and water, then dried and evaporated, leaving a partly crystalline residue which on purification by chromatography from light petroleum (b. p. 60—80°) on active aluminium oxide, followed by elution with the same solvent, gave 1 : 7-dimethylphenanthrene. This formed plates (0·68 g.), m. p. and mixed m. p. 85°, from methanol and gave a picrate, m. p. and mixed m. p. 132°.

Acidification of the aqueous sodium hydroxide extract gave a solid (0·15 g.). By the methyl sulphate–potassium carbonate method this gave a product which was purified by chromatography from light petroleum (b. p. 60—80°) on activated aluminium oxide. Concentration of the eluate gave 9-methoxy-1 : 7-dimethylphenanthrene, which separated from light petroleum (b. p. 60—80°) in plates (0·88 g.), m. p. and mixed m. p. 132°, having an infrared absorption spectrum identical with that of an authentic specimen (Found: C, 86·2; H, 6·5; OMe, 13·4. Calc. for $C_{16}H_{13}$·OMe: C, 86·4; H, 6·8; OMe, 13·1%).

Oxidation of the 9-methoxy-1 : 7-dimethylphenanthrene (0·2 g.) in acetic acid (2 ml.) with

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[2] King, Godson, and King, *J.*, 1955, 1117.
[3] King and King, *J.*, 1953, 4158.
[4] Ruzicka, de Graaf, and Müller, *Helv. Chim. Acta*, 1932, **15**, 1300.
[5] Le-van-Thoi and Ourgaud, *Bull. Soc. chim. France*, 1955, 317.

chromic oxide (0·3 g.) at 100° for 5 hr. furnished 1 : 7-dimethyl-9 : 10-phenanthraquinone which was condensed directly with *o*-phenylenediamine, yielding the requisite quinoxaline derivative,[6] m. p. and mixed m. p. 192° (Found: N, 8·9. Calc. for $C_{22}H_{16}N_2$: N, 9·1%).

iso*Rosenonolactone.*—A solution of rosenonolactone (1 g.) in alcohol (90 ml.) and hydrochloric acid (10 ml.) was heated under reflux for 2 hr., cooled, diluted with water (100 ml.), and basified with 2N-aqueous sodium hydroxide. The precipitate was isolated next day and on repeated crystallisation from methanol furnished, as the less soluble fraction, rosenonolactone (0·4 g.), m. p. and mixed m. p. 214°, with the requisite infrared absorption spectrum and specific rotation. The more soluble fraction consisted of *iso*rosenonolactone (0·1 g.), m. p. and mixed m. p. 144°. Acidification of the alkaline liquor gave an acid which separated from benzene or aqueous acetone in needles (50 mg.), m. p. 209° (decomp.) (Found: C, 75·7; H, 9·2%; equiv., 318·7. Calc. for $C_{20}H_{28}O_3$: C, 75·9; H, 8·9%; equiv., 316·4).

Under the same conditions *iso*rosenonolactone (1 g.) gave a mixture of rosenonolactone (0·2 g.), m. p. and mixed m. p. 214°, with the requisite infrared spectrum and specific rotation, and unchanged *iso*rosenonolactone (0·2 g.), plus the acid (50 mg.), m. p. and mixed m. p. 209°.

Rosenololactone.—When a solution of potassium borohydride (0·5 g.) in the minimum volume of water, containing 2 drops of 2N-sodium hydroxide, was added dropwise to rosenonolactone (1 g.) dissolved in methanol (200 ml.) at 35° (agitate), immediate effervescence occurred. Methanol was added as required to maintain a clear solution and 1 hr. later the mixture was diluted with water and the crystalline precipitate (0·9 g.) purified from benzene–chloroform, yielding *rosenololactone* in prisms (0·75 g.), m. p. 222° after softening at 218° (Found: C, 75·6; H, 9·6. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%). A mixture of this alcohol (0·1 g.), 2N-aqueous sodium hydroxide (5 ml.), and ethanol (7 ml.) was heated under reflux for 1¼ hr. On dilution with water (150 ml.) the cooled solution remained clear but subsequent acidification furnished a precipitate (0·09 g.) which on purification from methanol gave unchanged rosenololactone, m. p. and mixed m. p. 222° with softening from 218°. On oxidation by pyridine–chromic oxide for 12 hr. at 20° rosenololactone (0·5 g.) yielded rosenonolactone (0·4 g.), identical with an authentic specimen.

Prepared by the pyridine–acetic anhydride method, the *acetate* of rosenololactone separated from methanol in prisms, m. p. 186°, $[\alpha]_D^{20}$ +59·2° (*c* 0·15 in $CHCl_3$) (Found: C, 73·4; H, 9·1. $C_{22}H_{32}O_4$ requires C, 73·3; H, 9·0%), which on deacetylation with boiling 2N-aqueous sodium hydroxide (10 ml.) and alcohol (10 ml.) for 3 hr. regenerated the parent compound, m. p. and mixed m. p. 222°.

Rosenolic Acid.—A mixture of rosenololactone (0·5 g.), alcohol (90 ml.), and hydrochloric acid (10 ml.) was heated under reflux for 2 hr., cooled, basified with 2N-aqueous sodium hydroxide at 0°, extracted with ether, and acidified. The resulting precipitate was purified from acetone–light petroleum (b. p. 60—80°), giving *rosenolic acid* in needles (0·25 g.), m. p. 173°, $[\alpha]_D^{18}$ −97° (*c* 0·2 in $CHCl_3$) (Found: C, 75·5; H, 9·5. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%). The acid is readily soluble in sodium hydrogen carbonate solution, and in chloroform gives a yellow colour with tetranitromethane. There was almost no neutral fraction from this reaction.

iso*Rosenololactone.*—Prepared from *iso*rosenonolactone (1·0 g.) by reduction with potassium borohydride (0·5 g.) at room temperature, iso*rosenololactone* separated from methanol in needles (0·6 g.), m. p. 176°. On purification by chromatography from benzene solution on activated aluminium oxide this had m. p. 181° (Found: C, 75·1; H, 9·3. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%); admixed with rosenonolactone, it had m. p. *ca.* 128°. When the temperature of the reacting mixture was allowed to rise to *ca.* 50° the product was a mixture of rosenololactone, m. p. and mixed m. p. 222° (oxidised by chromic oxide–pyridine to rosenonolactone), and *iso*rosenololactone, m. p. and mixed m. p. 181°, which was separated by fractional crystallisation. Boiled for 1½ hr. with alcohol (8 ml.) and 2N-aqueous sodium hydroxide (8 ml.), *iso*rosenololactone (0·1 g.) was recovered unchanged.

On oxidation with chromic oxide (0·25 g.) in pyridine the lactone (0·25 g.) regenerated *iso*rosenonolactone (0·18 g.), m. p. and mixed m. p. 144°.

iso*Rosenolic Acid.*—A mixture of *iso*rosenololactone (1 g.), alcohol (90 ml.), and hydrochloric acid (10 ml.) was heated under reflux for 2 hr.; isolation of the acidic product in the usual manner gave iso*rosenolic acid*, needles (0·75 g.) (from aqueous methanol), m. p. 185°, $[\alpha]_D^{22}$ −138° (*c* 0·2 in $CHCl_3$) (Found: C, 75·5; H, 9·6%; equiv., 320. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%; equiv., 318·4). The neutral fraction from this reaction was negligible.

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[6] Ruzicka and Waldmann, *Helv. Chim. Acta*, 1932, **15**, 907.

The *acetate* separated from aqueous methanol in needles, m. p. 153° (Found: C, 73·3; H, 9·1. $C_{22}H_{32}O_4$ requires C, 73·3; H, 9·0%).

*Dehydrogenation of Dihydro*iso*rosenonolactone.*—A mixture of dihydro*iso*rosenonolactone (6·0 g.) and powdered selenium (12·0 g.) was kept at 320—330° for 48 hr., then cooled and extracted with ether. The filtered extract was washed successively with N-aqueous sodium hydrogen carbonate and N-aqueous sodium hydroxide, dried, and evaporated, leaving a neutral fraction which, on purification by chromatography on activated aluminium oxide from light petroleum (b. p. 60—80°) with elution with the same solvent and crystallisation from methanol, gave 1 : 7-dimethylphenanthrene in plates (1·3 g.), m. p. and mixed m. p. 85° (Found: C, 93·2; H, 6·8. Calc. for $C_{16}H_{14}$: C, 93·2; H, 6·8%). The picrate separated from methanol in yellow needles, m. p. and mixed m. p. 130°.

Obtained by acidification of the aqueous sodium hydroxide extracts, the buff precipitate (0·65 g.) was methylated by methyl sulphate–potassium carbonate, and the product purified by chromatography from light petroleum (b. p. 60—80°) on activated aluminium oxide, giving 9-methoxy-1 : 7-dimethylphenanthrene in plates (0·5 g.), m. p. and mixed m. p. 132°, the ultraviolet absorption spectrum of which in alcohol exhibited max. at 217, 250, 257, 278, 300, 309, 338, 352 mμ (log ε 4·49, 4·65, 4·68, 4·24, 3·88, 3·84, 3·03, and 2·99 respectively) (Found: C, 86·2; H, 6·5; OMe, 13·4. Calc. for $C_{16}H_{13}$·OMe: C, 86·4; H, 6·8; OMe, 13·1%).

*Dihydro*iso*rosenololactone.*—Reduction of dihydro*iso*rosenonolactone (1 g.) in methanol (5 ml.) with potassium borohydride (0·5 g.) in water (3 ml.), containing 2 drops of 2N-aqueous sodium hydroxide, for 1 hr. at 35° gave *dihydro*iso*rosenololactone* which separated from methanol in needles, m. p. 163°, and was then purified by chromatography from benzene on activated aluminium oxide; this lactone had m. p. 166° (Found: C, 74·5; H, 9·6. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·1%). This (4·5 g.) with powdered selenium (9·0 g.) in the manner employed for dihydro*iso*rosenonolactone gave pimanthrene (0·8 g.), m. p. and mixed m. p. 85°, and 9-methoxy-1 : 7-dimethylphenanthrene (0·06 g.), m. p. and mixed m. p. 132°.

12-*Hydroxy*iso(?)*rosan*-16-*oic Lactone.*—A slow stream of hydrogen chloride was led into a solution of dihydro*iso*rosenonolactone (1 g.) in ethanedithiol (1·7 ml.) at 0° for 1 hr. and next day the partly crystalline mass was diluted with methanol. Recrystallised from benzene–ethanol, the *mercaptal* formed prisms (1 g.), m. p. 209°, $[\alpha]_D^{19}$ −38° (*c* 0·2 in $CHCl_3$) (Found: C, 67·0; H, 8·6. $C_{22}H_{34}O_2S_2$ requires C, 67·0; H, 8·6%). Dihydrorosenonolactone furnished the same mercaptal, m. p. and mixed m. p. 209°, having an identical infrared absorption spectrum.

A solution of this mercaptal (1 g.) in dioxan (20 ml.) and alcohol (30 ml.) containing Raney nickel (8·0 g.) was boiled for 60 hr., filtered, and evaporated, leaving a viscous oil which crystallised on trituration with light petroleum (b. p. 60—80°). Purification from methanol gave 12-*hydroxy*iso(?)*rosan*-16-*oic lactone* in needles (0·45 g.), m. p. 101° (Found: C, 79·1; H, 10·5. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%), $[\alpha]_D^{22}$ +51° (*c* 0·2). On dehydrogenation with powdered selenium (8 g.) at 320—330° for 48 hr. this compound (3·9 g.) gave pimanthrene (1·9 g.), m. p. and mixed m. p. 85°, which furnished the picrate, m. p. and mixed m. p. 131°; a phenolic product was not formed. A clear solution resulted when a mixture of 12-hydroxy*iso*(?)rosan-16-oic lactone (0·5 g.), alcohol (7 ml.), and 2N-aqueous sodium hydroxide (7 ml.) was boiled for 45 min., cooled, and diluted with water (50 ml.). 24 Hr. later acidification of this gave the unchanged lactone (0·45 g.), m. p. and mixed m. p. 101° after purification.

iso(?)*Ros*-11 : 12-*en*-16-*oic Acid* [iso(?)*Rosenoic Acid*].—A solution of 12-hydroxy*iso*(?)rosan-16-oic lactone (1 g.) in alcohol (50 ml.) containing 2N-hydrochloric acid (50 ml.) was heated under reflux for 4 hr., cooled, diluted with water, and extracted with ether. The ethereal solution was washed with N-aqueous sodium hydroxide and the combined washings were acidified, giving iso(?)*ros*-11 : 12-*en*-16-*oic acid* which separated from aqueous methanol in plates (0·7 g.), m. p. 134°, $[\alpha]_D^{22}$ −146° (*c* 0·5 in $CHCl_3$) (Found: C, 79·0; H, 10·7%; equiv., 306. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%; equiv., 304·5). This compound is readily soluble in the common organic solvents and in 2N-aqueous hydrogen carbonate. There was no neutral fraction from this reaction.

The same acid was formed when a mixture of 12-hydroxy*iso*(?)rosan-16-oic acid lactone (1 g.) and naphthalene-2-sulphonic acid (0·08 g.) was melted on the steam-bath; the molten mixture crystallised after 5 min. A solution of this in ether was washed with N-aqueous sodium hydroxide, then with water, dried, and evaporated, leaving a negligible residue. Acidification of the alkaline extract gave *iso*(?)ros-11 : 12-en-16-oic acid (0·8 g.), m. p. and mixed m. p. 134°

after purification from methanol. Prepared with diazomethane, the *methyl ester* had b. p. 172°/0·5 mm., m. p. *ca.* 33° (Found: C, 79·1; H, 10·9; OMe, 9·8. $C_{20}H_{31}O{\cdot}OMe$ requires C, 79·2; H, 10·8; OMe, 9·7%).

When heated at 200° in a sealed tube for 1½ hr. *iso*(?)rosenoic acid (25 mg.) furnished a neutral oily *substance* (15 mg.) which was purified by distillation and had no hydroxyl or carbonyl infrared absorption (Found: C, 86·3; H, 11·9. $C_{19}H_{32}$ requires C, 87·6; H, 12·4%).

iso(?)Ros-11 : 12-en-16-oic acid (0·15 g.) was added to concentrated sulphuric acid (3 ml.) at −10° and the stirred mixture was kept at −5° to −10° for ¾ hr. After addition of crushed ice the product was isolated with ether and purified from methanol, to give allo*hydroxyrosanoic lactone* in prisms (65 mg.), m. p. 138°, $[\alpha]_D^{21}$ +26·7° (*c* 0·08), with a negative tetranitromethane reaction in chloroform (log ε 1·93 at 214 mμ). Dilution of the methanolic mother-liquors with water gave a semisolid product which was purified from methanol, to give *neo*hydroxyrosanoic lactone (3 mg.) identical with the product from rosololactone (see following paper).

iso(?)*Rosen*-16-*ol*.—A solution of methyl *iso*(?)ros-11 : 12-en-16-oate (7 g.) in ether (250 ml.) was added gradually to a slurry of lithium aluminium hydride (4 g.) in ether (200 ml.); the mixture was heated under reflux for 72 hr., the excess of reducing agent was destroyed with ethyl acetate, and the ethereal solution was washed with 2N-sulphuric acid (300 ml.), water, dried, and evaporated, leaving iso(?)*ros*-11 : 12-*en*-16-*ol* which separated from methanol in needles (4·1 g.), m. p. 115°, $[\alpha]_D^{22}$ −103° (Found: C, 82·4; H, 11·4. $C_{20}H_{34}O$ requires C, 82·7; H, 11·8%). This was insoluble in 2N-aqueous sodium hydroxide and gave a yellow tetranitromethane reaction in chloroform. On being slowly heated at 0·35 mm. a mixture of this alcohol (5 g.) and naphthalene-2-sulphonic acid (0·1 g.) reacted at 160° and an oil (3 g.) rapidly distilled. A solution in ether of the product (5·7 g.), from two experiments, was washed with 2N-aqueous sodium hydroxide, dried, and distilled, furnishing a *product* as an oil (4·8 g.), b. p. 140—144°/0·3 mm., $\lambda_{max.}$ 241 mμ (log ε 3·7), n_D^{24} 1·519, which gave an orange tetranitromethane reaction in chloroform (Found: C, 88·5; H, 11·9. $C_{20}H_{32}$ requires C, 88·2; H, 11·8%). Hydrogenation of this compound (12 g.) in ethyl acetate (280 ml.) with a catalyst (from 2 g. of palladium chloride and 1 g. of charcoal) occurred in 2 hr. (900 c.c., 1 mol. absorbed), giving a *hydrocarbon* (11·0 g.), b. p. 138—140°/0·5 mm. (log ε 3·66 at 216 mμ), n_D^{24} 1·510, which had a yellow tetranitromethane reaction in chloroform (Found: C, 87·9; H, 12·3. $C_{20}H_{34}$ requires C, 87·5; H, 12·5%).

On dehydrogenation with selenium (22 g.) at 330—340° for 60 hr. followed by isolation of the product with ether and preliminary purification from light petroleum (b. p. 60—80°) on aluminium oxide this hydrocarbon (11 g.) gave an oil (5·0 g.), b. p. 140—160°/0·1 mm., which was separated arbitrarily into four fractions. Fractions 2, 3, and 4 deposited a colourless solid which was isolated after dilution with alcohol and purified from benzene–light petroleum (b. p. 60—80°), yielding an *anthracene derivative* in plates (25 mg.), m. p. 240°, $\lambda_{max.}$ 227, 257, 343, 357, and 378 mμ ($E_{1\,cm.}^{1\%}$ 2·8, 3·91, 2·26, 2·31, and 218 respectively) (Found: C, 93·0; H, 7·4; *C*-Me, 6·0. $C_{17}H_{16}$ requires C, 92·7; H, 7·3; 3*C*-Me, 20·4. $C_{16}H_{14}$ requires C, 93·2; H, 6·8; 2*C*-Me, 14·5%). The combined fractions were treated with picric acid. Prolonged fractional crystallisation of the resulting picrates, followed by conversion into the trinitrobenzene derivatives and then regeneration of the picrates, ultimately furnished 1 : 7-dimethylphenanthrene picrate (80 mg.), m. p. and mixed m. p. 132°. The remaining picrates (1·3 g.) appeared to consist essentially of that of 1 : 7-dimethylphenanthrene.

iso(?)*Rosene*.—*iso*(?)Ros-11 : 12-en-16-ol (1 g.) dissolved in benzene (8 ml.) was oxidised with *tert.*-butyl chromate (from 0·8 g. of chromic oxide, 4 ml. of benzene, and 4 ml. of *tert.*-butyl alcohol) at 25° for 7 days and the resulting black precipitate decomposed by the addition of ether and water containing sulphur dioxide, giving *iso*(?)ros-11 : 12-en-16-al as a neutral oil which exhibited carbonyl absorption (1715 cm.$^{-1}$ in Nujol). The *semicarbazone* separated from methanol in needles (0·67 g.), m. p. 230° (Found: C, 73·0; H, 10·2; N, 12·4. $C_{21}H_{35}ON_3$ requires C, 73·0; H, 10·2; N, 12·2%).

A mixture of this semicarbazone (6 g.), sodium (4 g.), diethylene glycol (70 ml.), and hydrazine hydrate (0·75 ml.) was heated under reflux at 233° for 10 hr., then poured into water. Isolated with ether, the resulting iso(?)*rosene* separated from alcohol in needles (4 g.), m. p. 59° (Found: C, 87·2; H, 12·7. $C_{20}H_{34}$ requires C, 87·5; H, 12·5%). Dehydrogenation of this hydrocarbon (3 g.) with selenium (6 g.) at 320—330° for 36 hr. gave 1 : 7-dimethylphenanthrene (1·4 g.), m. p. and mixed m. p. 85°, forming the picrate, m. p. and mixed m. p. 132°.

Rosoic Acid.—Prepared as described previously,[1] this acid had a negative ferric reaction and was recovered unchanged when repeatedly heated above the m. p. Reduction of methyl rosoate (0·5 g.) in methanol (8 ml.) in 1 hr. by gradual addition of a solution of potassium borohydride (0·25 g.) in water (3 ml.), followed by acidification with 2N-hydrochloric acid, gave a *dilactone* which separated from methanol in needles (0·16 g.), m. p. 239°, mixed m. p. with rosoic acid 190—200° [Found: C, 71·7; H, 8·7%; OMe, 0. equiv., 173. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%; equiv. (dibasic), 167]. This product, which is insoluble in cold 2N-aqueous sodium hydroxide, has a negative tetranitromethane reaction in chloroform, and on being subjected to the conditions employed for the fission of rosoic acid is recovered unchanged.

Oxidation of the $C_{10}H_{18}O$ *Ketone* (With W. R. Smithies).—A vigorous reaction was initiated by heating a mixture of the ketone (1·8 g.), nitric acid (15 ml.), and water (15 ml.) on the steam-bath for *ca.* 5 min.; the oxidation was then allowed to proceed spontaneously. The mixture was next heated on the steam-bath for $\frac{3}{4}$ hr., cooled, and diluted with water (30 ml.). The clear solution was decanted from the sticky residue and evaporated on the steam-bath, and the residual solid was extracted with chloroform–light petroleum (b. p. 60—80°), leaving a crystalline residue of oxalic acid (0·08 g.). Evaporation of the extract furnished an oil, b. p. 200—220°/760 mm., a solution of which in ether was washed with 2N-aqueous sodium hydrogen carbonate and then evaporated. The residual gum was warmed on the steam-bath with 2N-aqueous sodium hydroxide (10 ml.), and the resulting homogeneous solution acidified, giving (+)- or (−)-*α-ethyl-α-methylsuccinic acid* which separated from ether–light petroleum (b. p. 40—60°) in prisms (0·12 g.), m. p. 98° (Found: C, 52·7; H, 7·2. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5%). The infrared absorption spectrum (in Nujol) and the potentiometric titration curve of this acid were identical with those of (±)-α-ethyl-α-methylsuccinic acid.[7]

Boiled with acetic anhydride for $2\frac{1}{2}$ hr., the keto-acid [1] $C_{10}H_{14}O_5$ from rosoic acid gave a sticky solid which on crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave the *anhydride* in large polyhedra, m. p. 95° (Found: C, 61·3; H, 6·3. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%). Hydrolysis with warm 2N-aqueous sodium hydroxide regenerated the parent keto-acid, m. p. and mixed m. p. 203—204° (decomp.), in quantitative yield.

The ultraviolet absorption spectra were determined in 95% alcohol with a Unicam S.P. 500 Spectrophotometer and the infrared spectra in CCl_4 solution (unless stated to the contrary) with a Perkin-Elmer, Model 21, Spectrophotometer. The analyses were by Mr. A. S. Inglis, M.Sc., and his associates of this Department.

University of Liverpool.

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[7] Smith and Horwitz, *J. Amer. Chem. Soc.*, 1949, **71**, 3419.