844. *The Chemistry of the Triterpenes and Related Compounds. Part XXI.* Some Aspects of the Chemistry of the Elemi Acids.*

By T. G. Halsall, G. D. Meakins, and R. E. H. Swayne.

The chemistry of the elemi acids is discussed and evidence presented for partial structures for hydroxyelemadienic and oxoelemadienic acids. The dehydro-derivatives of these acids have also been found in *Manila elemi* resin. " α-Elemonic acid " is shown to be a mixture.

The main acidic constituents of *Manila elemi* resin are α-elemolic acid (hydroxyelemadienic acid) and β-elemonic acid (oxoelemadienic acid †). The former is a diethenoid tetracyclic monohydroxy-acid, $C_{30}H_{48}O_3$, and the latter the corresponding ketone (Ruzicka, Rey, Spillman, and Baumgartner, *Helv. Chim. Acta*, 1943, **26**, 1638). (For a survey of the literature concerning the elemi acids see Elsevier's " Encyclopœdia of Organic Chemistry," Vol. 14, p. 598; Vol. 14S, p. 1203S.) One of the double bonds is present in an *iso*propylidene group (Ruzicka, Rey, and Spillman, *Helv. Chim. Acta*, 1942, **25**, 1375). Evidence concerning the unreactive double bond is given by the low wave-length ultraviolet absorption spectrum of methyl acetoxyelemenate. This is very similar to the spectra of oleanol (I) and dihydropolyporenic acid A (II), and indicates that the unreactive double bond is tetrasubstituted but not exocyclic (cf. Bladon, Henbest, and Wood, *J.*, 1952, 2737; Halsall, *Chem. and Ind.*, 1951, 867). Such an environment of the double bond is typical of the tetracyclic " triterpenes " ‡ and suggests that the structure of the elemi acids may well be based on the ring system (III) common to these " triterpenes." This is

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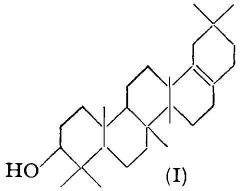
* Part XX, *J.*, 1953, 3024.

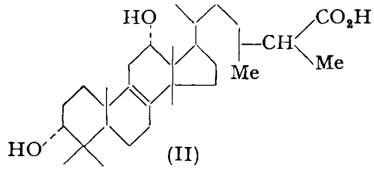
† The nomenclature used is derived systematically from the unknown, saturated C_{30} hydrocarbon elemane.

‡ The quotation marks are used because lanosterol and related compounds are not classical triterpenes.

supported by the isolation of phenanthrene derivatives on selenium dehydrogenation of α-elemolic acid (Ruzicka, Rey, and Spillman, *loc. cit.*).



(I)



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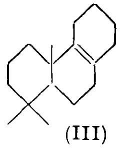
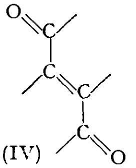


(III)

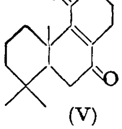


(IV)

Oxidation of methyl acetoxyelemenate with chromic acid (cf. Ruzicka, Rey, and Spillman, *loc. cit.*) gives an acetoxy-diketone (methyl acetoxydioxoelemenate) with an absorption maximum at 2720 Å ($\varepsilon = 8700$) characteristic of a *transoid* dione–ene system (IV). The infra-red spectrum of this diketone (in carbon tetrachloride) showed bands at 1742 cm.$^{-1}$ (ester groups) and 1677 cm.$^{-1}$ (conjugated carbonyl in a six-membered ring). The results are analogous to those obtained in the oxidation of lanostenyl and euphenyl acetates with chromic acid (cf. Christen, Dunnenberg, Roth, Heusser, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 1756) and, on the basis of (III), lead to the partial formulation of the diketone as (V).

Treatment of the acetoxy-diketone with zinc–acetic acid reduced the double bond and gave a saturated acetoxy-diketone (methyl acetoxydioxoelemanate), the infra-red spectrum of which showed a band at 1713 cm.$^{-1}$ indicative of a keto-group in a six-membered ring.

A typical reaction of tetracyclic "triterpenes" is that with selenium dioxide, dehydrogenation at positions α to the unreactive double bond giving a conjugated diene. Oxidation of methyl acetoxyelemenate with this reagent is reported to give a dehydro-compound with maximal ultra-violet light absorption at 2380 Å ($\varepsilon = 7900$) or 2390 Å ($\varepsilon = 8900$) (Ruzicka, Rey, and Spillman, *loc. cit.*; Kon and Bilham, *J.*, 1942, 544). The wave-length of maximum absorption is similar to that found for dehydroeuphenyl acetate (suggested structure VI) (λ 2400 Å; $\varepsilon = 20{,}000$) (Barbour, Bennett, and Warren, *J.*, 1951, 2540), but the intensity is appreciably less. The preparation of methyl acetoxy-dehydroelemenate by the action of selenium dioxide on methyl acetoxyelemenate has been repeated and maximal absorption has been found at 2320, 2390, and 2470 Å ($\varepsilon = 13{,}800$, 15,050, and 9700). These values are characteristic of the dienes obtained from derivatives of euphol (suggested structure VII; R = H) (Kyburz, Mijovic, Heusser, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 2073), euphorbol, and tirucallol (Barbour *et al.*, *loc. cit.*), but differ from those of dehydroeburicoic acid (Holker, Powell, Robertson, Simes, Wright, and Gascoigne, *J.*, 1953, 2422), agnosterol (Ruzicka, Denss, and Jeger, *Helv. Chim. Acta*, 1946, **29**, 204), and polyporenic acid C (Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548). This division of the tetracyclic "triterpenes" on the basis of light-absorption properties is supported by a comparison of the $[M]_D$ differences between the dienes and their precursors (Dawson, Halsall, and Swayne, *J.*, 1953, 590). Eburicoic acid, agnosterol, and polyporenic acid C probably differ from euphol at $C_{(14)}$, having a methyl group at this position instead of a hydrogen atom. These comparisons suggest the extension of partial structure (III) to (VIII). This is consistent with the partial structure (IX) put forward, without discussion, for α-elemolic acid by Kyburz, Mijovic, Heusser, Jeger, and Ruzicka (*loc. cit.*).



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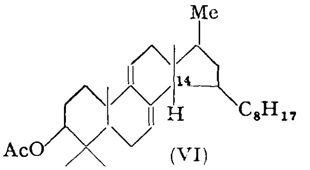
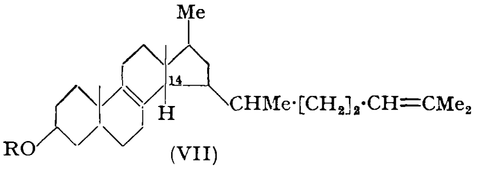


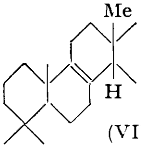
(VI)



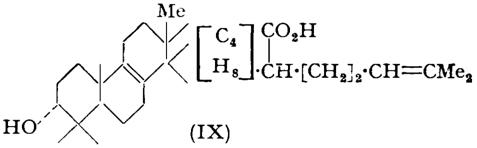
(VII)

Fractionation of the more polar by-products from the action of selenium dioxide on methyl acetoxyelemenate produced a crystalline compound which gave analytical data corresponding to either $C_{32}H_{48}O_6$ or $C_{33}H_{50}O_6$. It showed maximal absorption at 2585 Å

($\epsilon = 7300$) suggesting the presence of a fully substituted αβ-unsaturated ketone grouping (cf. 3β-acetoxy-11-oxolanost-8-ene : $\lambda_{max.}$ 2550 Å, $\epsilon = 8000$; McGhie, Pradhan, and Cavalla, *J.*, 1952, 3176). Its infra-red spectrum (determined in chloroform over the range 1500—1800 cm.$^{-1}$) showed bands at 1761, 1725, 1645, and 1618 cm.$^{-1}$. The most interesting of these is that at 1761 cm.$^{-1}$, which, allowing for the fact that the frequencies of bands in this region are generally lower than in carbon tetrachloride, indicates a saturated γ-lactone grouping. The structure of this compound will be discussed in a subsequent publication.

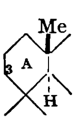


(VIII)

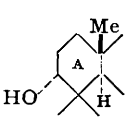


(IX)

When oxoelemadienic acid is reduced with sodium and *iso*butyl alcohol the resulting hydroxy-acid differs from α-elemolic acid, having an epimeric hydroxyl group (Ruzicka, Rey, Spillman, and Baumgartner, *loc. cit.*). This indicates that the hydroxyl group of α-elemolic acid has the less stable polar configuration, and that if it is located on a typical triterpene ring A (X) at $C_{(3)}$ then its configuration is α (XI). Support for this suggestion is provided by a comparison of the $[M]_D$ differences between hydroxyelemadienic acid and its acetate ($\Delta[M]_D$ $-104°$) and between *epi*hydroxyelemadienic acid and its acetate ($\Delta[M]_D$ $+84°$) (cf. Barton and Jones, *J.*, 1944, 659). In triterpenes with a 3β-hydroxyl group (cf. XII) the change in the molecular rotation on acetylation, although variable in size, is positive. The value for *epi*hydroxyelemadienic acid ($\Delta[M]_D$ $+84°$) is consistent with a 3β-hydroxyl group.as in (XII) while the negative shift ($\Delta[M]_D$ $-104°$) for α-elemolic acid agrees with the sign of the shift ($\Delta[M]_D$ *ca.* $-200°$) found for the 3α-hydroxyl group of polyporenic acid A (cf. II) (Curtis, Heilbron, Jones, and Woods, *J.*, 1953, 457; Halsall, Hodges, and Jones, *J.*, 1953, 3019). To test these suggestions methyl *epi*hydroxyelemenate was prepared by reduction of methyl oxoelemenate with sodium borohydride and by hydrogenation of the corresponding reduction product from methyl oxoelemadienate. Sodium borohydride reduces the 3-oxo-group of polyporenic acid C to the 3β-hydroxyl group. Methyl *epi*hydroxyelemenate was dehydrated with phosphorus pentachloride in petroleum, and the product ozonised; acetone was obtained in 75% yield as its 2 : 4-dinitrophenylhydrazone. This result is characteristic of the grouping (XII) (cf. Christen *et al.*, *loc. cit.*) which must, therefore, be present in methyl *epi*hydroxyelemenate. Partial structure (XI) follows for α-elemolic acid, and (VIII) may be expanded to (XIII).



(X)



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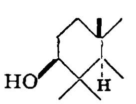

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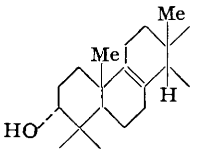
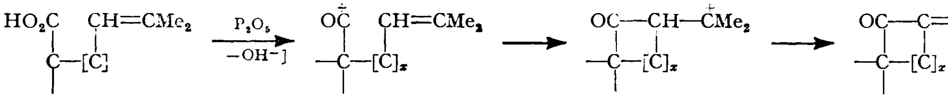


(XIII)

Following the proof that the side-chain of lanosterol was $\cdot CHMe\cdot[CH_2]_2\cdot CH{:}CMe_2$ (Voser, Mijovic, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1951, **34**, 1585; Barnes *et al.*, *Chem. and Ind.*, 1951, 1067), it appeared attractive to consider a similar side-chain, $\cdot CH(CO_2H)\cdot[CH_2]_2\cdot CH{:}CMe_2$, for hydroxyelemadienic acid. The partial structure (IX) put forward by Kyburz *et al.* (*loc. cit.*) incorporates this, but the published evidence does not distinguish between it and $\cdot CH_2\cdot CH(CO_2H)\cdot CH_2\cdot CH{:}CMe_2$ (Arnold, Koller, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 555; Mazur, Koller, Jeger, and Ruzicka, *ibid.*, 1952, **35**, 181). Before the publication of these two papers it appeared to the authors that a further study of the cyclisation reaction which occurs when acetoxyelemadienic acid is treated with phosphoric oxide (Ruzicka, Hiestand, Baumgartner, and Jeger, *ibid.*, 1947, **32**, 2119) would enable the number of carbon atoms between the carboxyl and *iso*propylidene groups to be determined. In the cyclisation these two groups interact to form an αβ-unsaturated ketone with the loss of one molecule of water. The reaction can be represented as:



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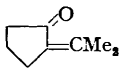
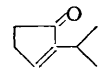
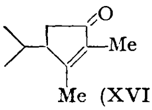


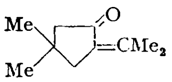
(XV)



(XVI)



(XVII)



(XVIII)

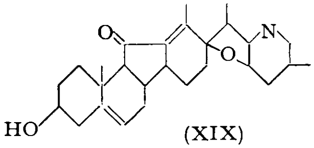
Examination of the infra-red spectrum of the resulting ketone (XIV) should enable the ring size and the value of x to be determined.

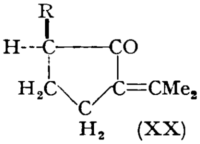
Treatment of acetoxyelemadienic acid with phosphoric oxide has given two cyclic products, anhydro-oxoelemadienyl acetate-I and anhydro-oxoelemadienyl acetate-II. One of these has the same constants as the single product obtained by Ruzicka, Hiestand, *et al.* (*loc. cit.*) from acetoxyelemadienic acid. It is of interest that these workers obtained two products in each case from oxoelemadienic acid and elemadienic acid. Both products from acetoxyelemadienic acid were αβ-unsaturated ketones showing maximal absorption at 2540 Å ($\varepsilon = 13,800$). The infra-red spectra of these compounds (in carbon tetrachloride) showed strong bands at 1732 and 1711 cm.$^{-1}$; the former band is caused by the acetoxy-group while the latter indicates the presence of a conjugated keto-group in a five-membered ring, as in (XV). Had the keto-group been in a six-membered ring, absorption at *ca.* 1660—1680 cm.$^{-1}$ would have been expected. The calculated position of maximal ultra-violet absorption of the chromophore (XV), *viz.*, 2540 Å, is in agreement with the observed values. This excludes the alternative structure (XVI), which would absorb at shorter wave-length [cf. XVII and XVIII having maximal absorption at 2310 Å and 2515 Å, respectively (Gillam and West, *J.*, 1942, 487; Eschenmoser, Shinz, Fischer, and Colonge, *Helv. Chim. Acta*, 1951, **34**, 2329)].

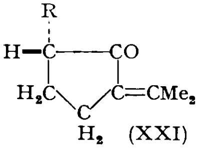
Hydrogenation of the two keto-acetates gave anhydro-oxoelemenyl acetates-I and -II, which, on hydrolysis, gave the same keto-alcohol. The infra-red spectrum of this compound (in carbon tetrachloride) had a strong band at 1738 cm.$^{-1}$, indicative of a keto-group in a five-membered ring. The frequency expected for saturated five-membered ring ketones is usually given as 1745 cm.$^{-1}$, dropping to about 1715 cm.$^{-1}$ in the αβ-unsaturated compound (see, *e.g.*, Grove and Willis, *J.*, 1951, 877). It is probable that these figures represent upper limits to the frequency ranges. Thus, while 17-keto-steroids absorb at 1742—1745 cm.$^{-1}$ (Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956), a number of triterpenoid five-membered ring ketones have frequencies of about 1735 cm.$^{-1}$ (Meyer, Jeger, Prelog, and Ruzicka, *Helv. Chim. Acta*, 1951, **34**, 747; Menard and Jeger, *ibid.*, 1953, **36**, 335). In dihydrojervine the band occurs at 1730 cm.$^{-1}$ (Anliker, Heusser, and Jeger, *ibid.*, 1952, **35**, 838), while jervine for which structure (XIX) has been proposed (Wintersteiner and Hosansky, *J. Amer. Chem. Soc.*, 1952, **74**, 4474) absorbs at 1705 cm.$^{-1}$ (Marion, Ramsay, and Jones, *ibid.*, 1951, **73**, 705).

As only one keto-alcohol is obtained on hydrolysis of the reduced acetates, the initial cyclisation products must differ at a centre at which alkali-catalysed inversion can occur. Structures such as (XX) and (XXI) probably represent the difference between the two anhydro-acetates. These could arise through partial inversion of the α-hydrogen atom in the ion $\cdot CHR\cdot \overset{+}{C}O$ formed by the action of phosphoric oxide on the carboxyl group of acetoxyelemadienic acid. From these results and those of Arnold *et al.* (*loc. cit.*) and Mazur *et al.* (*loc. cit.*) it follows that the side-chain is $-CH(CO_2H)\cdot CH_2\cdot CH_2\cdot CH{:}CMe_2$.

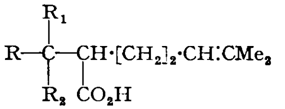
The infra-red spectra of anhydro-oxoelemadienyl acetates-I and -II, determined in carbon tetrachloride, show unusually strong carbon–carbon double-bond stretching bands at *ca.* 1635 cm.$^{-1}$, the intensities of these bands being similar to those of the carbonyl stretching (1711 cm.$^{-1}$). While the intensity of absorption due to an ethylenic bond is known to be increased by conjugation with a carbonyl group, the carbonyl intensity generally remains much the stronger. Other examples of this abnormal intensification are found in 4 : 4-dimethyl-2-*iso*propylidene*cyclo*pentanone (XVIII) (Eschenmoser *et al.*, *loc. cit.*) and in jervine (XIX) (Marion *et al.*, *loc. cit.*). A similar effect occurs in 3β-acetoxy-7-oxoergosta-8(14) : 22-diene, whereas the corresponding -8 : 22-diene shows only the expected intensification (Heusser, Saucy, Anliker, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 2090). The cause of these unusual effects is probably connected with the fact that in each case the double bond is exocyclic.


(XIX)

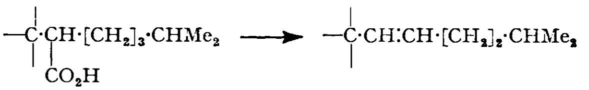

(XX)


(XXI)

Partial structure (XIII) suggests a comparison of acetoxyelemenic acid with euphenyl acetate (suggested structure VII; R = Ac). The latter is isomerised to *iso*euphenyl acetate by treatment with chloroformic hydrogen chloride (Dawson, Halsall, and Swayne, *loc. cit.*) or hydrochloric acid in acetic acid (Vilkas, Dupont, and Dulou, *Bull. Soc. chim.*, 1949, 813). Under similar conditions, however, no isomerisation occurred with acetoxyelemenic acid or oxoelemenic acid. A possible explanation is the absence of a hydrogen atom on the carbon atom to which the side-chain is attached (cf. XXII). It may be noted that in the degradation of the side-chain [(XXIII) ⟶ (XXIV)] (Arnold *et al.*, *loc. cit.*; Mazur *et al.*, *loc. cit.*) the double bond is formed away from the point of attachment of the side-chain to the remainder of the molecule.


$R\text{—}C(R_1)(R_2)\text{—}CH(CO_2H)\cdot[CH_2]_2\cdot CH{:}CMe_2$

R, R_1, and $R_2 \neq$ H (XXII)


$\text{—}C\cdot CH(CO_2H)\cdot[CH_2]_3\cdot CHMe_2 \longrightarrow \text{—}C\cdot CH{:}CH\cdot[CH_2]_2\cdot CHMe_2$

(XXIII) (XXIV)

Oxidation of hydroxyelemadienic acid with chromic acid gives the so-called " α-elemonic acid " (Ruzicka, Rey, and Spillman, *loc. cit.*; Bilham and Kon, *loc. cit.*) which has been characterised as its methyl ester. The absorption maximum of the ester at 2380 Å (ε = 6300) (Ruzicka *et al.*, *Helv. Chim. Acta*, 1943, **26**, 1628) was explained by assuming that the two double bonds moved into conjugation during the oxidation. This hypothesis is no longer tenable. The simplest explanation of the light-absorption properties is that oxidation gives rise to the diene system found in methyl acetoxydehydroelemenate. Comparison shows that the main peaks of the spectra of methyl acetoxydehydroelemenate (2390 Å; ε = 15,000) and methyl dehydro-oxoelemenate ($\lambda_{max.}$ 2390 Å; ε = 18,100) are at the same wave-length as that of " methyl α-elemonate " but have a much higher intensity for the pure dienes. The molecular-rotation shift ($[M]_D$ *ca.* −450°) for the formation of " methyl α-elemonate " is negative, as expected for the formation of the diene system (cf. Dawson *et al.*, *loc. cit.*) but its value is less than that found in the conversion of methyl hydroxyelemenate into methyl dehydro-oxoelemenate ($[M]_D$ *ca.* −640°). These facts suggest that " α-elemonic acid " is a mixture of, at least, oxoelemadienic and dehydro-oxoelemadienic acids. It is known that mixtures of tetracyclic " triterpenes " and their corresponding dehydro-derivatives are often very difficult to separate, *e.g.*, eburicoic and dehydroeburicoic acids (Gascoigne, Robertson, and Simes, *J.*, 1953, 1830).

If " methyl α-elemonate " were a mixture of only methyl oxoelemadienate and methyl dehydro-oxoelemadienate then the percentage of the latter present, calculated from the intensity of maximal absorption, would be about 40%. However, the rotation of the " methyl α-elemonate " indicates a diene content of about 65%, assuming that the rotation of methyl dehydro-oxoelemadienate is not appreciably different from that of methyl dehydro-oxoelemenate ($[\alpha]_D$ −152°).

The chromic acid oxidation of hydroxyelemadienic acid under various conditions has been reinvestigated. In one experiment a mixture was obtained which had absorption maxima at 2315, 2385, and 2470 Å, positions characteristic of methyl acetoxydehydroelemenate. The mixture was separated by chromatography into fractions, two of which showed maximal absorptions at 2390 Å of almost the same intensity, but with significantly different specific rotations. In addition to these diene-containing fractions, methyl dioxoelemadienate was obtained. It therefore appears that "α-elemonic acid," in addition to containing possibly a little dioxoelemadienic acid, is a mixture of at least three components, oxoelemadienic acid, dehydro-oxoelemadienic acid, and a compound with a large negative rotation, but no appreciable absorption at *ca.* 2400 Å. The nature of the last compound is not known. Possibly it is an isomer of oxoelemadienic acid differing from oxoelemadienic acid in the C/D ring fusion. Although caution is necessary in making comparisons between tetracyclic "triterpenes" and normal steroids it is of interest that a considerable negative shift in molecular rotation attends the conversion of the C/D ring fusion from *cis* into *trans* in the steroid molecule (cf. Fieser and Fieser, "Natural Products related to Phenanthrene," 3rd Edn., 1949, Reinhold Publ. Corp., p. 212).

The general method of extraction and separation of α-elemolic acid and β-elemonic acids was that used by Ruzicka and Hausserman (*Helv. Chim. Acta*, 1942, **25**, 445). In one extraction each step was followed spectroscopically and it was found that slight but definite light absorption occurred at 2320, 2390, and 2460—2480 Å, indicative of the presence of a conjugated diene (5—7%). The diene was present in the starting material, persisted throughout the separation of the acidic portion of the resin, and remained in both the ketonic and non-ketonic acids. The methyl esters of these acids could be separated by chromatography into pure methyl hydroxyelemadienate and methyl oxoelemadienate, and into enriched diene fractions.

It has been possible to examine spectroscopically samples of elemi acids extracted by (the late) Professor G. A. R. Kon, (the late) Dr. J. C. E. Simpson, and Professor H. Lieb. In all cases, even with the purest samples, small amounts of diene were found. Hence, in addition to hydroxyelemadienic and oxoelemadienic acids, the corresponding dehydro-compounds also occur in Nature.

EXPERIMENTAL

Rotations were determined in chloroform at room temperature. M. p.s were determined on a Kofler block and are corrected. Analytical samples were dried at a suitable temperature for 5—10 hr. in a high vacuum. Alumina of activity I—II was employed for chromatography unless otherwise stated, and except where specified light petroleum refers to the fraction, b. p. 40—60°. Ultra-violet spectra were determined in ethanol with a Unicam spectrophotometer. Infra-red spectra determinations were made with a Perkin-Elmer double-beam instrument, model 21, carbon tetrachloride solutions being used unless stated otherwise.

Extraction of Elemi Acids.—*Manilla elemi* resin (4 kg.), previously steam-distilled to remove ethereal oils, was dissolved in ether (25 l.), and the solution extracted with 2% sodium hydroxide solution (8 l.) by stirring at the interface for 4 hr. The aqueous layer was separated, and the ethereal solution extracted with water (3 × 8 l.) in the same way. All the aqueous extracts were combined and acidified to pH 7 with hydrochloric acid. The neutral solution was then extracted with ether (2 × 10 l.) and the extract concentrated, dried, and worked up to give a crystalline solid, m. p. 200—213° (from ethanol). Light absorption: 2385 (max.) and 2460 Å (infl.); $\varepsilon = 1065$ and 910.

The solid was separated into hydroxy- and oxo-elemadienic acids with Girard reagent-T. The hydroxyelemadienic acid crystallised from ethanol as needles, m. p. 212—222°, $[\alpha]_D$ $-21{\cdot}5°$ (*c*, 1·4) (Found: C, 78·8; H, 10·55. Calc. for $C_{30}H_{48}O_3$: C, 78·85; H, 10·6%). Light absorption: 2390 (infl.) and 2470 Å (infl.); $\varepsilon = 290$ and 200. By methylation with ethereal diazomethane and careful chromatography it was possible to obtain methyl hydroxyelemadienate, m. p. 148—149·5°, $[\alpha]_D$ $-14{\cdot}1°$ (*c*, 1·16), ε at 2390 Å = 390, with a negligible conjugated diene content.

The oxoelemadienic acid crystallised from ethanol as long needles, m. p. 207—223°, $[\alpha]_D$ $+24{\cdot}8°$ (*c*, 1·07). Light absorption: 2390 (max.) and 2470 Å (infl.); $\varepsilon = 760$ and 510. A sample of the acid, sublimed for analysis at 240/10^{-5} mm., had m. p. 204—218°; $[\alpha]_D$ $+33{\cdot}4°$ (*c*, 1·3) (Found: C, 79·05; H, 10·05. Calc. for $C_{30}H_{46}O_3$: C, 79·2; H, 10·2%). By repeated recrystallisation from ethanol of the oxoelemadienic acid (2·7 g.), m. p. 207—233°, described above, it was possible to obtain a sample (0·28 g.) with a conjugated-diene content of only 1% [m. p. 211—217°; $[\alpha]_D$ +37·2° (*c*, 1·6); light absorption : ε at 2390 Å = 200], and also needles (0·1 g.) [m. p. 250—260°, $[\alpha]_D$ −57·4° (*c*, 0·3); light absorption : Max. 2300, 2380, and 2470 (infl.) Å; ε = 1865, 1865, and 1190] consisting of a mixture containing oxoelemadienic and dehydro-oxoelemadienic acids.

Ultra-violet Light Absorption of Methyl Acetoxyelemenate.—Methyl acetoxyelemenate, m. p. 140—142·5°, $[\alpha]_D$ −41·8°, absorbed light in the low ultra-violet region as follows : ε at 2100 Å = 5100, ε at 2150 Å = 3300, ε at 2200 Å = 1800, and ε at 2230 Å = 1000.

Methyl Acetoxydioxoelemenate.—Chromic acid (1·4 g.) in acetic acid (100 c.c.) was added with stirring during 45 min. to a solution of methyl acetoxyelemenate (2 g.) in acetic acid (100 c.c.) at 90°. After being stirred for a further 1½ hr. at 90°, the solution was kept at 20° overnight. Dilution with water followed by extraction with ether gave an orange-coloured oil (1·76 g.) which was adsorbed from benzene on alumina (170 g.). Elution with benzene (4 × 250 c.c.) gave the following fractions : (i) 33 mg., needles, m. p. 154—156° (from methanol); (ii) 176 mg., oil; (iii) 332 mg., yellow oil; and (iv) 217 mg., yellow oil. Crystallisation of fraction (iii) from methanol and ethyl acetate gave methyl acetoxyoxoelemenate as needles, m. p. 189—191·5°. Light absorption : Max. 2545 and 3160 Å; ε = 10,000 and 137. Fraction (iv) was crystallised from methanol, giving methyl acetoxydioxoelemenate as yellow crystals, m. p. 145·5—147°, $[\alpha]_D$ −33° (*c*, 0·7) (Found : C, 73·05; H, 9·4. Calc. for $C_{33}H_{50}O_6$: C, 73·05; H, 9·3%). Light absorption : Max. 2720 Å; ε = 8700. Infra-red absorption bands at 1742, 1677, and 1245 cm.$^{-1}$.

Reduction of Methyl Acetoxydioxoelemenate.—Methyl acetoxydioxoelemenate (200 mg.) in acetic acid (30 c.c.) was stirred at 90°, and zinc dust (2 g.) was added in portions during 10 min. After being decanted from inorganic material the hot solution was diluted with water. Extraction with ether yielded an oil (152 mg.) which was adsorbed from light petroleum on alumina (15 g.); elution with benzene (450 c.c.) gave an oil (113 mg.) which did not crystallise. It was sublimed at 140°/10^{-5} mm. to give *methyl acetoxydioxoelemanate* as an amorphous solid, softening at 70°, $[\alpha]_D$ −138° (*c*, 0·43) (Found : C, 72·35; H, 9·65. $C_{33}H_{52}O_6$ requires C, 72·75; H, 9·6%). Infra-red light absorption bands at 1743 and 1713 cm.$^{-1}$.

Sodium Borohydride Reduction of Methyl Oxoelemadienate.—Sodium borohydride (85 mg.) in aqueous dioxan (1 : 1; 14 c.c.) was added to a solution of methyl oxoelemadienate (0·56 g.) in dioxan (50 c.c.) which was kept at 20° for 1 hr. Dilution with water precipitated a solid which was collected and adsorbed from benzene on alumina (50 g.). Elution with benzene–ether (9 : 1; 500 c.c.) yielded an oil (0·51 g.) which crystallised from acetic acid to give methyl *epi*-hydroxy elemadienateas plates, m. p. 100—102°, $[\alpha]_D$ −5·5° (*c*, 1·7). Acetylation of this hydroxy-compound (0·065 g.) with acetic anhydride–pyridine gave *methyl* epi*acetoxyelemadienate* (0·062 g.) as needles, m. p. 123—126° (from methanol) (Found : C, 77·6; H, 10·3. $C_{33}H_{54}O_4$ requires C, 77·3; H, 10·2%).

Methyl epi*Hydroxyelemenate.*—(*a*) Methyl *epi*hydroxyelemadienate (0·39 g.) in acetic acid (50 c.c.) was shaken with Adams's catalyst (40 mg.) and hydrogen at 20° for 30 min. (uptake of hydrogen : 1 mole). After removal of the catalyst, evaporation yielded an oil (0·39 g.) which was precipitated from acetic acid to give *methyl* epi*hydroxyelemenate* as an amorphous solid, softening at 90°, $[\alpha]_D$ +2° (*c*, 1·26). This was sublimed at 170°/10^{-5} mm. to a clear glass (Found : C, 78·9; H, 11·3. $C_{31}H_{52}O_3$ requires C, 78·7; H, 11·1%). Methyl *epi*acetoxyelemenate, prepared by acetylation in pyridine, formed short rods (from acetic acid and methanol), m. p. 140—141°, $[\alpha]_D$ +13·5° (*c*, 0·46) (Found : C, 77·15; H, 10·8. Calc. for $C_{33}H_{54}O_4$: C, 76·95; H, 10·6%).

(*b*) Methyl oxoelemenate (0·63 g.), prepared from methyl acetoxyelemenate by hydrolysis and oxidation, was dissolved in dioxan (55 c.c.) and kept at 20° for 1 hr. with sodium borohydride (102 mg.) in aqueous dioxan (1 : 1; 16 c.c.). Dilution with water and extraction with ether yielded an oil which was adsorbed from benzene on alumina (60 g.). After elution with benzene (250 c.c.), elution with ether (250 c.c.) gave methyl *epi*hydroxyelemenate as an oil (526 mg.) which was characterised by conversion into methyl *epi*acetoxyelemenate (short rods from methanol), m. p. 138—139° undepressed on admixture with a sample obtained by method (*a*).

Dehydration of Methyl epi*Hydroxyelemenate.*—Phosphorus pentachloride (0·20 g.) was added to methyl *epi*hydroxyelemenate (0·34 g.) in light petroleum (50 c.c.), and the mixture kept at 20° under anhydrous conditions for 30 min., with occasional shaking. Addition of water followed by extraction with ether yielded an oil (0·31 g.) which was adsorbed from light petroleum on alumina (30 g.). Elution with light petroleum (1000 c.c.) gave an oil (0·128 g.), $[\alpha]_D$ +18·7°

(*c*, 1·28). Further elution with ether (250 c.c.) gave an oil (0·17 g.) which was re-treated with phosphorus pentachloride to give a further petroleum-elutable fraction as an oil (0·073 g.), $[\alpha]_D$ +20·5° (*c*, 0·73). The two petroleum-elutable fractions were combined to give the uncrystallisable dehydration product. A Beilstein test for halogen was negative. In a subsequent experiment a higher yield (72%) of dehydration product was obtained by allowing the phosphorus pentachloride to react for 1 hr.

Ozonolysis of the Dehydration Product.—A stream of ozonised oxygen (6%) was passed through a solution of the dehydration product in carbon tetrachloride at 20° for 1 hr. Ferrous sulphate solution was added and the mixture was distilled into a solution of 2 : 4-dinitrophenylhydrazine sulphate; a 2 : 4-dinitrophenylhydrazone was formed which was extracted with benzene and adsorbed on alumina (30 g.). Elution with benzene (250 c.c.) separated and removed a coloured band. Evaporation of the solution containing this fraction afforded a solid (0·11 g.) which gave acetone 2 : 4-dinitrophenylhydrazone as rods (from ethanol), m. p. 124·5—125° undepressed on admixture with an authentic sample (Found: N, 23·3. Calc. for $C_9H_{10}O_4N_4$: N, 23·5%).

Anhydro-oxoelemadienyl Acetate-I.—Acetoxyelemadienic acid (5·0 g.) was heated under reflux in dry benzene (300 c.c.), and phosphoric oxide was added with stirring to the boiling solution during 25 min. After a further 2 hr., the warm solution was filtered and the solvent removed, leaving a yellowish oil (4·1 g.) which was adsorbed from benzene on alumina (150 g.). Benzene (250 c.c.) eluted a pale yellow solid which was crystallised from ethyl acetate and chloroform–ethanol to give anhydro-oxoelemadienyl acetate-I as thick rods (1·3 g.), m. p. 185—189°, $[\alpha]_D$ −58·2° (*c*, 1·6) (Found: C, 79·8; H, 10·05. Calc. for $C_{32}H_{48}O_3$: C, 79·95; H, 10·05%). Light absorption: Max. 2540 and 3420—3450 Å; ε = 13,750 and 86. Infra-red absorption: bands at 1732 and 1711 cm.$^{-1}$.

Anhydro-oxoelemadienyl Acetate-II.—By use of the same conditions as in the preparation of anhydro-oxoelemadienyl acetate-I an isomeric product, *anhydro-oxoelemadienyl acetate-II*, was obtained as rods, m. p. 188—192°, $[\alpha]_D$ −15·3 (*c*, 0·45) (Found: C, 80·25; H, 10·2. $C_{32}H_{48}O_3$ requires C, 79·95; H, 10·05%). Light absorption: Max. 2540 Å; ε = 13,800. Infra-red absorption: bands at 1732 and 1711 cm.$^{-1}$.

Anhydro-oxoelemenol.—(*a*) Anhydro-oxoelemadienyl acetate-II (0·55 g.) in ethyl acetate–acetic acid (10 : 1; 55 c.c.) was shaken with hydrogen at 20° in the presence of Adams's catalyst (11 mg.) until absorption was complete (2 hr.). After filtration and evaporation of the filtrate the residual brown syrup (0·54 g.) was adsorbed from light petroleum–benzene (3 : 1) on alumina (25 g.). Elution with the same solvent gave a fraction which was crystallised several times from methanol and ethanol, giving *anhydro-oxoelemenyl acetate-II* as rods, m. p. 166—174° (Found: C, 79·9; H, 10·4. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). Infra-red absorption in Nujol: band at 1738 cm.$^{-1}$. The acetate (300 mg.) in benzene (20 c.c.) was heated under reflux for 3 hr. with 10% methanolic potassium hydroxide (20 c.c.). Dilution with water and extraction with ether yielded an oil which was triturated with light petroleum, and the resulting needles crystallised from ethyl acetate, giving anhydro-oxoelemenol as rods, m. p. 192—197°, $[\alpha]_D$ +88·5° (*c*, 0·5) (Found: C, 82·1; H, 11·1. Calc. for $C_{30}H_{48}O_2$: C, 81·8; H, 11·0%). Infra-red absorption: band at 1738 cm.$^{-1}$.

(*b*) Hydrogenation of anhydro-oxoelemadienyl acetate-I as above yielded anhydro-oxoelemenyl acetate-I as plates (from methanol), m. p. 134—138°, $[\alpha]_D$ −53·5° (*c*, 1·1). This acetate (125 mg.) was heated under reflux with 10% methanolic potassium hydroxide (50 c.c.) for 6 hr. Dilution with water and extraction with ether yielded an oil (102 mg.) which was crystallised from nitromethane and methanol to give anhydro-oxoelemenol as rods, m. p. and mixed m. p. with a sample obtained by method (*a*) 190—195°, $[\alpha]_D$ +88·5° (*c*, 0·5).

Anhydro-oxoelemadienol.—Anhydro-oxoelemadienyl acetate-II (0·47 g.) was heated under reflux with 10% methanolic potassium hydroxide (25 c.c.) for 2 hr. Dilution with water and extraction with ether yielded an oil (0·38 g.) which was crystallised from chloroform–methanol and chloroform–ethyl acetate, giving anhydro-oxoelemadienol as needles, m. p. 237—244°, $[\alpha]_D$ −34° (*c*, 0·4) (Found: C, 82·0; H, 10·85. Calc. for $C_{30}H_{46}O_2$: C, 82·1; H, 10·55%). Infra-red absorption in Nujol: band at 1691 cm.$^{-1}$.

Ozonolysis of Anhydro-oxoelemadienyl Acetate-II.—A stream of ozonised oxygen (6%) was passed through a solution of anhydro-oxoelemadienyl acetate-II (0·46 g.) in ethyl acetate (100 c.c.), at 20° for 1 hr. Raney nickel was added and the solution kept at 20° for 4 days. It was then distilled into an aqueous solution of 2 : 4-dinitrophenylhydrazine sulphate and the resulting two layers were separated. The aqueous layer was extracted with ethyl acetate. The combined ethyl acetate solution gave a residue which was adsorbed from benzene on alumina

(60 g.). Elution with benzene (500 c.c.) gave a dark red oil which was crystallised from ethanol, giving acetone 2 : 4-dinitrophenylhydrazone as needles (0·15 g.; 66%), m. p. and mixed m. p. 126—127° (Found : N, 23·4. Calc. for $C_9H_{10}O_4N_4$: N, 23·5%).

Methyl Acetoxydehydroelemenate.—Methyl acetoxyelemenate (0·3 g.) and selenium dioxide (2·0 g.) were heated under reflux in glacial acetic acid (25 c.c.) for 20 hr. Filtration, dilution with water, and extraction with benzene yielded a red oil (0·25 g.) which was adsorbed from light petroleum–benzene (1 : 1) on alumina (40 g.). Elution with the same solvent yielded a fraction (107 mg.) which was crystallised from methanol and ethanol to give *methyl acetoxydehydroelemenate* as rods (53 mg.), m. p. 134—136°, $[\alpha]_D$ −115° (*c*, 0·3) (Found : C, 77·1; H, 10·35. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·25%). Light absorption : Max. 2320, 2390, and 2450—2480 Å; ε = 13,800, 15,050, and 9700.

Methyl Dehydrohydroxyelemenate.—Methyl acetoxydehydroelemenate (2·6 g.) was heated under reflux with 10% methanolic potassium hydroxide (100 c.c.) for 5 hr. After dilution with water, extraction with ether yielded an oil (2·45 g.) which was methylated with diazomethane. The crude ester was crystallised from ethyl acetate and ethanol giving crystals (0·85 g.), m. p. 144—146°. The residue from the mother-liquor was adsorbed from benzene on alumina (180 g.). After elution with benzene (500 c.c.) and benzene–ether (1 : 1; 250 c.c.), elution with ether (750 c.c.) gave a fraction which formed granular crystals, m. p. 142—147°, from methanol. These were combined with the first crop and crystallised from nitromethane to give *methyl dehydrohydroxyelemenate* as prisms, m. p. 144—145°, $[\alpha]_D$ −98·5° (*c*, 1·8) (Found : C, 79·0; H, 10·75. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). Light absorption : Max. 2330 and 2395 Å, inflection 2470 Å; ε = 13,300, 14,650, and 9450.

Methyl Dehydro-oxoelemenate.—Methyl dehydrohydroxyelemenate (0·54 g.) in benzene (50 c.c.) was kept at 20° for 2 hr. with a solution of chromic acid (0·6 g.) in acetic acid (50 c.c.), acetone (85 c.c.), and water (5 c.c.). After dilution with water, extraction with ether yielded an oil (525 mg.) which was adsorbed from light petroleum–benzene (3 : 1) on alumina (50 g.). Elution with benzene gave a crystalline fraction (0·27 g.) which gave *methyl dehydro-oxoelemenate* as prisms (from ethanol), m. p. 142° (sublimation to long needles)—146·5°, $[\alpha]_D$ −152° (*c*, 0·9) (Found : C, 79·45; H, 10·45. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%). Light absorption : Max. 2320 and 2390 Å, infl. 2450—2480 Å; ε = 16,350, 18,100, and 11,500. Infra-red absorption : bands at 1736 and 1714 cm.$^{-1}$.

Fractionation of the Product of the Oxidation of Methyl Acetoxyelemenate with Selenium Dioxide.—Methyl acetoxyelemenate (18·6 g.) was heated under reflux in acetic acid (250 c.c.) with selenium dioxide (20 g.) for 20 hr. After filtration and dilution of the filtrate with water, extraction with benzene and ether yielded a dark red oil (19 g.) which was adsorbed from light petroleum on alumina (200 g.). Elution with light petroleum (1800 c.c.), light petroleum–benzene (9 : 1; 500 c.c.), light petroleum–benzene (4 : 1; 250 c.c.), and benzene (150 c.c.) yielded a series of fractions (total wt. 8·8 g.) which were mainly methyl acetoxydehydroelemenate. Further elution with benzene (350 c.c.; 900 c.c.), benzene–ether (1 : 1; 500 c.c.) and ether (500 c.c.) yielded the following fractions : (i) yellow oil (1·64 g.); (ii) pale yellow oil (0·47 g.); (iii) yellow oil (0·67 g.); and (iv) yellow oil (0·21 g.). Fractions (i), (iii), and (iv) corresponded to three separate yellow bands on the chromatographic column. Fraction (i) crystallised from light petroleum, ethyl acetate, and methanol as *rods*, m. p. 205—207°, $[\alpha]_D$ −4·5° (*c*, 0·3%) (Found : C, 73·3; H, 9·3. $C_{32}H_{48}O_6$ requires C, 72·7; H, 9·15. $C_{33}H_{50}O_6$ requires C, 73·05; H, 9·25%). Light absorption : Max. 2585 Å; ε = 7300; infra-red absorption bands at 1761, 1725, 1645, and 1618 cm.$^{-1}$.

Attempted Isomerisation of Methyl Acetoxyelemenate.—(*a*) Methyl acetoxyelemenate (0·44 g.; m. p. 140—142·5°; $[\alpha]_D$ −41·8°) was dissolved in acetic acid (10 c.c.) containing concentrated hydrochloric acid (0·5 c.c.), and the mixture kept on the steam-bath for 2½ hr. and then concentrated to half the volume. After dilution with water, extraction with ether yielded an oil (0·38 g.) from which starting material, m. p. 138—140°, $[\alpha]_D$ −39·6° (*c*, 1·4), was obtained.

(*b*) Methyl acetoxyelemenate (0·26 g.) was dissolved in acetic acid (20 c.c.), and concentrated hydrochloric acid (3 c.c.) was added. The mixture was kept at 20° for 3 days, concentrated to half the volume, and then kept at 20° for a further 2 days. After dilution with water, extraction with ether yielded starting material (0·2 g.), m. p. 137—141°, $[\alpha]_D$ −38·7° (*c*, 1·8). Light absorption : $\varepsilon_{2100\,Å}$ = 5300; $\varepsilon_{2150\,Å}$ = 3100, $\varepsilon_{2200\,Å}$ = 1300, and $\varepsilon_{2230\,Å}$ = 1050.

Attempted Isomerisation of Oxoelemenic Acid.—A rapid stream of dry hydrogen chloride was passed through a solution of oxoelemenic acid {0·13 g.; m. p. 233—237°; $[\alpha]_D$ +46·5° (*c*, 0·49)} in dry chloroform at 0° for 1 hr. The solution was then worked up in the usual manner, giving unchanged material (0·11 g.), m. p. 233—238°, $[\alpha]_D$ +41·4° (*c*, 0·59).

Attempted Isomerisation of Methyl Acetoxyelemadienate.—Methyl acetoxyelemadienate (0·13 g.; m. p. 117—118°; $[\alpha]_D$ −50°) was kept at 20° for 4 hr. in 6% formic acid–benzene (20 c.c.). Unchanged material, m. p. 120°, $[\alpha]_D$ −49° (*c*, 0·7), was recovered. Light absorption: $\varepsilon_{2100\text{Å}} = 5500$, $\varepsilon_{2150\text{Å}} = 3355$, $\varepsilon_{2200\text{Å}} = 1490$, and $\varepsilon_{2230\text{Å}} = 1020$.

Oxidation of Hydroxyelemadienic Acid.—(*a*) A solution of chromic acid (1·75 g.) in acetic acid (30 c.c.) containing a few drops of water was added dropwise (5 min.) to a warm (60°) stirred solution of hydroxyelemadienic acid (5 g.) in acetic acid (70 c.c.). Stirring was continued while the solution cooled until precipitation commenced. The solution was then filtered and the precipitate washed with water, the washings being collected in the filtrate. The precipitate (3·1 g.), m. p. 238—249°, $[\alpha]_D$ −30·5°, was repeatedly crystallised from acetic acid and from ethanol, and sublimed at 250°/10^{-3} mm., yielding needles, m. p. 254—256°, $[\alpha]_D$ −73° (*c*, 0·33) (Found: C, 78·95; H, 10·1. Calc. for $C_{30}H_{44}O_3$: C, 79·6; H, 9·8%. Calc. for $C_{30}H_{46}O_3$: C, 79·2; H, 10·2%). Light absorption: 2295 (infl.), 2375 (max.), and 2460—2470 Å (infl.); ε = 3080, 3000, and 1930. The needles are a mixture containing oxoelemadienic acid and dehydro-oxoelemadienic acid.

The filtrate was cooled to 20°, and the resulting precipitate collected by filtration. The product (1·6 g.), m. p. 205—217, $[\alpha]_D$ +10·4°, appeared to be oxoelemadienic acid contaminated with dehydro-oxoelemadienic acid.

(*b*) Hydroxyelemadienic acid (5·0 g.) in acetic acid (125 c.c.) was warmed in the steam-bath and a solution of chromic acid (1·65 g.) in water (25 c.c.) added with stirring during 10 min. The solution was cooled and the precipitate collected. The filtrate was diluted with water and the further precipitate collected and combined with the first. Evaporation of the filtrate gave oxoelemadienic acid as needles (from ethanol–acetic acid) (0·87 g.), m. p. 205—215°, $[\alpha]_D$ +35·9° (*c*, 2·3). Light absorption: 2360—2390 (infl.) and 2440—2490 Å; ε = 680 and 580.

The combined precipitates were crystallised from ethanol–acetic acid, giving needles, m. p. 235—252°, $[\alpha]_D$ −33·5° (*c*, 1·08). Light absorption: Max. 2315, 2385, and 2470 Å; ε = 2270, 2410, and 1880. The needles were methylated with ethereal diazomethane, and the solid product (2·08 g.), m. p. 125—149°, was adsorbed from light petroleum on alumina (200 g.). After elution with light petroleum (440 c.c.) and benzene (300 c.c.), further elution with benzene (110 c.c.; 120 c.c.) gave two fractions: (i) oil (344 mg.), $[\alpha]_D$ −14·4° (*c*, 0·8), $\varepsilon_{2390\text{Å}} = 2270$; (ii) oil (364 mg.), $[\alpha]_D$ −50·1° (*c*, 1·3), $\varepsilon_{2390\text{Å}} = 2480$. The column was then cut into six equal portions and each portion eluted separately with 30% methanol–ether.

The second fraction (97 mg.) from the top was crystallised from methanol, giving *methyl dioxoelemadienate* as plates (50 mg.), m. p. 199—203°, $[\alpha]_D$ −34·5° (*c*, 0·35) (Found: C, 77·0; H, 9·8. $C_{31}H_{46}O_4$ requires C, 77·1; H, 9·6%). Light absorption: Max. 2520 Å; ε = 9350. Infra-red absorption: bands at 1733, 1713, and 1666 cm.$^{-1}$.

Comparison of the Ultra-Violet Spectra of Samples of Hydroxy- and Oxo-elemadienic Acids.

Source of sample	Compound (Author's description)	ε at the maxima or inflections at *ca.*		
		2320	2390	2470 Å
Prof. G. A. R. Kon	α-Elemolic acid (purified by two treatments with Girard Reagent-T)	725	645	590
	α-Elemolic acid (Puriss.)	935	850	775
	β-Elemonic acid (m. p. 212—214°; $[\alpha]_D$ +45°)	355	205	130
Prof. H. Lieb	Elemi acid (crude)	1230	1105	1035
	Elemi acid (m. p. 221°)	1100	1005	925
	Elemi acid (from elemi acetate)	270	180	125
Dr. J. C. E. Simpson	α-Elemolic acid (crude)	350	290	200
	β-Elemonic acid (crude)	1000	875	695
Present work......	Mixed acids	1000	1065	910
	α-Elemolic acid (from Girard separation)	—	290	200
	β-Elemolic acid (from Girard separation)	840	760	510
Compare methyl acetoxyelemenate (no maximum or inflection)..................		215	75	0

The authors thank Professor E. R. H. Jones, F.R.S., for his interest and advice, and Professor H. Lieb (Graz) and the late Dr. J. C. E. Simpson for making available samples of the elemi acids. One of them (R. E. H. S.) is indebted to the Ministry of Education for a F.E.T.S. grant. Thanks are also proffered to Mr. E. S. Morton and Mr. H. Swift for the microanalyses.

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[*Received, August 22nd,* 1953.]