464. *The Chemistry of Cedrelone.*[1]

By R. Hodges, S. G. McGeachin, and R. A. Raphael.

Chemical evidence is presented for the structure (I) for cedrelone, and the constitutions of rearrangement products of the substance are elucidated.

The isolation of the natural product, cedrelone, was first reported by Parihar and Dutt, who obtained it, along with an essential oil, by benzene extraction of the heartwood of *Cedrela toona* Roxb.[2] These workers assigned the formula $C_{25}H_{30}O_5$ to cedrelone; on the basis of some colour tests, and the formation of an acetate, an oxime, and a dibromide, they considered it to be phenolic and to possess a ketonic carbonyl group, an ethylenic double bond, and a $\beta\gamma$-unsaturated lactone ring.

Repetition of the Indian workers' isolation procedure gave cedrelone without difficulty as a highly crystalline substance which, in contrast to the analogously constituted " bitter principles," is quite tasteless. Elemental analysis and an accurate mass-spectrometric determination of the molecular weight showed that the previous molecular formula had to be amended to $C_{26}H_{30}O_5$.

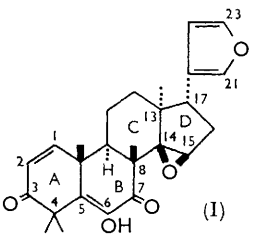
The spectral properties of cedrelone and its simple derivatives were in good agreement

[1] Preliminary communications: (*a*) Grant, Hamilton, Hamor, Hodges, McGeachin, Raphael, Robertson, and Sim, *Proc. Chem. Soc.*, 1961, 444; (*b*) Arigoni, Gopinath, Govindachari, Parthasarathy, Viswanathan, and Wildman, *ibid.*, 1961, 446.

[2] Parihar and Dutt, *J. Indian Chem. Soc.*, 1950, **27**, 77.

with the functional groups present. Thus, in the infrared spectrum three bands at 3130w, 1505w, and 878s cm.$^{-1}$, characteristic of the furan ring, were present. A peak in the carbonyl region at 1678 cm.$^{-1}$, with an inflection at 1685 cm.$^{-1}$, indicated the two unsaturated carbonyl groups in the molecule. In addition, the presence of a hydroxyl group was shown by a band at 3425 cm.$^{-1}$. The position of this band and its insensitivity to dilution indicated that the diosphenol hydroxyl was intramolecularly hydrogen bonded to the adjacent carbonyl function. The ultraviolet spectrum of cedrelone had $\lambda_{max.}$ 217 mμ (ε 11,800) consistent with a summation of furan and ring-A-enone chromophores, and a maximum at 279 mμ (ε 9100) shifting in base to 327 mμ (ε 5550) which was particularly characteristic for the diosphenol function. The position and intensities observed for cedrelone and other diosphenols in the series were in good agreement with those for limonin diosphenol [$\lambda_{max.}$ 278 mμ (ε 10,000), shifting in base to 336 mμ (ε 6150)],[3] in which the diosphenol has an environment similar to that in cedrelone.

Methylation of cedrelone gave a monomethyl ether, and acetylation readily gave a monoacetate and similarly a chloroacetate. Cedrelone acetate had bands in the infrared at 1770 cm.$^{-1}$, highly characteristic for the enol acetate carbonyl, and 1702 cm.$^{-1}$, associated with the two enone carbonyls. The shift to higher frequency of the diosphenol carbonyl after acetylation can be attributed mainly to removal of the hydrogen bonding.



(I)

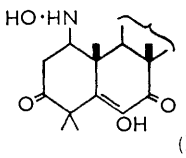
The ultraviolet spectrum had maxima at 222 (16,400) with an inflection at 245 mμ (ε *ca.* 8000), and 320 mμ (ε 170), in agreement with the normal neutralisation of the bathochromic effect of the hydroxyl in an α-hydroxyenone after acetylation.[4] The successful hydrolysis of cedrelone acetate to cedrelone was very dependent upon the reaction conditions, owing to the lability of cedrelone itself in base (see below). The ready chloroacetate formation led to the preparation of the crystalline iodoacetate which was submitted for *X*-ray structural examination while the chemical work was proceeding. This led to the determination of the structure and relative stereochemistry of cedrelone as (I) (see preceding paper). The chemistry of cedrelone as described herein was fully consistent with this constitution.

Catalytic hydrogenation of cedrelone under mild conditions yielded a dihydro-derivative in which the double bond in ring A had been saturated. The ultraviolet subtraction curve of dihydrocedrelone from cedrelone had $\lambda_{max.}$ 225 mμ (ε 8100) which is the contribution of the enone chromophore in ring A to the total ultraviolet absorption of cedrelone. By the use of platinum in acetic acid, hydrogenation proceeded further to a hexahydro-derivative in which the furan ring was also reduced.

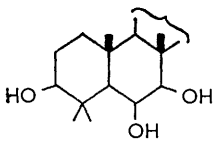
The diosphenol function in cedrelone was found to be completely resistant to quinoxaline formation under a variety of conditions. A number of attempts were made to cleave it to the corresponding dicarboxylic acid by the use of the standard oxidative reagents. Cedrelone was recovered unchanged from treatment with sodium periodate. With lead tetra-acetate it afforded a yellow crystalline unstable acetoxylated product, probably the 5-acetoxy-6,7-dione. Attempted cleavage of the diosphenol by the action of hydrogen peroxide and alkali led to the isolation of a neutral compound, $C_{26}H_{30}O_6$, which was formulated as the 1,2-epoxide, since its ultraviolet spectrum [$\lambda_{max.}$ 201 mμ (ε 7200), and 276 mμ (ε 10,700)] established the retention of the diosphenol function but loss of the ring-A-enone. The infrared spectrum, with carbonyl bands at 1719 (α-oxygenated cyclohexanone) and 1681 cm.$^{-1}$ (diosphenol), and no absorption below 700 cm.$^{-1}$, confirmed this. Subtraction of the ultraviolet spectrum from that of cedrelone gave $\lambda_{max.}$ 225 mμ (ε 7300), in good agreement with the previous value estimated for this enone chromophore.

[3] Barton, Pradhan, Sternhell, and Templeton, *J.*, 1961, 255.
[4] Gillam and Stern, " An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold Ltd., London, 1957, p. 112.

Parihar and Dutt [2] reported the formation of a crystalline oxime from cedrelone by treatment with hydroxylamine hydrochloride and sodium acetate in refluxing acetic acid. In our hands this procedure afforded only amorphous solids which decomposed on attempted purification, and which had a number of the infrared characteristics of the acid-catalysed rearrangement product from cedrelone (see below). However, oximation in pyridine–



(II)



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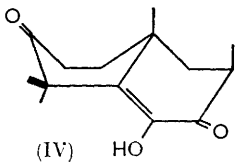
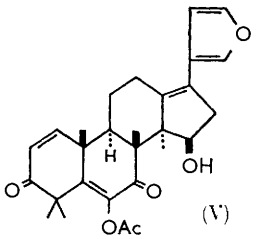




(V)

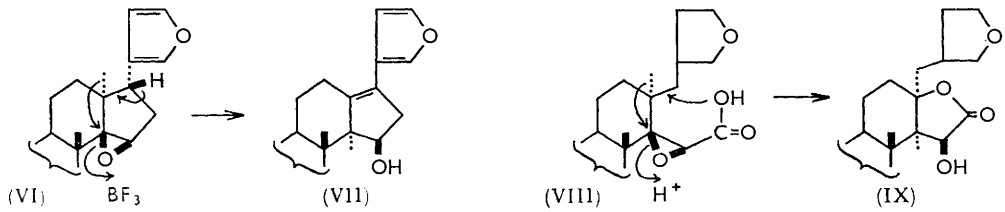
ethanol solution gave a nitrogen-containing derivative, $C_{26}H_{33}NO_6$, whose formula showed it to be an adduct with hydroxylamine and not an oxime. It decomposed at the melting point with re-formation of cedrelone and this, in conjunction with the spectral properties, indicated the structure (II). The formation of β-hydroxyamino-oximes from αβ-unsaturated ketones on oximation is well known; [5] it is, however, of interest to note that the carbonyl group at C-3 was resistant to oximation even after prolonged treatment with the reagent. An entirely analogous reaction is the reduction of cedrelone with an excess of sodium borohydride at room temperature in aqueous dioxan,[1b] to the same dihydro-derivative as is obtained by catalytic hydrogenation. Reduction of the carbon–carbon double bond in conjugated systems by sodium borohydride has been previously observed; thus the butenolide system of iresin was reduced to the butanolide to give dihydroiresin,[6] and conjugated nitroalkenes gave the saturated nitro-compounds.[7] However, saturation of the double bond in an enone by sodium borohydride has hitherto been accompanied by concomitant reduction of the carbonyl grouping; [8] thus, the system most closely comparable to cedrelone occurs in gedunin which gave dihydrogedunol by treatment with sodium borohydride [9] under conditions in which only the double bond of cedrelone is reduced. Drastic reduction of cedrelone to the triol (III) by borohydride has been reported.[1b]

The failure of the ring-A-carbonyl of dihydrocedrelone to undergo oximation, and its considerable resistance to borohydride reduction, contrast strongly with the normal reactivity of the carbonyl function in 3-oxo-triterpenes, which readily undergo both of these reactions. The reasons for this are probably steric in origin. A consideration from models of the non-bonded interactions associated with chair and flexible forms of ring A in dihydrocedrelone suggests that the preferred conformation is the boat (IV), since only in it is the severe eclipsed interaction between the 4-α-methyl group and the 6-substituent absent. In this conformation the carbonyl group is shielded from attack on the β-face by the 10-methyl, and on the α-face by the pseudo-axial 4α-methyl group. Further, nucleophilic addition to the carbonyl would be energetically unfavourable as it requires that C-3 become tetrahedral, and the resulting product would have a severe non-bonded interaction of the 1,4-" boat-flagpole " type between the 3β-substituent and the 10-methyl group. Nucleophilic addition to the carbonyl group when ring A is in the chair conformation would be free from these objections, but, as has already been stated, this conformation is energetically the less favourable.

[5] Kötz and Grethe, *J. prakt. Chem.*, 1909, **80**, 499.
[6] Djerassi and Rittel, *J. Amer. Chem. Soc.*, 1957, **79**, 3528.
[7] Schechter, Ley, and Robertson, *J. Amer. Chem. Soc.*, 1956, **78**, 4984.
[8] Albrecht and Tamm, *Helv. Chim. Acta*, 1957, **40**, 2216; Sondheimer, Velasco, Batres, and Rosenkranz, *Chem. and Ind.*, 1954, 1482.
[9] Akisanya, Bevan, Hirst, Halsall, and Taylor, *J.*, 1960, 3827; Akisanya, Bevan, Halsall, Powell, and Taylor, *J.*, 1961, 3705; Robertson, Sim, and Sutherland, *Proc. Chem. Soc.*, 1962, 222.

It is suggestive that the *X*-ray examination of cedrelone iodoacetate showed ring A to possess the boat-like conformation rather than the alternative half-chair. Although some part may be played by intermolecular forces in the crystal, this conformation may be preferred because it minimises non-bonded interactions between the 4-methyl groups and the bulky 6-substituent; in the half-chair this substituent is eclipsed by the 4α-methyl group.

Treatment of cedrelone acetate with boron trifluoride etherate yielded an isomeric compound, isocedrelone acetate. Comparison of its infrared and ultraviolet spectra with those of cedrelone acetate established that the enone and diosphenol type of function were still present, and that a hydroxyl group and a new chromophore had been introduced. Subtraction of the ultraviolet spectrum of cedrelone acetate from that of isocedrelone acetate showed this chromophore to have $\lambda_{max.}$ 242 mμ (ε 13,200) assignable to the substituted 3-vinylfuran system. The hydroxyl group was not acetylated under mild conditions but it was acetylated in refluxing acetic anhydride–sodium acetate solution, which suggested that it was a tertiary or hindered secondary alcohol. The latter was favoured on the basis of a new peak in the infrared spectrum at 1061 cm.$^{-1}$, incompatible with the carbon–oxygen single-bond stretching vibration of a tertiary alcohol. This was confirmed by comparison of the nuclear magnetic resonance spectra of cedrelone and isocedrelone acetates. These were fairly similar but the former showed a peak at τ 6·35, attributable to the epoxide proton at C-15 in cedrelone acetate; this position, lower by one unit than the recorded value for such a proton,[10] is explicable in terms of deshielding by the nearby C-7 carbonyl function. In isocedrelone acetate this peak had moved downfield to τ 5·42, compatible with a similar deshielded proton on a carbon bearing a hydroxyl group.



The above spectral observations, combined with the mode of formation, indicated that structure (V) was the most probable. This arises through Lewis acid-catalysed cleavage of the epoxide ring with concomitant methyl migration from C-13 to C-14 and generation of a double bond in conjugation with the furan ring (VI ⟶ VII). The stereochemistry of cedrelone is such that ring C of necessity exists in a boat conformation, whereas it becomes a chair in isocedrelone acetate. It is considered that the driving force for the rearrangement arises from the attendant relief of steric strain. Excellent analogy for this exists in the acid-catalysed conversion of the stereochemically similar epoxy-acid, hexahydrolimoninic acid (VIII) into the isomeric hydroxy-γ-lactone (IX).[3] Analogous rearrangement products were similarly obtained from dihydrocedrelone and its acetate.

It has recently been reported [11] that cedrelone, on treatment with acetic anhydride in the presence of toluene-*p*-sulphonic acid, gave a diacetate, m. p. 245—247°. The reaction conditions employed would have been expected to give isocedrelone diacetate but this, however, has a much lower melting point. We have reinvestigated this compound, and found that it analysed as a triacetyl derivative of cedrelone. Its infrared spectrum [$\nu_{max.}$ (in carbon tetrachloride) 1767, 1742, 1699, and 1688 cm.$^{-1}$] clearly showed, by comparison with that of isocedrelone diacetate [$\nu_{max.}$ (in carbon tetrachloride) 1766, 1742, and 1698 cm.$^{-1}$], that it was a derivative of the latter into which a third acetyl group had been

[10] Jackson, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 55.
[11] Aghoramurthy, Dass, Mukherjee, and Rao, *J. Sci. Ind. Res., India*, 1962, **21**,*B*, 95.

introduced. The ultraviolet spectrum [$\lambda_{max.}$ 223 (20,400) and 276 mμ (ε 14,000)] provided the clue as to the position of this acetyl group, by indicating that the vinylfuran chromophore had undergone extended conjugation. This required that a Friedel–Crafts acetylation of the furan had taken place; that this was so was proved by the appearance of only one furan α-proton (multiplet at τ 2·44) and one β-proton (multiplet at τ 3·04) in the nuclear magnetic resonance spectrum. The well-known sensitivity of the Friedel–Crafts reaction to steric hindrance would support the compound's being the 23-acetyl derivative of isocedrelone diacetate rather than the 21-acetyl isomer. This acetylation of the furan ring is quite unexceptional; furan itself gives 2-acetylfuran in moderate yield by treatment with acetic anhydride and toluene-*p*-sulphonic acid.[12] In addition to the above product there was isolated, in an amount too small to permit complete characterisation, a second compound, whose ultraviolet and infrared spectra were consistent with its being the 21-acetyl isomer.

Treatment of cedrelone with aqueous-alcoholic potassium hydroxide under reflux afforded in moderate yield an acid, $C_{26}H_{32}O_6$, hereafter termed isocedrelonic acid. That it was a monocarboxylic acid was shown by its solubility in aqueous sodium hydrogen carbonate solution, and the formation of a neutral monomethyl ester by treatment with diazomethane. The acid had bands in its solid-state infrared spectrum, at 3550, 3540, 3250, 1706, 1672, and 875 cm.$^{-1}$; the peaks at 1672 and 875 cm.$^{-1}$ indicated that the ring-A-enone and furan ring, respectively, had been retained. Those at 3604 and 3525 cm.$^{-1}$ in the ester established that it was a derivative of a mono- or a di-hydroxy-acid. That the latter was correct was proved by the conversion of the ester into an acetate which still showed a hydroxyl band in its infrared spectrum. The presence of two hydroxyl groups, the furan ring, and the enone function in ring A, taken in conjunction with the molecular formula of the acid, indicated that the epoxide ring could no longer be intact. The same conclusion was also reached from the observation that the acid was stable to boron trifluoride etherate.

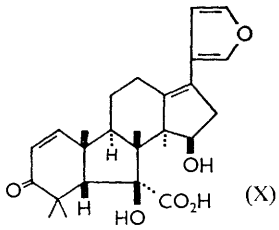
The ultraviolet spectrum of isocedrelonic acid [$\lambda_{max.}$ 235 mμ (ε 20,000), unaltered in base] suggested that the diosphenol function was no longer present and that the epoxide had been opened in the same manner as in isocedrelone acetate, with the attendant formation of a vinylfuran. This was confirmed by the near identity of this absorption with the ultraviolet subtraction curve of hexahydrocedrelone acetate from isocedrelone acetate, which had $\lambda_{max.}$ 236 mμ (ε 18,000), the contribution of the ring-A-enone and vinylfuran chromophores to the ultraviolet spectrum of isocedrelone acetate.

The above evidence strongly indicated that isocedrelonic acid had the structure (X), formed by benzilic acid rearrangement of the diosphenol function of cedrelone together with the epoxide rearrangement detailed above. Further support for this structure came from two sources. First, similar basic hydrolysis of isocedrelone acetate gave the same acidic rearrangement product. Secondly, oxidation of isocedrelonic acid by lead tetra-acetate in dioxan–benzene at room temperature afforded a neutral compound, $C_{25}H_{30}O_4$. That this was the norketone (XI; R = H) expected on the basis of structure (X) for the acid was shown by its ultraviolet spectrum, identical with that of the acid, and bands at 3470 (hydrogen-bonded hydroxyl), 1718 (hydrogen-bonded cyclopentanone), and 1691 cm.$^{-1}$ (ring-A-enone) in its infrared spectrum. The norketone on acetylation gave a monoacetate (XI; R = Ac) [$\nu_{max.}$ (in carbon tetrachloride) 1739 with an inflection at 1745, and 1690 cm.$^{-1}$] in which the cyclopentanone carbonyl absorption had moved up to a more normal value.

The probable stereochemistry assigned to isocedrelonic acid results from the following observations. The hydroxyl group on C-15 must be β since the same acid results from hydrolysis of isocedrelone acetate. The norketone was obtained from the acid by a very mild reaction during which quantitative epimerisation at C-5 would appear unlikely to

[12] Hartough and Kosak, *J. Amer. Chem. Soc.*, 1947, **69**, 3093.

occur. It was shown to be the more stable epimer since it was recovered unchanged after treatment with boiling aqueous-alcoholic alkali. Inspection of models of the *cis*- and *trans*-A/B-fused norketones corresponding to (XI) showed that the latter is the more strained and has serious 1,3-non-bonded interactions between the β-methyl groups at C-4, C-10, and C-8. By comparison the *cis*-fused isomer can adopt a conformation in which there



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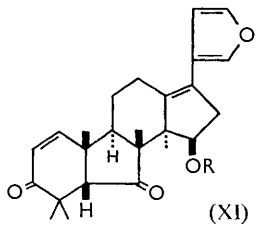

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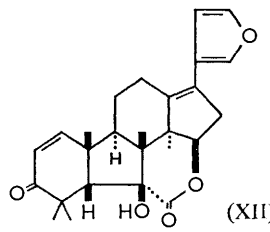


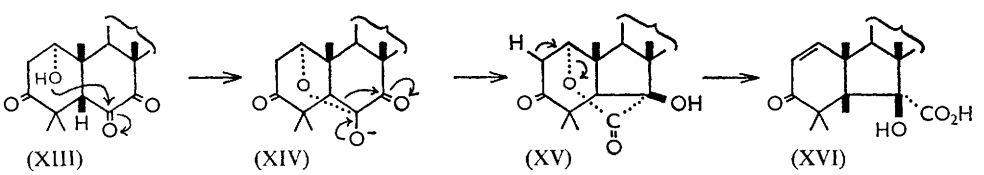
(XII)

is no interaction between the 4β-methyl group and that at C-10, and in which the interaction between the C-8 and C-10 methyl is diminished. The stereochemistry of isocedrelonic acid (X) at C-6 was established through the formation of a lactone (XII), described in more detail below. Molecular models indicate that for either a *cis*- or a *trans*-A/B-fused ring junction, lactonisation can take place most readily if the carboxyl group is placed α on C-6.

It is of some interest to enquire into the reasons and mechanism for the opening of the epoxide ring under seemingly basic conditions during formation of isocedrelonic acid. It is noteworthy that, even under forcing conditions of basic hydrolysis, dihydrocedrelone and isodihydrocedrelone acetates were merely deacetylated to the corresponding parent compounds, with formation of only traces of acidic by-products.

This seeming paradox was resolved by isolating the initial potassium salt from the reaction mixture, and measuring its ultraviolet spectrum. This had $\lambda_{max.}$ 220 mμ (ε 9700), consistent with the presence of only the ring-A-enone and furan chromophores; only after acidification of the solution did the spectrum change immediately to that of isocedrelonic acid with its characteristic vinylfuran chromophore. It would therefore seem highly probable that the epoxide ring is unaffected during the benzilic acid rearrangement *per se*, but undergoes an extremely facile opening on acidification, owing to the very considerable strain inherent in a boat ring C *trans*-fused to two five-membered rings.

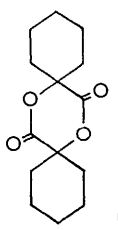
As previously mentioned, dihydro- and isodihydro-cedrelone cannot be induced to undergo the benzilic acid rearrangement, behaviour which contrasts markedly with that of cedrelone. A possible explanation, in terms of current views on the benzilic acid rearrangement, is as follows. As noted above, the ring-A-enone is highly susceptible to nucleophilic attack at C-1, and in aqueous methanolic alkali the 1,2-dihydro-1α- and -1β-hydroxycedrelones will exist in equilibrium with cedrelone. In the case of the 1α-*cis*-A/B-fused diketo-tautomer (XIII) intramolecular addition of the anion generated by base on the 1-hydroxyl group to the 6-carbonyl group would lead to the intermediate (XIV)



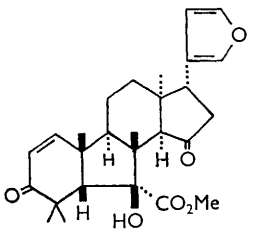
(XIII) (XIV) (XV) (XVI)

which could then undergo benzilic rearrangement to the α-hydroxy-acid (XVI) of the same stereochemistry deduced on other grounds by way of an intermediate such as (XV). Such a mechanism is of course precluded when the ring-A double bond has been removed.

Dehydration of isocedrelonic acid by dicyclohexylcarbodi-imide afforded two products, readily separable by chromatography. The more polar substance, $C_{26}H_{30}O_5$, had an ultraviolet spectrum identical with that of the acid, and showed peaks at 3593 (hydrogen bonded hydroxyl), 1753 (δ-lactone), and 1686 cm.$^{-1}$ (ring-A-enone). These spectral properties, and the reconversion of the compound into isocedrelonic acid by hydrolysis, indicated its formulation as the lactone (XII). The less polar substance was shown to be the norketone (XI; R = H), by a direct comparison of its physical properties with those of the product resulting from oxidation of isocedrelonic acid. The lactone decomposed on melting, with evolution of a gas, and the decomposition product was again the norketone. Rather surprisingly, however, the lactone did not yield any of the norketone by treatment with dicyclohexylcarbodi-imide, thus indicating that, under the reaction conditions employed, it was not an intermediate in the formation of the norketone. The formation of the norketone during the di-imide reaction may have the following explanation. Lactides are known to undergo a synchronous double decarbonylation on pyrolysis;[13] thus the spirolactide (XVII) gives two molecules each of carbon monoxide and cyclohexanone. If a lactide were formed from two molecules of isocedrelonic acid, as an alternative to lactonisation, then it would seem reasonable that this lactide, highly destabilised by non-bonded interactions between the two linked molecules, might undergo a particularly ready double decarbonylation with the consequent formation of the norketone.



(XVII)



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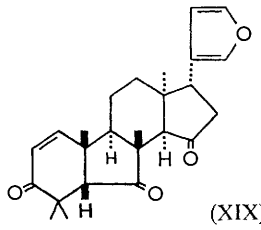

(XIX)

The mother liquors from crystallisation of crude isocedrelonic acid were treated with diazomethane. Chromatography of the resulting methyl esters gave not only the expected methyl isocedrelonate but also a new isomeric methyl ester whose light-absorption properties were fully compatible with the structure (XVIII). The production of this isomer in the cedrelone–isocedrelonic acid rearrangement can be readily rationalised by the alternative and more usual mode of epoxide opening to yield the isomeric ketone. Lead tetra-acetate oxidation of the free acid derived from (XVIII) gave the corresponding norketone (XIX), a formulation fully in accord with its spectral properties and its resistance to rearrangement by boron trifluoride etherate.

Cedrelone is thus revealed as a member of the growing class of skeletally-related C_{26} modified triterpenes of the euphol type exemplified by limonin,[3, 14] obacunone,[3, 15] nomilin,[3, 15] gedunin,[9] khivorin,[16] and cedrelide,[17] which have in common a number of structural features such as a β-substituted furan, a β-epoxide function involving C-14 and C-15, a β-methyl at C-8, and oxygen substitution at C-7. Biogenetically, cedrelone is of some interest in that it alone of the series so far possesses an intact carbocyclic ring D. It is also unusual in containing a diosphenol function, a structural feature of rare occurrence in Nature.

[13] Golomb and Ritchie, *J.*, 1962, 838.
[14] Arigoni, Barton, Corey, Jeger, and collaborators, *Experientia*, 1960, **16**, 41; Arnott, Davie, Robertson, Sim, and Watson, *ibid.*, p. 49.
[15] Kubota, Matsuura, Tokoroyama, Kamikawa, and Matsumoto, *Tetrahedron Letters*, 1961, No. 10, 325.
[16] Bevan, Halsall, Nwaji, and Taylor, *J.*, 1962, 768.
[17] Henderson, McCrindle, and Overton, personal communication.

Experimental

M. p.s were determined on the Kofler block. Specific rotations are for chloroform solutions at room temperature, unless otherwise specified. Infrared spectra of solutions were recorded on a Unicam S.P. 100 Mark II instrument, with a prism-grating monochromator, and operated with evacuated optics; Nujol spectra were obtained with a Perkin-Elmer Infracord spectrophotometer. Ultraviolet maxima below 215 mμ were recorded on a Hilger Uvispek photoelectric spectrophotometer, and above 215 mμ on a Perkin-Elmer ultraviolet recording spectrophotometer (Model 137), both for ethanol solutions. Microanalyses were by Mr. J. M. L. Cameron, B.Sc., and his associates. Brockmann-standardised alumina was used for chromatography.

Extraction of Cedrelone.—Dry powdered heartwood of *Cedrela toona* Roxb. was extracted continuously with benzene in a Soxhlet apparatus. Addition of light petroleum to the extract, after concentration *in vacuo*, precipitated crude cedrelone (0·4% of the weight of dried wood). This, on recrystallisation several times from chloroform–ethanol, afforded pure cedrelone as rhombs, m. p. 209—214°, $[\alpha]_D$ −64·5° (*c* 1·0), $\lambda_{max.}$ 217 (11,800) and 279 (9100) shifting in base to 327 mμ (ε 5550), $\nu_{max.}$ ($CHCl_3$) 3425 (hydroxyl), 1678 with a shoulder at 1685 $cm.^{-1}$ (αβ-unsaturated ketones), (Nujol) 3130, 1505, 878 $cm.^{-1}$ (furan) (Found: C, 74·1; H, 7·4. Calc. for $C_{26}H_{30}O_5$: C, 73·9; H, 7·15%). It gave a dark-green colour with alcoholic ferric chloride.

Cedrelone Acetate.—Cedrelone (2 g.) was acetylated in acetic anhydride (2 ml.) and pyridine (2 ml.) at room temperature for 24 hr. The solution was poured into water and extracted with ether. The extract was washed with dilute sulphuric acid, sodium hydrogen carbonate solution, and water. Drying, removal of solvent, and crystallisation of the residue from 80% aqueous ethanol gave *cedrelone acetate* (2 g.) as plates, m. p. 156—159°, $[\alpha]_D$ −56° (*c* 0·99), $\lambda_{max.}$ 222 (16,400), shoulder at 245 (*ca.* 8000), and 320 mμ (ε 170), $\nu_{max.}$ (CCl_4) 1770 (enol acetate), 1702 $cm.^{-1}$ (αβ-unsaturated carbonyls) (Found: C, 72·5; H, 7·05. $C_{28}H_{32}O_6$ requires C, 72·4; H, 6·95%).

Hydrolysis of Cedrelone Acetate to Cedrelone.—Cedrelone acetate (20 mg.) was dissolved in dioxan (0·5 ml.) and N-potassium hydroxide solution (0·2 ml.), and kept at room temperature for 2 days. The solution was diluted with water and extracted with ether to give cedrelone (13 mg.).

Cedrelone Chloroacetate.—Cedrelone (100 mg.) and chloroacetic anhydride (97 mg.; 2·4 equiv.) were dissolved in benzene (1 ml.) containing pyridine (0·02 ml.) at room temperature. After 16 hr. the solution was poured into water and the product extracted with ether. Removal of the solvent and crystallisation from chloroform–ethanol gave *cedrelone chloroacetate* (114 mg.) as needles, m. p. 171·5—173°, $[\alpha]_D$ −39° (*c* 1·1), $\lambda_{max.}$ 222 (15,900), 320 mμ (ε 442), $\nu_{max.}$ (Nujol) 1769 and 1702 $cm.^{-1}$ (Found: C, 67·2; H, 6·35. $C_{28}H_{31}ClO_6$ requires C, 67·4; H, 6·25%).

Cedrelone Iodoacetate.—Cedrelone chloroacetate (100 mg.) and sodium iodide (200 mg.) were refluxed under nitrogen in "AnalaR" acetone (8 ml.) for 8 hr. After concentration, the solution was poured into water and the product extracted with ether. Crystallisation from aqueous ethanol afforded *cedrelone iodoacetate* as plates, m. p. 149—149·5°, $[\alpha]_D$ −24° (*c* 1·0), $\lambda_{max.}$ 223 (15,600), shoulder at 250 mμ (ε *ca.* 8500) (Found: C, 56·7; H, 5·15. $C_{28}H_{31}IO_6$ requires C, 56·95; H, 5·3%).

Cedrelone Methyl Ether.—Cedrelone (1 g.) and dimethyl sulphate (2 ml.) were dissolved in dioxan (25 ml.). Small additions (2·5 ml.) of N-potassium hydroxide solution were made at intervals sufficient to maintain the yellow colour of the solution. When addition of alkali no longer re-established the colour, a further quantity (10 ml.) was added to hydrolyse the excess of dimethyl sulphate. Dissolution of the resulting precipitate in benzene–chloroform (1 : 1), followed by filtration through Grade II alumina and evaporation, gave *cedrelone methyl ether* (800 mg.), which crystallised from chloroform–ethanol as prisms, m. p. 207—210°, $[\alpha]_D$ −13·4° (*c* 0·97), $\lambda_{max.}$ 216 (13,200) and 262 mμ (ε 9000), $\nu_{max.}$ ($CHCl_3$) 1692 $cm.^{-1}$ (Found: C, 74·2; H, 7·5; $C_{27}H_{32}O_5$ requires C, 74·3; H, 7·4%).

The Lead Tetra-acetate Oxidation of Cedrelone.—Cedrelone (550 mg.) in benzene (10 ml.) was shaken at room temperature with lead tetra-acetate (630 mg.; 1·05 equiv.) and the resulting mixture, after dilution with ether, was thoroughly washed with dilute sodium hydroxide solution and water. Removal of the solvent, and crystallisation of the residue from ethyl acetate–light petroleum, afforded the unstable oxidation product which gave one spot on a silica

chromatoplate, m. p. 212°, $[\alpha]_D$ −12·8° (*c* 1·25), $\lambda_{max.}$ 215 (11,600), 273 (5200), 433 mμ (in chloroform) (ε 34), $\nu_{max.}$ (Nujol) 3100, 1500, 874 (furan), 1744, 1240 (acetate), 1690 (enone and α-diketone), and 690 cm.$^{-1}$ (*cis*-double bond). After a day the product showed several additional spots when examined on a silica chromatoplate.

Dihydrocedrelone.—(*a*) Cedrelone (38·8 mg.) in " AnalaR " ethyl acetate (10 ml.) was hydrogenated over 5% palladium–charcoal (11 mg.) until the uptake of hydrogen (2·41 ml.; theoretical for 1 mol. = 2·25 ml.) ceased. The product was chromatographed over Grade II alumina. Elution with 15% chloroform in benzene gave *dihydrocedrelone*, prisms (from chloroform), m. p. 211—214° (sealed capillary), $[\alpha]_D$ −60° (*c* 0·97), $\lambda_{max.}$ 210 (6100) and 279 mμ (ε 9950), $\nu_{max.}$ ($CHCl_3$) 3430, 1712·5, 1677, and 1636w cm.$^{-1}$, (Nujol) no band at 690 cm.$^{-1}$ (Found: C, 73·25; H, 7·6. $C_{26}H_{32}O_5$ requires C, 73·55; H, 7·6%).

Dihydrocedrelone, on acetylation with 1 : 1 acetic anhydride–pyridine (1 ml.) at room temperature for 24 hr., gave dihydrocedrelone acetate as plates (from aqueous ethanol), m. p. 176—180°, $[\alpha]_D$ −76° (*c* 0·84), $\lambda_{max.}$ 217 (8500) and 245 mμ (ε 9000), $\nu_{max.}$ ($CHCl_3$) 1764, 1714, 1702·5, and 1610w cm.$^{-1}$ (Found: C, 71·85; H, 7·5. $C_{28}H_{34}O_6$ requires C, 72·1; H, 7·35%).

(*b*) Cedrelone (100 mg.), dissolved in dioxan (1·5 ml.) and water (0·15 ml.), was treated with sodium borohydride (10 mg.; 11 mol.) at room temperature for 1·5 hr. Addition of water precipitated crystalline dihydrocedrelone, identical with the product obtained by hydrogenation of cedrelone.

Hexahydrocedrelone.—Cedrelone (1 g.) in " AnalaR " acetic acid (180 ml.) was hydrogenated over prereduced platinum oxide (250 mg.). Hydrogenation was complete after 1·5 hr. during which 214 ml. had been absorbed (theoretical for 3 mol. uptake = 175 ml.). The product was adsorbed from benzene on Grade IV alumina (50 g.). Elution with benzene gave *hexahydrocedrelone* (700 mg.) as a mixture of C-20 epimers. Repeated crystallisation from chloroform–ethanol afforded one pure isomer as needles, m. p. 222—225°, $[\alpha]_D$ −44·5° (*c* 0·86), $\lambda_{max.}$ 279 (11,000) shifting in base to 329 mμ (ε 7500), $\nu_{max.}$ ($CHCl_3$) 3435 (hydroxyl), 1712 (cyclohexanone), 1676 (diosphenol), and 1624w cm.$^{-1}$ (diosphenol double bond) (Found: C, 73·1; H, 8·55. $C_{26}H_{36}O_5$ requires C, 72·85; H, 8·45%). Hexahydrocedrelone (145 mg.), on acetylation as for dihydrocedrelone, gave *hexahydrocedrelone acetate* as plates (from aqueous ethanol), m. p. 185—190°, $[\alpha]_D$ −44·5° (*c* 0·92), $\lambda_{max.}$ 245 mμ (ε 9400), $\nu_{max.}$ (CCl_4) 1770·5 (enol acetate), 1720·5 (cyclohexanone), and 1705 cm.$^{-1}$ (diosphenol) (Found: C, 71·55; H, 7·9. $C_{28}H_{38}O_6$ requires C, 71·45; H, 8·15%).

1,2-*Epoxycedrelone.*—Cedrelone (150 mg.) was dissolved in dioxan (20 ml.); hydrogen peroxide (30%; 5 ml.) and N-sodium hydroxide solution (5 ml.) were added, and the solution was set aside for 36 hr. at room temperature. The product was isolated by chloroform extraction of the solution after dilution with water. 1,2-*Epoxycedrelone* crystallised from chloroform–ethanol as needles, m. p. 222—228°, $[\alpha]_D$ −10·6° (*c* 0·71), $\lambda_{max.}$ 201 (7200) and 276 mμ (ε 10,700), $\nu_{max.}$ ($CHCl_3$) 3428 (hydroxyl), 1719 (α-oxygenated cyclohexanone), 1681 (diosphenol), and 1630w cm.$^{-1}$ (diosphenol double bond) (Found: C, 71·25; H, 6·8. $C_{26}H_{30}O_6$ requires C, 71·2; H, 6·9%). Acetylation as for dihydrocedrelone gave 1,2-*epoxycedrelone acetate*, plates (from aqueous ethanol), m. p. 214—217°, $[\alpha]_D$ −26° (*c* 0·88), $\lambda_{max.}$ 217 (8900) and 244 mμ (ε 9900), $\nu_{max.}$ (CCl_4) 1769 (enol acetate), 1722 (α-oxygenated cyclohexanone), and 1707·5 cm.$^{-1}$ (diosphenol) (Found: C, 69·9; H, 6·95. $C_{28}H_{32}O_7$ requires C, 69·95; H, 6·7%).

1,2-*Dihydro*-1-*hydroxyaminocedrelone* (II).—Cedrelone (200 mg.) and hydroxylamine hydrochloride (220 mg.) were dissolved in pyridine (4 ml.) and ethanol (2 ml.), and the solution was set aside at room temperature for 9 days. Addition of water precipitated the product in crystalline form. 1,2-*Dihydro*-1-*hydroxyaminocedrelone* formed prisms from dioxan–petrol, m. p. 188—190° (decomp.), $[\alpha]_D$ −24° (*c* 0·9 in dioxan), $\lambda_{max.}$ 211 (6950) and 281 mμ (ε 9300), $\nu_{max.}$ (Nujol) 3450 (hydroxyl), 3300 (N–H), 1695 (hydrogen-bonded cyclohexanone), and 1678 cm.$^{-1}$ (diosphenol) (Found: C, 68·55; H, 7·15; N, 3·3. $C_{26}H_{33}NO_6$ requires C, 68·55; H, 7·3; N, 3·1%). A sample was melted under nitrogen and kept at 200° for 15 min. The resulting red gum was absorbed from benzene on silica. Elution with 10% chloroform in benzene afforded cedrelone (infrared spectrum and mixed m. p.). The same adduct resulted from refluxing cedrelone with hydroxylamine hydrochloride in pyridine–methanol solution.

Isocedrelone Acetate (V).—Cedrelone acetate (100 mg.) in ether (4 ml.) was treated with boron trifluoride etherate (4 ml.) for 2 hr. The solution was diluted with ether and washed with dilute sodium hydrogen carbonate solution and water. Removal of the solvent afforded a gum which was purified by filtration through Grade IV alumina in benzene–ether (9 : 1),

followed by crystallisation from chloroform–ethanol. *Isocedrelone acetate* formed plates, m. p. 223—227° (decomp.), $[\alpha]_D$ −61° (*c* 0·98), $\lambda_{max.}$ 210 (23,100) and 238 mμ (ε 26,300), $\nu_{max.}$ ($CHCl_3$) 3606w (unbonded hydroxyl), 3415 (hydroxyl), 1764 (enol acetate), 1696 (cyclohexenone), and 1667 cm.$^{-1}$ (diosphenol) (Found: C, 72·4; H, 6·9. $C_{28}H_{32}O_6$ requires C, 72·4; H, 6·95%).

Cedrelone, by a similar 12 hr. treatment with boron trifluoride, gave isocedrelone as an uncrystallisable gum, $\nu_{max.}$ ($CHCl_3$) 1684 (cyclohexenone), 1659w (diosphenol double bond), and 1619s cm.$^{-1}$ (diosphenol carbonyl).

Isodihydrocedrelone.—This was prepared from dihydrocedrelone and boron trifluoride as in the cognate preparation of isocedrelone acetate, with the modification that the reaction was allowed to proceed for 12 hr. *Isodihydrocedrelone* crystallised from benzene–petrol as fine needles of a solvate, m. p. 115—118°, $[\alpha]_D$ −45° (*c* 1·03) (Found: C, 75·4; H, 7·5. $C_{26}H_{32}O_5,\frac{1}{2}C_6H_6$ requires C, 75·15; H, 7·55%); after sublimation it had m. p. 168—172°, $\lambda_{max.}$ 239 (13,900) and 287 (11,400), shifting in base to 345 mμ (ε 7000, $\nu_{max.}$ ($CHCl_3$) 3418 (hydroxyl), 1712·5 (cyclohexanone), 1658w (diosphenol double bond), and 1620s cm.$^{-1}$ (diosphenol carbonyl) (Found: C, 73·4; H, 7·7. $C_{26}H_{32}O_5$ requires C, 73·55; H, 7·6%).

Isodihydrocedrelone acetate was obtained by the analogous boron trifluoride rearrangement of dihydrocedrelone acetate for 2 hr. It crystallised from chloroform–ethanol in plates, m. p. 221—223°, $[\alpha]_D$ −73·8° (*c* 1·0), $\lambda_{max.}$ 212 (15,200) and 242 mμ (ε 20,700), $\nu_{max.}$ (CCl_4) 1772, 1721, and 1672 cm.$^{-1}$ (Found: C, 72·25; H, 7·6. $C_{28}H_{34}O_6$ requires C, 72·1; H, 7·35%).

Isocedrelone Diacetate.—Isocedrelone acetate was refluxed in acetic anhydride (5 ml.) containing anhydrous sodium acetate (300 mg.) for 3 hr. Removal of the acetic anhydride under reduced pressure left a residue which was taken up in ether–water. The ether layer was thoroughly washed with dilute aqueous sodium hydrogen carbonate to remove any unchanged acetic anhydride. Removal of the solvent gave a gum which was purified by filtration through Grade II alumina in benzene–ether (9 : 1), followed by crystallisation from chloroform–ethanol. *Isocedrelone diacetate* formed plates, m. p. 195—200°, $[\alpha]_D$ −8·7° (*c* 0·86), $\lambda_{max.}$ 238 mμ (ε 26,860), $\nu_{max.}$ (CCl_4) 1766 (enol acetate), 1743 (normal acetate), and 1698 cm.$^{-1}$ (enone and diosphenol) (Found: C, 71·35; H, 6·5. $C_{30}H_{34}O_7$ requires C, 71·15; H, 6·75%).

23-*Acetylisocedrelone Diacetate.*—Cedrelone (60 mg.) and toluene-*p*-sulphonic acid (30 mg.) were refluxed in acetic anhydride (3 ml.) for 6 hr. After removal of the acetic anhydride under reduced pressure the residue was dissolved in ether and washed with dilute sodium hydroxide solution and water. Examination of the crude product on a silica chromatoplate showed that it contained no isocedrelone diacetate. The product, a black gum, was adsorbed on Grade II alumina from benzene. Elution with benzene–ether (1 : 1) gave a product (21 mg.) which showed one spot and a trace of a second on a silica chromatoplate. This fraction was crystallised from ethanol to give needles, m. p. 245—252°, $[\alpha]_D$ −12·5° (*c* 0·65), $\lambda_{max.}$ 223 (20,400) and 276 mμ (ε 14,000), $\nu_{max.}$ (CCl_4) 1767 (enol acetate), 1742 (normal acetate), 1699 (cyclohexenone and diosphenol), and 1688 cm.$^{-1}$ (furan acetyl) (Found: C, 70·0; H, 6·35. $C_{32}H_{36}O_8$ requires C, 70·05; H, 6·6%).

Elution with ether gave a second fraction (9 mg.). This crystallised from ethanol as needles, m. p. 237—242°, $\lambda_{max.}$ 227 (24,250), 256 (19,200), and 282 mμ (ε 16,600), $\nu_{max.}$ (CCl_4) 1767, 1744, 1697, and 1692 cm.$^{-1}$, and is believed to be 21-acetylisocedrelone diacetate.

Isocedrelonic Acid (X).—Cedrelone (5 g.) was suspended in methanol (200 ml.). A solution of potassium hydroxide (100 g.) in water (150 ml.) which had been deoxygenated by the passage of nitrogen for 0·5 hr. was added and the resulting solution was refluxed under nitrogen for 7 hr. After cooling it was extracted with ether (2 × 200 ml.) and then poured slowly into ice-cold concentrated hydrochloric acid (200 ml.) and methanol (200 ml.). The resulting solution was set aside overnight and was then diluted to 1 l. with water, to give the product in an easily filterable form. Crystallisation from chloroform–methanol afforded *isocedrelonic acid* (2·136 g.) as prisms, m. p. 295—300° (decomp.), $[\alpha]_D$ −50° (*c* 0·5 in 1 : 1 chloroform–ethanol), $\lambda_{max.}$ 235 mμ (ε 20,000) unchanged by the addition of base, $\nu_{max.}$ (Nujol) 3550 and 3450 (hydroxyls), 3250 (carboxyl), 1706 (carboxyl), and 1672 cm.$^{-1}$ (cyclohexenone) (Found: C, 70·8; H, 7·55. $C_{26}H_{32}O_6$ requires C, 70·9; H, 7·3%). Concentration of the mother-liquors gave a further quantity of pure (chromatoplate) isocedrelonic acid (400 mg.). The mother-liquors, after evaporation to dryness, yielded a mixture of acids (500 mg.) used for the preparation of the norketone (XIX) as described below. Extraction of the aqueous filtrate with chloroform gave a foam (800 mg.) which was not further examined. Isocedrelonic acid was suspended in ether and treated with an excess of ethereal diazomethane to give, in the usual manner, *methyl isocedrelonate* which

crystallised from chloroform–benzene as plates, m. p. 270—272°, $[\alpha]_D$ −49° (*c* 1·25), $\lambda_{max.}$ 236 mμ (ε 20,400), $\nu_{max.}$ ($CHCl_3$) 3604 and 3525 (hydroxyl), 1703 (ester), and 1677 cm.$^{-1}$ (cyclohexenone) (Found: C, 71·45; H, 7·65. $C_{27}H_{34}O_6$ requires C, 71·35; H, 7·55%).

Isocedrelonic acid (50 mg.) in methanol (2 ml.) was neutralised by the addition of sufficient 5% aqueous potassium hydroxide to make the solution just alkaline to litmus. *p*-Nitrobenzyl bromide (29 mg.) was added and the solution was refluxed for 24 hr. Crystallisation of the neutral fraction, isolated by ether extraction, afforded p-*nitrobenzyl isocedrelonate* (47 mg.) from ethanol as plates, m. p. 240—242·5°, $[\alpha]_D$ −28° (*c* 1·0), $\lambda_{max.}$ 241 mμ (ε 22,000), $\nu_{max.}$ (Nujol) 1700 (ester), 1666 (cyclohexenone), 1505s, and 1340 cm.$^{-1}$ (nitro-group) (Found: C, 68·85; H, 6·35. $C_{33}H_{37}NO_8$ requires C, 68·85; H, 6·5%).

Intermediate Potassium Salt in the Alkaline Rearrangement of Cedrelone.—Cedrelone (0·5 g.) was hydrolysed as in the preparation of isocedrelonic acid. The solution, after extraction with ether, was diluted with water till cloudy, clarified by warming, and allowed to cool slowly to give the potassium salt (244 mg.), which, after being dried under a high vacuum at 50° for 2 days, had $\lambda_{max.}$ 220 mμ (ε 9700), $\nu_{max.}$ 3445—3455 (hydroxyl), 1678 (cyclohexenone), and 1580 cm.$^{-1}$ (carboxylate anion).

Rearrangement of Isocedrelone Acetate.—A solution of isocedrelone acetate (V) (160 mg.) in methanol (5 ml.) and 50% aqueous potassium hydroxide (5 ml.) was refluxed under nitrogen for 4 hr. The solution, after extraction with ether, was acidified and the acids were extracted with chloroform. Crystallisation gave an acid (130 mg.) identical with isocedrelonic acid (m. p. and infrared spectrum); by treatment with ethereal diazomethane in the usual way it gave a methyl ester identical with methyl isocedrelonate (m. p., mixed m. p., and infrared spectrum).

Hydrolysis of Dihydrocedrelone Acetate.—Dihydrocedrelone acetate (100 mg.), 50% aqueous potassium hydroxide (4 ml.), and methanol (4 ml.) were refluxed under nitrogen for 15 hr. The methanol was removed under reduced pressure and the neutral fraction was isolated by extraction with ether. Crystallisation from chloroform–ethanol afforded dihydrocedrelone (83 mg.) identical with an authentic sample. Acidification of the aqueous solution, followed by extraction with chloroform, yielded only a trace of gum, which was not further examined. Hydrolysis as above, by 60% aqueous-methanolic potassium hydroxide for 24 hr., gave somewhat less pure dihydrocedrelone.

Hydrolysis of Isodihydrocedrelone Acetate.—Hydrolysis of isodihydrocedrelone acetate (100 mg.), under the same conditions as for dihydrocedrelone acetate, in 25% aqueous-methanolic potassium hydroxide for 18 hr. gave only isodihydrocedrelone (85 mg.).

Norketone (XI; R = H).—A solution of isocedrelonic acid (550 mg.) in dry dioxan (10 ml.) was added to lead tetra-acetate (800 mg.) in benzene (15 ml.), and the resulting solution was set aside for 3 hr. at room temperature. After dilution with ether it was washed with dilute sodium hydroxide solution and water. Crystallisation of the residue, after removal of the solvent, afforded the *norketone* (XI; R = H) as rhombs (from chloroform–ethanol), m. p. 206—208°, $[\alpha]_D$ −87° (*c* 1·0), $\lambda_{max.}$ 234 mμ (ε 19,000), $\nu_{max.}$ (CCl_4) 3470, 1718 (hydrogen-bonded cyclopentanone), and 1691 cm.$^{-1}$ (cyclohexenone) (Found: C, 75·85; H, 7·6. $C_{25}H_{30}O_4$ requires C, 76·1; H, 7·65%). The norketone (50 mg.), treated with hydroxylamine hydrochloride (50 mg.) in pyridine (0·5 ml.) for 3 hr. on the steam-bath, gave a *mono-oxime* (ring B), prisms (from methanol–benzene), m. p. 240—243°, $[\alpha]_D$ +60·7° (*c* 0·65 in dioxan), $\lambda_{max.}$ 210 (25,900) and 237 mμ (ε 27,450), $\nu_{max.}$ (Nujol) 3380 (N–H and OH) and 1696 cm.$^{-1}$ (cyclohexenone) (Found: N, 3·5. $C_{25}H_{31}NO_4$ requires N, 3·4%).

The norketone (40 mg.) was refluxed with anhydrous sodium acetate (300 mg.) in acetic anhydride (5 ml.). The product was isolated by removal of the acetic anhydride under reduced pressure, extraction of the residue with ether, and filtration through Grade I alumina in benzene–ether (1 : 1). The *norketone acetate* (XI; R = Ac) formed prisms (from ether–petrol), m. p. 133—136°, $[\alpha]_D$ −27° (*c* 1·35), $\lambda_{max.}$ 234 mμ (ε 17,350), $\nu_{max.}$ (CCl_4) 1739, with an inflection at 1745 (acetate and cyclopentanone), and 1690 cm.$^{-1}$ (cyclohexenone) (Found: C, 74·3; H, 7·1. $C_{27}H_{32}O_5$ requires C, 74·3; H, 7·4%).

The norketone was refluxed in ethanol (1·6 ml.) and 50% aqueous potassium hydroxide (0·4 ml.) for 1·5 hr. Isolation of the product by extraction with ether and examination of it on a silica chromatoplate indicated that it contained only starting material.

Isocedrelonic Acid Lactone (XII).—A solution of isocedrelonic acid (300 mg.) and dicyclohexylcarbodi-imide (300 mg.) in benzene (15 ml.) was refluxed for 14 hr. After removal of the solvent the residue was adsorbed on Grade IV alumina (30 g.) from chloroform (5 ml.). Elution

with benzene (3 × 15 ml.) gave unchanged dicyclohexylcarbodi-imide. Further elution with benzene (3 × 30 ml.), and crystallisation of the product, gave the norketone (XI; R = H) (87 mg.), identical with material obtained by oxidation of isocedrelonic acid (m. p., mixed m. p., infrared spectrum, and silica chromatoplate). Elution with 5% and 10% ether in benzene (60 ml. of each) gave dicyclohexylurea. Elution with 20% ether in benzene (100 ml.), and crystallisation of the product from ethanol, gave *isocedrelonic acid lactone* (140 mg.) as fine needles, m. p. 219—221° (decomp.), $[\alpha]_D$ −90° (*c* 0·8), $\lambda_{max.}$ 236 mμ (ε 23,500), $\nu_{max.}$ (CCl_4) 3593 (hydroxyl), 1752 (δ-lactone), and 1686 cm.$^{-1}$ (cyclohexenone) (Found: C, 73·9; H, 7·0. $C_{26}H_{30}O_5$ requires C, 73·9; H, 7·15%).

The lactone was recovered unchanged from further treatment with dicyclohexylcarbodi-imide. The lactone was completely hydrolysed to isocedrelonic acid (m. p. and infrared spectrum) by refluxing with 25% aqueous-methanolic potassium hydroxide solution for 12 hr.

The lactone (19 mg.) was heated under nitrogen at 240° until gas evolution had ceased. The product, after filtration through Grade IV alumina in benzene–ether (95 : 5) and crystallisation from ethanol, gave the norketone (XI; R = H) (10 mg.).

Methyl Ester (XVIII).—Methylation, with ethereal diazomethane, of the crystallisation residues (1·5 g.) from the preparation of isocedrelonic acid gave a mixture of esters (chiefly methyl isocedrelonate and one other product as judged from the behaviour on a silica chromatoplate). This was chromatographed over Grade III alumina (100 g.), and elution with 40% chloroform in benzene (100 ml.) gave a new ester, contaminated with a little methyl isocedrelonate. Rechromatography of this fraction (436 mg.) afforded the new *methyl ester* (XVIII) which crystallised from ethanol as plates, m. p. 180—185°, $\lambda_{max.}$ 210 mμ (ε 11,200), $\nu_{max.}$ ($CHCl_3$) 3520, 1735 (ester and cyclopentanone), and 1683 cm.$^{-1}$ (Found: C, 71·65; H, 7·65. $C_{27}H_{34}O_6$ requires C, 71·35; H, 7·55%).

Norketone (XIX).—Hydrolysis of the methyl ester (XVIII) and treatment of the resulting hydroxy-acid with lead tetra-acetate gave the norketone (XIX). A larger quantity was obtained from the crystallisation residues of the isocedrelonic acid preparation as follows.

The acid mixture (200 mg.) in dioxan (5 ml.) was treated with lead tetra-acetate (400 mg.) in benzene (10 ml.) for 2 hr. The neutral fraction was isolated as before, and was adsorbed on Grade II alumina (20 g.) from benzene. Elution with 5%, 10%, and 15% ether in benzene (20 ml. of each) followed by crystallisation gave the norketone (XI; R = H) derived from isocedrelonic acid. Elution with benzene–ether (1 : 1) gave the isomeric *norketone* (XIX) which formed prisms (from chloroform–ethanol), m. p. 229—231°, $[\alpha]_D$ −35° (*c* 1·0), $\lambda_{max.}$ 220 mμ (ε 12,600), $\nu_{max.}$ ($CHCl_3$) 1751·5 (cyclopentanone) and 1683 cm.$^{-1}$ (cyclohexenone) (Found: C, 76·35; H, 7·85. $C_{25}H_{30}O_4$ requires C, 76·1; H, 7·65%). The norketone was recovered unchanged from treatment with boron trifluoride etherate under the conditions used to form isocedrelone acetate. Attempts were made to confirm the 1,4-relationship of the two carbonyl groups in this norketone by reaction with hydrazine to form a dihydropyrazine; the lack of success can be attributed to the strain involved in such a structure.

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