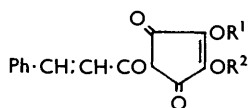


843. *The Structure of Linderone and Methyl-linderone.*¹

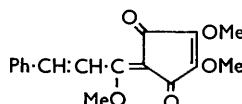
By A. K. KIANG, H. H. LEE, and K. Y. SIM.

Linderone and methyl-linderone, two coloured crystalline compounds isolated from *Lindera pipericarpa* (*Lauraceae*), have been shown to possess $\beta\beta$ -triketone structures (I) and (II), respectively. Their derivatives and degradation products are discussed.

LINDERA PIPERICARPA belongs to a relatively large genus of trees of the family Lauraceae grown in Western Malaysia. The seeds and bark of the tree have been used by the natives in making cosmetic powders, and the fruits as a flavouring agent as well as a substitute for cubebs in medicine.² The bark and leaves are said to be slightly poisonous and to contain a small amount of the alkaloid laurotetanine. There is no recorded use of the root, although the root of a related plant, *Lindera strychnifolia*, had been used by the Chinese as a tonic, astrigent, and carminative. This work reports structural studies on two coloured crystalline compounds from ether extracts of the root of *L. pipericarpa*. These have been named linderone (I) and methyl-linderone (II).¹ They are easily separated from each other, as the latter is neutral while the former is enolic, giving a dirty-green colour with ferric chloride and forming difficultly soluble deep orange ammonium, sodium, and potassium salts.



(I); R¹ = R² = Me (IV); R¹ = R² = H
(III); R¹ = Me, R² = H



(II)

Linderone, C₁₆H₁₄O₅, contains one active hydrogen (pK_a 6.4 in 70% aqueous acetone) and two methoxyl groups. It forms a crystalline acetate, benzoate, and toluene-*p*-sulphonate. Its infrared spectrum shows strong absorption at 1715, 1630, and 1595 cm.⁻¹ and bands at 765 and 695 cm.⁻¹ (monosubstituted benzene). Its ultraviolet spectrum (Fig. 1) shows bathochromic shifts of the maxima in alkaline solution, demonstrating that the enolic function is part of a highly conjugated chromophore. Linderone also forms a mono-2,4-dinitrophenylhydrazone and an orange-brown copper derivative, indicating the presence of an enolisable 1,2-dicarbonyl or 1,3-dicarbonyl grouping.

Methyl-linderone, C₁₇H₁₆O₅, contains three methoxyl groups and no active hydrogen and gives a negative ferric chloride test. Its infrared spectrum shows bands at 1725, 1675, 1640, and 1585 cm.⁻¹. Its ultraviolet spectrum (Fig. 1) is similar to that of linderone (I) of which it is a methyl ether. This relation is certain because methyl-linderone is converted into linderone by mild acid or basic hydrolysis, and treatment with dimethyl sulphate effects the reverse change with 75% yield (use of diazomethane leads to a resin from which methyl-linderone was isolated in only 15% yield; a small amount of an unstable colourless crystalline compound, C₁₉H₂₀O₅N₄, was also obtained, but this was not further studied).

Both linderone and methyl-linderone, when heated with hydrobromic (or less readily hydrochloric) acid and acetic acid yield a demethyl compound which can be further demethylated to 2-cinnamoyl-4,5-dihydroxycyclopentene-1,3-dione (IV). Dimethyl sulphate reconverts the demethyl compound into linderone or methyl-linderone, but the

¹ A preliminary communication appears in *Proc. Chem. Soc.*, 1961, 455.

² Burkill, "Dictionary of the Economic Products of the Malay Peninsula," Crown Agents, London, 1935.

compound (IV) gives only a 10% yield of linderone. The interconversion of the compounds (I)—(IV) shows that the basic skeleton remains intact.

The demethyl compound (III), $C_{15}H_{12}O_5$, contains one methoxyl group and gives a green-brown colour with ferric chloride. Unlike linderone, it is readily soluble in aqueous sodium hydrogen carbonate and has pK_a 4.6 in 70% aqueous acetone. It forms a mono- and a di-acetate, the former giving a positive ferric chloride test. The infrared spectra of this monoacetate and of linderone acetate show strong absorption at 1770 cm^{-1} characteristic of a vinyl ester, and this band is more intense in the spectrum of the di-acetate. The ultraviolet spectra of the acetates of (III) show a close resemblance to those of linderone and methyl-linderone. The spectrum of the demethyl compound (III) also shows bathochromic shifts in the presence of alkali. These results indicate that

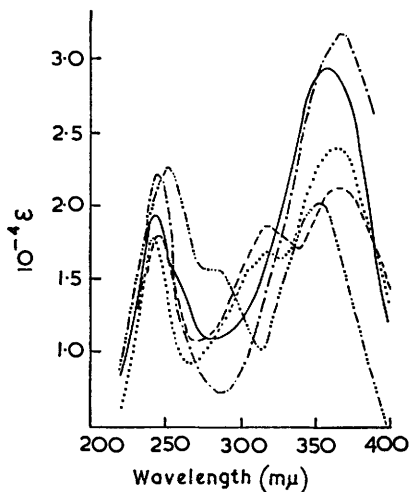


Fig. 1.

FIG. 1. Ultraviolet absorption spectra of: linderone in (—) 95% EtOH and (· · · · ·) 0.09N-ethanolic NaOH; (— · — · —) methyl-linderone in 95% EtOH; (---) demethyl derivative from linderone; and (· · ·) 2-cinnamoyl-4,5-dihydroxycyclopent-4-ene-1,3-dione in 95% EtOH.

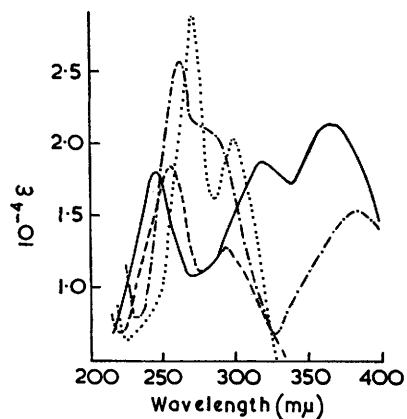


Fig. 2.

FIG. 2. Ultraviolet absorption spectra of demethyl (monohydroxy-) products from: linderone in (—) 95% EtOH and (— · — · —) 0.09N-ethanolic NaOH; and dihydrolinderone in (---) 95% EtOH and (· · ·) 0.09N-ethanolic NaOH.

its newly formed enolic group is also part of the highly conjugated chromophore of linderone. However, attempts to prepare 2,4-dinitrophenylhydrazone and copper derivatives of the demethyl compound (III) gave amorphous products.

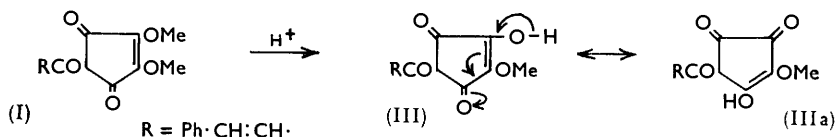
The chemical evidence for the structures of linderone (I) and methyl-linderone (II) is based on oxidation and hydrolysis. When linderone is heated in a sealed tube with concentrated ammonia, cinnamamide can be isolated. Alkaline hydrolysis of linderone or the demethyl derivative gives benzaldehyde, cinnamic acid, and oxalic acid. The demethyl derivative with sodium metaperiodate* yields benzaldehyde, benzylideneacetone, and cinnamic acid. These reactions show the presence of the group $Ph\cdot CH=CH\cdot CO-$ outside a ring which is relatively unstable to alkalis and to oxidation. Consideration of the molecular formula establishes the structure (III) for the demethyl compound and therefore (I) for linderone.

* For periodate oxidation of cyclic 1,3-diketones, see Wolfram and Bobbie, *J. Amer. Chem. Soc.*, 1956, **78**, 2489.

To date, the only one other naturally occurring substance having a similar cyclopentenedione system is calythrone³ (IX). Cyclopentene-1,3-dione⁴ and some analogous compounds,^{5,6} including calythrone,⁷ have been synthesised. The infrared absorption of linderone at 1715 cm.⁻¹ is in accord with the $\beta\beta$ -triketone group, as Birch³ found that absorption in this region can be assigned to it and Elliot⁶ confirmed this for synthetic cyclopentenediones.

The relatively easy cleavage of one methoxyl group from linderone (I) may be explained by its being part of a vinylogue of a methyl ester. The resonance structure (IIIa) would make the hydrolysis of the second methoxy-group more difficult.

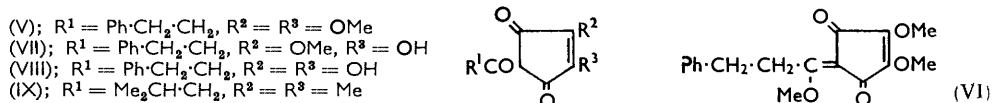
The low pK_a of the demethyl compound (III) is also consistent with the assigned structure and parallels that of dihydroresorcinol,⁸ reductic acid,⁹ and analogous compounds containing the $-\text{CO}\cdot\text{C}(\text{OH})\cdot\text{C}(\text{OH})-$ grouping. In the case of compound (III), the acidity is accentuated by the presence of another carbonyl group adjacent to the enol.



A reaction which, so far as we are aware, is without precedent and is difficult to explain is the formation of methyl cinnamate in 35% yield on zinc dust distillation of linderone (I).

Linderone, methyl-linderone, and the demethyl derivative (III) are hydrogenated in the presence of 2% palladium-strontium carbonate with saturation of the cinnamoyl double bonds. Dihydromethyl-linderone (VI) is, however, best prepared by methylation of dihydrolinderone (V) with diazomethane.

The demethyldihydro-derivative (VII) is hydrolysed by alkali to benzylacetone and β -phenylpropionic and methoxyacetic acid, is oxidised by alkaline peroxide to β -phenylpropionic acid, and on ozonolysis gives benzylacetone. It is demethylated to the monohydrate of 4,5-dihydroxy-2- β -phenylpropionylcyclopentene-1,3-dione (VIII), which is a strong acid.



Dihydromethyl-linderone (VI) forms a 2,4-dinitrophenylhydrazone, and with *o*-phenylenediamine gives a monoanil that forms a cream-coloured acetyl derivative.

The structure of methyl-linderone (II) was established by ozonolysis of its dihydro-derivative (VI), which gives methyl β -phenylpropionate and oxalic acid, in contrast to ozonolysis of dihydrolinderone (V) which gives benzylacetone, β -phenylpropionic acid, and oxalic acid. These ozonolyses confirm the site of the third methoxyl group in methyl-linderone (II). Moreover, the nuclear magnetic resonance spectrum of methyl-linderone shows two methoxyl bands, at 245 and 251 cycles/sec. (relative to tetramethylsilane) with relative intensities 1 : 2, in accord with the structure (II) containing two equivalent methoxyl groups, and excludes the other possible structure (X) where the three methoxyl

³ Birch, J., 1951, 3026; Birch and Elliott, *Austral. J. Chem.*, 1956, **9**, 95.

⁴ De Puy *et al.*, *J. Amer. Chem. Soc.*, 1959, **81**, 4920; 1960, **82**, 2909.

⁵ Birch and English, J., 1957, 3805.

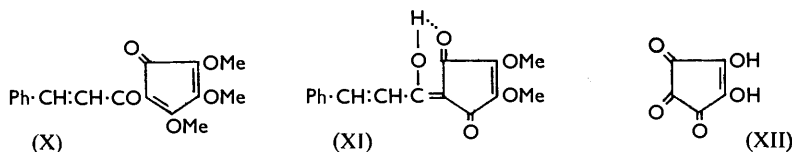
⁶ Elliot, *Proc. Chem. Soc.*, 1960, 406.

⁷ Elliot and Jeffs, *Proc. Chem. Soc.*, 1961, 374.

⁸ Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1162.

⁹ Reichstein and Oppenhauer, *Helv. Chim. Acta*, 1933, **16**, 988.

groups are non-equivalent. In any case the compound (X), being a cyclopentadienone, would be expected to be much less stable than compound (II). The spectrum also shows two doublets at 471, 486, and 442, 457 cycles/sec. due to vinylic hydrogen. The second doublet, however, has the same chemical shift as the aromatic protons and is distinguished



from the latter with difficulty. The positions of the doublets indicate that these hydrogen atoms are on unsaturated carbon atoms in a conjugated system, and the large coupling constant of the doublets (15 cycles/sec.) is characteristic of *trans*-vinylic hydrogen atoms.

With the structures of (I), (II), and (III) established, re-examination of the ultraviolet spectra revealed some interesting features. The absorption of dihydrolinderone (V) [λ_{max} (in EtOH) 258 (log ϵ 4.29), 282 $\mu\mu$ (log ϵ 4.25)], and of calythrone (IX) [λ_{max} (in EtOH) 240 (log ϵ 4.29), 266 $\mu\mu$ (log ϵ 4.26)] are in agreement with the bathochromic shift expected of the methoxyl groups.

Comparison of the spectra of linderone in neutral and basic media (Fig. 1) suggests that linderone exists mainly in the chelated enol-enedione form (XI). This is again supported by its nuclear magnetic resonance spectrum. This shows the presence of an acidic hydrogen at 692 cycles/sec. and a doublet of almost equal intensity due to two groups of non-equivalent methoxyl-hydrogen atoms at 252 and 249 cycles/sec.

The ultraviolet spectra indicate a greater degree of enolisation in the demethyl compound (III) and the compound (IV). This is supported by their failure to react with *o*-phenylenediamine. The compounds (IV) and (VIII) are reminiscent of croconic acid (XII).¹⁰ More quantitative aspects of the keto-enol equilibrium in these compounds are being studied.

EXPERIMENTAL

M. p.s are corrected. Microanalyses are by Dr. W. Zimmermann and Mrs. H. K. Tong. "Light petroleum" refers to a fraction of b. p. 60—80°. Solutions were dried by Na₂SO₄.

Isolation of Linderone and Methyl-linderone.—(a) Ground root bark (2.2 kg.) of *Lindera pipericarpa* was extracted continuously with ether. The ether extracts on evaporation gave an orange-brown sticky solid (156 g.) with a smell of methyl cinnamate. This was redissolved in ether (2 l.), and the solution was shaken with saturated aqueous sodium hydrogen carbonate and then with 2% aqueous potassium hydroxide (3 × 300 ml.).

Acidification of the hydrogen carbonate extracts and extraction with ether gave a dark brown resin (11.5 g.), which yielded cinnamic acid (6 g.), m. p. 132—134° (from aqueous ethanol).

The potassium hydroxide extracts containing some insoluble red solid were acidified and extracted with chloroform. Removal of the solvent gave a solid (55 g., 2.5% of bark), m. p. 85—92°, recrystallisation of which from aqueous ethanol gave *linderone*, orange needles, m. p. 92—93° [Found: C, 67.2, 67.4; H, 4.9, 5.1; O, 28.4, 27.6; active H, 0.44; OMe, 21.4, 21.3%; *M*, 286 (mass spectroscopy). C₁₆H₁₄O₅ requires C, 67.1; H, 4.9; O, 28.0; 1H, 0.35; 2OMe, 20.6%; *M*, 286], λ_{max} (in EtOH) 244 (log ϵ 4.29), 262 (sh, log ϵ 4.15), and 357 $\mu\mu$ (log ϵ 4.47); λ_{max} (in 0.09*N*-ethanolic NaOH) 252 (log ϵ 4.36), 285 (sh, log ϵ 4.20), and 352 $\mu\mu$ (log ϵ 4.31), ν_{max} (in KBr) 1715, 1630, 1595, 985, 765, and 695 cm.⁻¹.

The neutral ether solution was evaporated and the oily residue extracted with light petroleum

¹⁰ Yamada, Mizuno, and Hirata, *Bull. Chem. Soc. Japan*, 1958, **31**, 543.

(5 × 200 ml.). Evaporation of the extract gave a solid (11 g.), m. p. 82—85°. Recrystallisation from light petroleum yielded *methyl-linderone*, yellow needles, m. p. 83—85° [Found: C, 68.0; H, 5.4; O, 27.0; active H, 0.1; OMe, 28.9; *M*, 300 (mass spectroscopy). $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.4; O, 26.6; 3OMe, 31%; *M*, 300], $\lambda_{max.}$ (in EtOH) 244 (log ϵ 4.35) and 368 $m\mu$ (log ϵ 4.50), $\nu_{max.}$ (in KBr) 1725, 1675, 1640, 1585, 970, 760, and 695 cm^{-1} .

(b) By a similar procedure, 72 g. of crude linderone and 6 g. of crude methyl-linderone were obtained from 1.84 kg. of the root wood.

Preparations of Methyl-linderone (II) from Linderone.—Linderone (0.38 g.), anhydrous potassium carbonate (2.5 g.), dimethyl sulphate (0.8 ml.), and acetone (30 ml.) were refluxed for 28 hr. After removal of the acetone, 2% aqueous sodium hydroxide (20 ml.) was added and the mixture was extracted with ether (3 × 30 ml.). The extracts were washed with water, dried, and evaporated. Recrystallisation of the residue (0.3 g.) from light petroleum gave methyl-linderone, m. p. and mixed m. p. 83—85°.

2-Cinnamoyl-4-hydroxy-5-methoxycyclopent-4-ene-1,3-dione (III) by Demethylation of Linderone.—Linderone (2 g.), concentrated hydrochloric acid (20 ml.), and acetic acid (40 ml.) were refluxed for 1 hr., after which more hydrochloric acid (10 ml.) was added and the heating continued for 5 hr. The yellow solid *product* (1.25 g.) was filtered off and recrystallised from aqueous ethanol; it had m. p. 217—218° (Found: C, 66.2, 65.85, 66.4; H, 4.7, 4.7, 4.5; active H, 0.76; OMe, 9.84. $C_{15}H_{12}O_5$ requires C, 66.2; H, 4.4; 2H, 0.74; OMe, 11.4%; $\lambda_{max.}$ (in EtOH) 246 (log ϵ 4.25), 316 (log ϵ 4.27), and 366 $m\mu$ (log ϵ 4.32), $\lambda_{max.}$ (in 0.09N-ethanolic NaOH) 261 (log ϵ 4.41), 285 (sh, log ϵ 4.32), and 382 $m\mu$ (log ϵ 4.19), $\nu_{max.}$ (in KBr) 1680, 1640, 1595, 970, 755, and 695 cm^{-1} .

The same product was obtained in 75% yield by refluxing a solution of linderone in (1 : 1) 48% hydrobromic acid-acetic acid for 1 hr.

Dihydrolinderone (4,5-Dimethoxy-2- β -phenylpropionylcyclopent-4-ene-1,3-dione (V).—Linderone (2 g.) was hydrogenated in methyl acetate (120 ml.) and at 25°/1 atm. with 2% palladium-strotrium carbonate (0.4 g.). After slightly more than 1 mol. of hydrogen had been absorbed, hydrogenation was stopped, filtration, and evaporation under diminished pressure left the *propionyl derivative* as a yellow oil (1.9 g.), b. p. 200—210°/0.15 mm., which crystallised as yellow needles, m. p. 38—40° (Found: C, 66.8, 66.8; H, 5.8, 5.8. $C_{16}H_{16}O_5$ requires C, 66.7; H, 5.6%), $\lambda_{max.}$ (in EtOH) 258 (log ϵ 4.29) and 282 $m\mu$ (log ϵ 4.25), $\nu_{max.}$ (in KBr) 1730, 1665, and 1635 cm^{-1} .

4-Hydroxy-5-methoxy-2- β -phenylpropionylcyclopent-4-ene-1,3-dione (VII).—The monohydroxycyclopentenedione (III) (2.5 g.) in ethyl acetate (350 ml.) was hydrogenated as above. After 1 mol. had been taken up, the mixture was filtered and the solvent removed, to give a yellow solid *product* (2.25 g.). Recrystallisation from benzene gave yellow needles, m. p. 195—197° (Found: C, 65.9; H, 5.2. $C_{15}H_{14}O_5$ requires C, 65.7; H, 5.2%), $\lambda_{max.}$ (in EtOH) 256 (log ϵ 4.26) and 293 $m\mu$ (log ϵ 4.11), $\lambda_{max.}$ (in 0.09N-ethanolic NaOH) 270 (log ϵ 4.46) and 298 $m\mu$ (log ϵ 4.31), $\nu_{max.}$ (in KBr) 1685, 1645, and 1635 cm^{-1} .

Dihydromethyl-linderone[4,5-Dimethoxy-2-(1-methoxy-3-phenylpropylidene)cyclopent-4-ene-1,3-dione] (VI).—Ethereal diazomethane, prepared from nitrosomethylurea (4 g.), was gradually added with stirring to suspension of the hydroxy-compound (VII) (2 g.) in ether (150 ml.). After $\frac{1}{2}$ hr. the ether was allowed to evaporate. Trituration of the residue with a small quantity of methanol removed a viscous brown uncharacterisable oil and left the *product* (VI). Recrystallisation from cyclohexane gave yellow needles, m. p. 117—119° (Found: C, 67.5; H, 6.0. $C_{17}H_{18}O_5$ requires C, 67.8; H, 5.8%), $\lambda_{max.}$ (in EtOH) 256 (log ϵ 4.35) and 292 $m\mu$ (log ϵ 4.29), $\nu_{max.}$ (in KBr) 1720, 1670, 1640, and 1610 cm^{-1} .

Derivatives and Reactions of Linderone.—*Copper chelate.* A solution of linderone (1 g.) in chloroform (100 ml.) was shaken with aqueous cupric acetate (100 ml.). The chloroform layer containing a light brown precipitate was warmed with additional chloroform (250 ml.) until a clear solution was obtained. This was washed with water, dried, and evaporated. Recrystallisation of the residue from chloroform gave fine brownish-orange needles of the *copper salt*, m. p. 256—257° (decomp.) [Found: C, 60.4, 60.1; H, 4.4, 4.3; ash, 12.6. $Cu(C_{16}H_{13}O_5)_2$ requires C, 60.6; H, 4.1; ash, 12.6%].

When hydrogen sulphide was passed into a solution of the salt in benzene, linderone was quantitatively recovered.

2,4-Dinitrophenylhydrazone. Two forms of the same m. p. 241—243° and infrared spectra were obtained, (a) vermilion crystals extractable by hot benzene, and (b) scarlet prisms, insoluble in hot benzene but crystallisable from ethanol [Found: (a) C, 56.7; H, 4.0; N, 12.1; (b) C, 57.0; H, 3.9; N, 12.1. $C_{22}H_{18}N_4O_8$ requires C, 56.5; H, 3.9; N, 12.0%].

Acetate. By heating linderone with acetic anhydride and pyridine, two forms of the same m. p. 160—161° were obtained: rapid cooling from aqueous ethanol gave yellow feathery needles while slow cooling gave glistening prisms (Found: C, 65.8, 65.9; H, 5.0, 5.2; O, 28.9; OMe, 18.2, 18.2. $C_{18}H_{16}O_6$ requires C, 65.9; H, 4.9; O, 29.2; 2-OMe, 18.9%); both forms had λ_{\max} . (in EtOH) 244 (log ϵ 4.26), 269 (log ϵ 4.02), and 366 μ . (log ϵ 4.54), ν_{\max} . (in KBr) 1770 and 1250 cm^{-1} .

Benzoate. Reaction with benzoyl chloride and potassium carbonate in acetone yielded the *benzoate* as yellow needles (from acetone), m. p. 192—193° (Found: C, 71.0; H, 4.9. $C_{23}H_{18}O_6$ requires C, 70.8; H, 4.7%).

Toluene-p-sulphonate. Similar reaction with toluene-*p*-sulphonyl chloride gave this *ester* as light orange needles (from acetone), m. p. 170—171° (Found: C, 62.8; H, 4.7. $C_{23}H_{20}O_7S$ requires C, 62.7; H, 4.6%).

Picrate. A mixture of linderone (0.1 g.) and ethanolic picric acid (5 ml.) was heated to boiling and cooled. The precipitate that formed was recrystallised from warm ethanol to give red plates, m. p. 106—108°, of the *picrate* (Found: C, 51.8, 51.4; H, 3.5, 3.6; N, 8.0. $C_{16}H_{14}O_5 \cdot C_6H_3N_3O_7$ requires C, 51.3; H, 3.3; N, 8.2%).

Urea adduct. A mixture of linderone (0.5 g.) and urea (0.2 g.) in the minimum amount of methanol was heated to boiling and left to cool. The *adduct* crystallised as pale yellow needles, m. p. 147—150° (Found: C, 58.8; H, 5.7. $C_{16}H_{14}O_5 \cdot CH_4N_2O$ requires C, 59.0; H, 5.2%).

o-Phenylenediamine adduct. Linderone (0.14 g.) and *o*-phenylenediamine (0.07 g.) in ethanol (6 ml.) were warmed on a water-bath for 15 min. On cooling, yellow crystals of an *adduct* were obtained, having m. p. 106—108° (Found: C, 66.9; H, 6.1; N, 7.9. $C_{16}H_{14}O_5 \cdot C_6H_8N_2$ requires C, 66.9; H, 5.6; N, 7.1%).

Reaction with diazomethane. Ethereal diazomethane, prepared from nitrosomethylurea (2 g.), was added to a solution of linderone (0.5 g.) in ether (60 ml.). After 3 hr., removal of the ether left a pale orange gum which, after extraction with ether, yielded a solid *substance* that crystallised from ethanol as colourless rods, sintering at 134° and melting at 139—140° (decomp.) (Found: C, 59.5, 59.9; H, 5.4; O, 21.2; N, 13.7; OMe, 22.6, 23.3. $C_{19}H_{20}N_4O_5$ requires C, 59.4; H, 5.2; O, 20.8; N, 14.6; 3OMe, 24.2%). The compound partially decomposed on further recrystallisations and resinified on storage.

The ether extracts were washed with dilute sodium hydroxide and water, and dried. Removal of the ether left methyl-linderone which crystallised from light petroleum as yellow needles (0.08 g.), m. p. and mixed m. p. 83—85°.

Reaction with ammonia. Linderone (1 g.) and concentrated ammonia (5 ml.) were heated in a sealed tube in boiling water for 1 hr. The mixture was diluted with water and extracted with benzene; chromatography on alumina of the residue from benzene yielded cinnamamide, m. p. 145—146° (Found: C, 73.6; H, 6.4; N, 9.5. Calc. for C_9H_9NO : C, 73.5; H, 6.1; N, 9.5%).

Oxidation by nitric acid. Linderone (1 g.) and concentrated nitric acid (10 ml.) were refluxed for 4 hr. The mixture was diluted with water and extracted with ether. The aqueous layer on evaporation yielded oxalic acid (0.24 g.). The ether extract afforded benzoic acid (0.1 g.).

Zinc-dust distillation. Linderone (2.5 g.) was ground with zinc dust (30 g.). The mixture, placed in a tube and covered with more zinc dust (10 g.), was heated in a metal-bath in a stream of nitrogen. At about 220°, a pale yellow oil began to condense in ice-cooled U-tubes. The temperature of the bath was gradually raised to, and kept at, 360° until no more oil distilled. The oil was extracted with ether and the extracts were shaken with saturated aqueous sodium hydrogen carbonate and 2% aqueous sodium hydroxide, washed with water, and dried. Evaporation and distillation of the residue gave a liquid, b. p. 77—80°/0.7 mm. (0.3 g., 35%), which solidified. Recrystallisation from light petroleum gave colourless crystals, m. p. 35—36°, undepressed on admixture with methyl cinnamate and further identified by its infrared spectrum.

Alkaline degradation. Linderone (1.5 g.) and 2% aqueous potassium hydroxide (120 ml.) were warmed on a steam-bath with stirring. After 6 hr. the brown mixture was centrifuged, filtered, brought to pH 9, and steam-distilled. The distillate possessed the smell of benzaldehyde and gave a 2,4-dinitrophenylhydrazone, m. p. 234—236°. The residual alkaline solution, on acidification and extraction with ether, gave a solid (0.8 g.) whence hot water removed cinnamic acid.

Demethylation of Methyl-linderone (II).—Methyl-linderone (3.5 g.) in acetic acid (40 ml.) and 66% hydrobromic acid (20 ml.) were heated under reflux for 1 hr., and the mixture cooled in ice. The solid (2.8 g.) was collected and, after recrystallisation from ethanol, gave the monohydroxy-compound (III), m. p. 213—215°.

Derivatives and Reactions of the Demethyl Compound (III).—Warming this compound with acetic anhydride on a steam-bath for 1 hr. yielded a *monoacetate* as pale yellow needles (from aqueous methanol), m. p. 156—157°, which gave a deep purple colour with ferric chloride (Found: C, 65.3; H, 4.8. $C_{17}H_{14}O_6$ requires C, 65.0; H, 4.5%), λ_{max} (in EtOH) 240 (log ϵ 4.34), 288 (log ϵ 4.13), and 345 $m\mu$ (log ϵ 4.38), ν_{max} (in Nujol) 1770 and 1250 cm^{-1} .

Gentle refluxing with acetic anhydride for 2 hr. yielded pale yellow crystals of the *diacetate* (from aqueous methanol), m. p. 141—143° (Found: C, 64.0; H, 4.7. $C_{19}H_{16}O_7$ requires C, 64.0; H, 4.5%), λ_{max} (in EtOH) 247 (log ϵ 4.18) and 357 $m\mu$ (log ϵ 4.54), ν_{max} (in Nujol) 1770 and 1250 cm^{-1} .

Reaction with dimethyl sulphate, as described for linderone, gave, after 5 hr., linderone (20% yield), and, after 40 hr., methyl-linderone (60% yield).

A solution of sodium metaperiodate (9 g.) in water (120 ml.) was gradually added to a suspension of the monohydroxy-compound (III) (3 g.) in methanol (50 ml.). The mixture was left at room temperature for 12 hr., then diluted with water (300 ml.), and extracted with ether. The extract was shaken with saturated aqueous sodium hydrogen carbonate and then with saturated aqueous sodium hydrogen sulphite. The hydrogen carbonate extract, on acidification, yielded cinnamic acid (0.04 g.). Decomposition of the hydrogen sulphite extract with aqueous potassium carbonate yielded benzaldehyde, identified by its 2,4-dinitrophenylhydrazone, m. p. 234—236°. The ether extract, on evaporation, gave a small amount of brown oil which formed a mixture of 2,4-dinitrophenylhydrazones (0.265 g.). This was chromatographed on bentonite-kieselguhr¹¹ (100 g.). Elution with chloroform containing 5% of methanol yielded compounds (a) m. p. 202—205° (85 mg.), (b) 223—225° (70 mg.), and (c) 199—201° (45 mg.). Compound (b) was identified as benzylideneacetone 2,4-dinitrophenylhydrazone by its m. p., mixed m. p., and infrared spectrum.

The monohydroxy-compound (III) (0.6 g.), 48% hydrobromic acid (12 ml.), and acetic acid (24 ml.) were refluxed for 1½ hr., left at room temperature for 12 hr., and then cooled in ice. The solid (0.13 g.) that separated was filtered off and washed with water. Three recrystallisations from benzene gave light orange crystals of 2-cinnamoyl-4,5-dihydroxycyclopent-4-ene-1,3-dione, sintering at 243° and melting at 253° (decomp.) (Found: C, 65.2; H, 4.2. $C_{14}H_{10}O_5$ requires C, 65.1; H, 3.9%), λ_{max} (in EtOH) 242 (log ϵ 4.25), 318 (log ϵ 4.23), and 362 $m\mu$ (log ϵ 4.38), ν_{max} (in KBr) 1695, 1635, 1600 cm^{-1} . This gave a pale green colour with ferric chloride, and with dimethyl sulphate afforded linderone in about 10% yield.

Ozonolysis of Dihydrolinderone (V).—A solution of compound (V) (2 g.) in chloroform (120 ml.) at 0° was ozonised. The solvent was then removed at room temperature under reduced pressure and the residue treated with water, refluxed for 15 min., and steam-distilled. The distillate (400 ml.) was extracted with ether, and the extract shaken with aqueous sodium hydrogen carbonate, washed with water, and dried. Evaporation of the ether solution left an oil (0.19 g.) which yielded two fractions, distilling at 75—90° and at 130—145° at 0.15 mm. Redistillation of the former gave a colourless liquid identified as benzylacetone by its scarlet 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 128—129°, with the correct infrared spectrum. The higher-boiling fraction could not be characterised. The hydrogen carbonate washings were acidified and extracted with ether which removed an oil, partly extractable by hot light petroleum. Evaporation of the petroleum extract and distillation of the oily residue yielded a liquid, b. p. 90—100°/0.15 mm., solidifying to crystals of β -phenylpropionic acid, m. p. 46—48° (correct infrared spectrum). The aqueous residue after steam-distillation was extracted with ether, but the extract gave only a dark oil which could not be characterised; evaporation of the aqueous layer yielded oxalic acid (0.4 g.).

Derivatives and Reactions of Dihydromethyl-linderone (VI).—The 2,4-dinitrophenylhydrazone, prepared in the usual way, crystallised from ethyl acetate as red needles, m. p. 239—240° (decomp.) (Found: C, 57.5; H, 5.0; N, 11.5. $C_{23}H_{22}N_4O_8$ requires C, 57.3; H, 4.6; N, 11.6%).

A solution of compound (VI) (0.1 g.) and *o*-phenylenediamine (0.04 g.) in ethanol (4 ml.) was warmed on a water-bath for 15 min. On cooling, a yellow crystalline *anil* was formed,

¹¹ Elvidge and Whalley, *Chem. and Ind.*, 1955, 589.

which crystallised from cyclohexane as pale yellow needles, m. p. 148—149° (decomp.) (Found: C, 70.4; H, 6.1; N, 6.9. $C_{23}H_{24}N_2O_4$ requires C, 70.4; H, 6.2; N, 7.1%). With acetic anhydride ($\frac{1}{2}$ hr.; 100°) this gave a cream-coloured *acetyl derivative*, m. p. 160—161° (Found: C, 69.1; H, 6.0. $C_{25}H_{26}N_2O_5$ requires C, 69.1; H, 6.0%).

A solution of compound (VI) (2 g.) in chloroform (120 ml.) was ozonised at 0°. The products were separated as discussed under dihydrolinderone. The ether extract of the steam-distillate yielded only methyl β -phenylpropionate, b. p. 75—80°/0.15 mm., n_D^{25} 1.504, the infrared spectrum of which was identical with that of an authentic sample.

Reactions of the Demethyl Compound (VII).—(a) *Alkaline hydrolysis.* A solution of the compound (5 g.) in 2*N*-sodium hydroxide was heated on the steam-bath under nitrogen for 1½ hr. The products were separated into neutral and acidic fractions. The former yielded benzylacetone, b. p. 58—60°/0.3 mm., n_D^{25} 1.5100 (2,4-dinitrophenylhydrazone, m. p. 126—127°; and correct infrared spectrum). The acids extracted by ether, yielded, on distillation at 0.2 mm., fractions (a), b. p. below 80°, a colourless liquid (0.36 g.), (b) b. p. 80—100°, a viscous oil (0.1 g.), and (c) b. p. 110°, β -phenylpropionic acid (0.25 g.), m. p. 42—45°. Fraction (a) was identified as methoxyacetic acid by comparison of its infrared spectrum with that of an authentic sample prepared by Friedman's method,¹² as well as by the m. p. and mixed m. p. of the 4-bromophenacyl ester,¹³ m. p. 76—78°. The residual acid portion, when continuously extracted by ether, yielded oxalic acid.

(b) *Ozonolysis.* A suspension of the compound (VII) (1 g.) in chloroform (100 ml.) was ozonised at 0°, and the products were separated as described for dihydrolinderone. The ether extract of the steam-distillate yielded, as the main product, benzylacetone distilling at 80—90°/0.15 mm. The aqueous solution after steam-distillation did not give recognisable products.

(c) *Demethylation.* Compound (VII) (1 g.), 58% hydrobromic acid (15 ml.), and acetic acid (35 ml.) were refluxed for 6 hr. and left at room temperature overnight. The mixture was cooled with ice, and the solid (0.36 g.) was filtered off and washed with water. Three recrystallisations of the solid from benzene gave yellow crystals, m. p. 200—202° (decomp.), of 4,5-dihydroxy-2- β -phenylpropionylcyclopent-4-ene-1,3-dione (Found, for sample dried at 80° *in vacuo*: C, 60.8, 60.6; H, 5.4, 5.25; active H, 1.4; OMe, 0. $C_{14}H_{12}O_5 \cdot H_2O$ requires C, 60.4; H, 5.1; 4H, 1.64%), λ_{max} (in EtOH) 253 (log ϵ 4.18) and 292 $m\mu$ (log ϵ 4.01), ν_{max} (in KBr) 1695 and 1630 cm^{-1} .

We thank the Chief Research Officer, Forest Research Institute, Kepong, and Mr. A. H. Millard, Department of Chemistry, Petaling Jaya, for collection of plant material, Professor K. Nakanishi for the infrared spectra, Professor S. M. Goodwin for the nuclear magnetic resonance spectra and their interpretation, Professor K. Biemann for the molecular-weight determinations, and Mrs. H. K. Tong for microanalysis.

CHEMISTRY DEPARTMENT, UNIVERSITY OF SINGAPORE.

[Received, February 12th, 1962.]

¹² Friedman, *Zhur. obshchei Khim.*, 1954, **24**, 642; *Chem. Abs.*, 1955, **49**, 6231.

¹³ Kenner and Richards, *J.*, 1953, 2240.