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THE CONSTITUENTS OF *CACALEA DECOMPOSITA* A. GRAY

STRUCTURES OF CACALOL AND CACALOME

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Abstract—Cacalol and cacalone, isolated from the roots of *Cacalea decomposita* A. Gray, have been shown to be furotetralin derivatives with structures Ia and IX.

Cacalea decomposita, a compositae widely distributed in the northern part of México, is a shrub popularly known as "matarique" and "maturín". Extracts from the root have been used for the treatment of diabetes and other diseases.[1]

The present communication is concerned with the isolation of two crystalline substances, which we propose to name cacalol (Ia) and cacalone (IX). Their structure belong to the furotetralin ring system, not at this time known to occur in nature.

Extensive chromatography of an hexane extract of the roots, afforded cacalol (Ia) and cacalone (IX) in the less polar fractions. Cacalol (Ia; $C_{15}H_{18}O_2$), has m.p. 92–94°, $[\alpha]_D$ +10°. A solution in concentrated sulfuric acid has a pink colour, on addition of a few crystals of sodium nitrite, the colour becomes red which after a short time changes to purple, then to blue and finally green. The T.N.M. test is positive. It has a complex UV spectrum (λ max 218, 256, 264 and 286 mμ; ε, 30400, 10500, 10000, 1840), suggesting the presence of an aromatic structure.[2]

Cacalol (Ia), a phenol as shown by the following evidence, has IR spectral bands at 3550, 1635 and 1602 cm^{-1} and can be partially extracted from an ethereal solution by strong alkali. Cacalol (Ia), forms a crystalline monoacetate, (Ib), which shows the phenolic acetate IR band at 1760 cm^{-1}) and an oily methyl ether (Ic), on treatment of a methanolic solution with ethereal diazomethane. Since cacalol has no carbonyl groups, the other oxygen atom must be involved in a bridge system. Cacalol has a furan nucleus condensed with a fully substituted phenolic ring as shown in the following manner. The NMR spectrum of cacalol[3] (Ia), indicates the presence of three methyl groups; a doublet centered at 8·90 t (J = 7 c/s) corresponding to a methyl group inserted in a secondary carbon atom and two singlets at 7·78 and 7·67 t ascribed to a vinylic and aromatic methyl groups. The proton of the phenolic hydroxyl group is

[1] Maximino Martínez, *Las Plantas Medicinales de México*. Ediciones Botas, Méx. (1939).

[2] H. H. Jaffé and Milton Orchin. *Theory and Applications of Ultraviolet Spectroscopy*. J. Wiley, New York (1962).

[3] The NMR spectra were run by Mr. Eduardo Díaz, to whom we are indebted; on a Varian A-60 spectrometer, in $CDCl_3$ and CCl_4, using tetramethylsilane as internal standard (t = 10·00).

responsible for a sharp signal at 4·91 t, which disappears on acetylation. Cacalol (Ia), only posesses one vinylic proton, a singlet at 3·17 t. The vinylic methyl group and the vinylic proton are inserted in the furan double bond, since Pd–C catalysed hydrogenation of cacalol (Ia) yields a dihydroderivative (II; λ max 288 mμ; ε, 1920), whose NMR spectrum does not exhibit the vinylic methyl group, nor the vinylic proton. Furthermore, in the methyl region, two doublets partially superimposed are centered at 8·88 and 8·77 t (intensity 6 protons; J = 7 c/s), corresponding to two CH_3–CH groups and a singlet at 7·90 t, ascribed to the aromatic methyl group. A multiplet centered at 5·70 t (intensity 2 protons) indicates the presence of the furan methylene group. A singlet at 4·91 t is assigned to the proton of the hydroxyl group. Treatment of a chloroform solution of cacalol acetate (Ib) with one equivalent of bromine, affords a monobromoderivative (Id), the NMR spectrum of which does not show the vinylic proton.

Carefully controlled ozonolysis of cacalol acetate, followed by mild alkaline hydrolysis, yields the dihydroxyacetophenone (IIIa; λ max 270 mμ; ε, 3900) which is soluble in alkali and gives positive ferric chloride (green colour) and iodoform tests. The IR spectrum shows a band at 3500 (hydroxyl groups) and a carbonyl band of an hydrogen bonded hydroxyacetophenone[4] at 1630 cm^{-1}. The methyl region of its NMR spectrum indicates the presence of three methyl groups: a doublet centered at 8·91 t (J = 7 c/s) and two singlets, (intensity three protons each), at 7·71 and 7·53 t, corresponding to the CH_3—CO— group and the aromatic methyl group. The protons of the hydroxyl groups, are responsible for the singlets, at 4·41 t (not *ortho* to the acetyl group) and at −1·17 t (*ortho* to the acetyl group). Methylation of a methanolic solution of the dihydroxyacetophenone (IIIa) with ethereal diazomethane, yields the monomethyl ether (IIIb). The hydroxyl *ortho* to the acetyl group was methylated, since the IR spectrum shows bands at 3500 cm^{-1} (hydroxyl group) and at 1690 cm^{-1} (non bonded α,β-unsaturated carbonyl group). The NMR spectrum shows the presence of a methoxyl group (singlet at 6·35 t) and a signal at 4·00 t, corresponding to the nonchelated hydroxyl group.

The sequence of substituents in the phenolic ring, was ellucidated in the following manner. The hydroxyl group of cacalol is in *ortho* position with the oxygen bridge of the furan ring, since the dihydroxyacetophenone (IIIa), on Clemmensen reduction furnishes an oily *ortho* diphenol (IV) giving a green colour in the ferric chloride test. The ethereal solution of this diol (IV), upon oxidation with silver oxide, yields a red *ortho* quinone, which was not purified, but characterized as its quinoxaline derivative, (V) by treatment with *o*-phenylenediamine. The relative position of the aromatic methyl group was established as follows. Cacalol (Ia), affords a yellow nor-*p*-quinone (VI; $C_{14}H_{14}O_3$), upon mild oxidation with chromium trioxide, (λ max 283 mμ; ε, 8300); IR bands at 1655 (α,β-unsaturated carbonyl groups) and at 1615 and 1590 cm^{-1} (C–C double bonds). The aromatic methyl group was eliminated by degradative oxidation, as shown by the NMR spectrum, which, in the methyl region, exhibits a doublet centered at 8·86 t (J = 7 c/s; intensity 3 protons), corresponding to the CH_3—CH grouping. The furan methyl group and the vinylic proton are responsible for two singlets at 7·77 t (intensity 3 protons) and at 2·60 t (intensity 1 proton). Reductive acetylation, furnishes the hydroquinone diacetate (VII) with the IR acetyl band at 1760 cm^{-1}.

[4] L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*. Methuen, London.

Besides the chemical and spectroscopical evidence cited, further proof was obtained by aromatization of cacalol acetate (Ib) with chloranil to a naphthofuran derivative (VIII), which shows λ max 244, 250, 320, 330 and 346 mμ; ε, 34800, 38000, 8750, 8200 and 7300; IR bands at 1770 cm^{-1} (carbonyl of the acetate) and weak bands at 1660, 1620 and 1580 cm^{-1}. The NMR spectrum exhibits in the methyl region, four singlets (intensity 3 protons each), at 7·58, 7·49,7·07 and 6·89 t and four vinylic protons; a complex signal centered at 2·70 t, (intensity 3 protons) and a multiplet at 2·20 t (intensity 1 proton). Furthermore, the results of the drastic ozonolysis of cacalol (Ia), in acetic acid, permit positions 6 or 7 for the attachment of the methyl group in the naphthofuran ring. An acidic mixture isolated from this reaction was esterified with diazomethane and submitted to vapour phase chromatography.[5] Three peaks were obtained whose retention times are identical with those of methylsuccinic, β-methylglutaric and β-methyladipic dimethyl esters. Using the addition method,[6] the height of the peak due to β-methyladipic dimethyl ester, was increased when an authentic sample was added.

Further evidence, for the position of this methyl group, was secured by consideration of the properties of cacalone (IX); a substance closely related to cacalol (Ia) and obtained only in small amounts from the hexane extract of the roots of *Cacalea decomposita*.

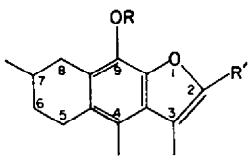
Cacalone (IX; $C_{15}H_{16}O_3$), m.p. 120–121°, $[\alpha]_D$ +84°: (λ max 212, 250 and 320 mμ: ε, 6600, 11200 and 8500) is a hydroxyketone, as shown by its IR spectrum; bands at 3550 cm^{-1} (hydroxyl group) and at 1660 cm^{-1} (α,β-unsaturated ketone) though we could not obtain carbonyl or hydroxyl derivatives under the usual conditions. Its structure was ellucidated as shown by the following evidence. Clemmensen or lithium aluminium hydride reductions of cacalone, yield cacalol (Ia). The reduction of the keto group to a methylene in the latter reaction, confirm an α-tetralone formulation. Position C-5 for the ketonic group is justified on spectroscopical grounds. The chemical shift of the phenolic hydroxyl proton in the NMR spectrum (singlet at 6·14 t, intensity 1 proton, which disappears on equilibration with D_2O) does not indicate hydrogen bonding with the carbonyl group, furthermore, the position of the IR band of the latter is not in keeping with chelation. Accordingly structure IX is assigned to cacalone. Hydrogenation of cacalone (IX), saturates the furan double bond, yielding two isomeric dihydroderivatives (X). Both, show IR bands at 3400 (hydroxyl group) and at 1680 cm^{-1} (α,β-unsaturated carbonyl group).

When cacalone (IX) in ethylene glycol is refluxed with hydrazine, the hydroxyl and carbonyl groups are eliminated, furnishing desoxycacalol (XI; λ max 216, 258, 284 and 294 mμ; ε, 35000, 11800, 2800 and 2800). The NMR spectrum exhibits in the methyl region, a doublet centered at 8·83 t, (J = 7 c/s, intensity three protons) ascribed to the CH_3-CH grouping. The vinylic and aromatic methyl groups are responsible for two singlets (intensity three protons each), at 7·66 and 7·48 t. Two singlets at 3·10 and 2·86 t (intensity 1 proton each) correspond to the furan and aromatic hydrogens. The methyl group of the nonaromatic ring, in cacalone and cacalol, must be placed at C-7 since cacalone retains its optical activity after alkaline treatment.

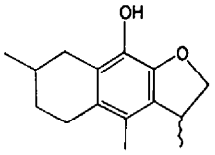
Further investigations are in progress and will be reported later.

[5] We are grateful to Dr. Armando Manjarrez, of this Institute, who kindly carried out this chromatography.

[6] A. I. M. Keulemans, *Gas Chromatography* Chap. 2; p. 26. Reinhold, New York (1957).



I a, R=H ; R'=H
b, R=Ac ; R'=H
c, R=CH_3; R'=H
d, R=Ac ; R'=Br



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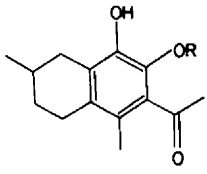
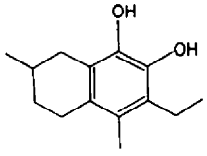


III a, R=H
b, R=CH_3



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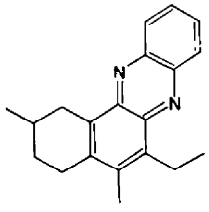

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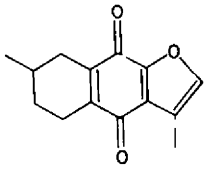

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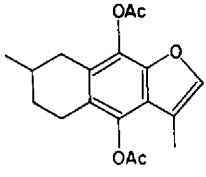

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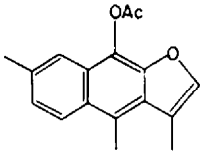
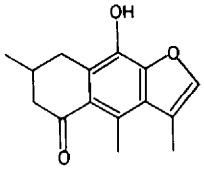


VIII



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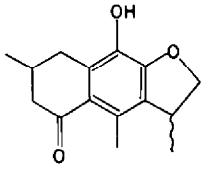
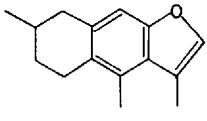


X



XI

EXPERIMENTAL[7]

Isolation of cacalol (Ia) *and cacalone* (IX). *Cacalea decomposita* was collected in Chihuahua (México).[8] The ground root (950 g) was extracted with hexane (8 l) for 12 hr. The extract was filtered, evaporated to dryness (wt 45 g), dissolved again in hexane (leaving a small insoluble residue) and chromatographed on alumina (400 g). Several fractions eluted with hexane, crystallized. They were combined and by recrystallization from ether–pentane, yield 9·1 g cacalol m.p. 89–91°. Further

[7] M.ps. are uncorrected, rotations were determined at 20° in $CHCl_3$. The IR spectra were run in $CHCl_3$ solution (unless otherwise noted), on a Perkin–Elmer 21 double beam spectrophotometer. The UV absorption spectra were determined in 95% ethanol solution, in a Beckman DK2 spectrophotometer. The microanalyses and mol wt determinations were performed by Dr. Franz Pascher, Bonn, Germany. We are grateful to Syntex, S. A., for the determination of the rotations and UV spectra.

[8] We are grateful to Mr. Javier Valdez of the Botanical Garden (U.N.A.M.) for the classification of the roots.

crystallizations from ether–pentane, furnished the analytical sample, as prisms m.p. 92–94°, negative $FeCl_3$ test, $[\alpha]$ +10°; λ max 218, 256, 264 and 286 mμ; ε, 30400, 10500, 10000, 1840; ν max 3550 (hydroxyl group), weak bands at 1635 and 1602 cm^{-1}. (Found: C, 78·23; H, 7·82; O, 14·17. Calc. for $C_{15}H_{18}O_2$: C, 78·23; H, 7·88; O, 13·89%). M.W. (Rast) 229.

Several fractions eluted with benzene–hexane (1:1) were combined and recrystallized from acetone–hexane, yielding cacalone (3·2 g), m.p. 116–118°. The analytical sample, showed m.p. 120–121°, (prisms from acetone–hexane); $[\alpha]_D$ +84°; negative $FeCl_3$ test, yellow colour with T.N.M.; λ max 212, 250 and 320 mμ; ε, 6600, 11200, 8500; ν max 3550 (hydroxyl group); 1660 (α,β-unsaturated carbonyl group); at 1620 and 1595 cm^{-1} (C—C double bonds). (Found: C, 73·70; H, 6·90; O, 19·44. Calc. for $C_{15}H_{16}O_2$: C, 73·75; H, 6·60; O, 19·65%).

Cacalone (IX; 75 mg), was refluxed in methanol (8 ml) with 200 mg KOH for 1 hr. The solution was diluted with water and extracted with ether. The ethereal extract was washed with water and evaporated. Crystallization from ether–pentane afforded recovered cacalone (50 mg), m.p. 116°, $[\alpha]_D$ +86°.

Cacalol acetate (Ib). The acetate (acetic anhydride and pyridine, 1 hr on a steam bath) showed m.p. 103–104° (prisms from acetone–hexane), $[\alpha]_D$ −9°; λ max 218, 255, 280 and 292 mμ; ε, 27000, 12000, 2100, 1320; ν max; 1760 (acetyl group); weak bands at 1630 and 1600 cm^{-1}. (Found: C, 75·06; H, 7·21; O, 17·57. Calc. for $C_{17}H_{20}O_3$: C, 74·97; H, 7·40; O, 17·63).

Dihydrocacalol (II). A solution of cacalol (Ia; 400 mg), in ethyl acetate (40 ml), was hydrogenated with 10% Pd-C, (the absorption of H_2 ceased, after 1 equiv. was consumed). The catalyst was filtered off and the solvent evaporated to dryness, leaving an oily residue which did not crystallize. It was sublimed *in vacuo* and the crystalline product, washed with a small amount of cold pentane, m.p. 78–79°, $[\alpha]_D$ −23°; λ max 288 mμ; ε, 1920; ν max 3550 (hydroxyl group); weak bands at 1710, 1630 cm^{-1} and shoulder at 1600 cm^{-1}. (Found: C, 77·74; H, 8·61; O, 13·86. Calc. for $C_{15}H_{20}O_2$: C, 77·55; H, 8·68; O, 13·77%).

Bromocacalol acetate (Id). To a solution of cacalol acetate (Ib; 100 mg), in $CHCl_3$ (8 ml), one equiv. Br_2 in acetic acid (12 ml) was added, with mechanical stirring. The Br_2 was absorbed immediately. The solution was then washed with a dil. Na_2SO_3 aq and water and the solvent evaporated to dryness *in vacuo*. The oily residue crystallized from hexane, m.p. 136–139° (yield 120 mg). The analytical sample was obtained after several crystallizations from acetone–hexane yielding prisms, m.p. 145°, $[\alpha]_D$ −1°; λ max 215 and 260 mμ; ε, 29600, 16200; ν max 1765 cm^{-1} (acetyl band), shoulder at 1628 and a weak band at 1595 cm^{-1}. (Found: C, 57·63; H, 5·55; O, 13·79; Br, 23·31. Calc. for $C_{17}H_{19}O_3Br$: C, 58·11; H, 5·45; O, 13·66; Br, 22·77%).

Ozonolysis of cacalol acetate (Ib). Cacalol acetate (Ib; 2 g) dissolved in ethyl acetate (60 ml) was cooled to −70° and O_3 passed for 20 min (aprox. 0·6 g of O_3). The solution was then hydrogenated with 10% Pd-C catalyst (130 mg), until the absorption of H_2 ceased. The catalyst was filtered off and the solution evaporated to dryness *in vacuo*. The oily residue was dissolved in ether and extracted with 10% NaOH aq. The alkaline solution was acidified with HCl aq, precipitating a brown oil which was extracted with ether. The ethereal extract was washed with water, dried (Na_2SO_4) and evaporated. Crystallization from ether–hexane yielded the dihydroxyketone (IIIa), as yellow prisms (470 mg), m.p. 95–98°. Further crystallizations from acetone–hexane, raised the m.p. to 102–104°, $[\alpha]_D$ −20°, green colour with $FeCl_3$ λ max 270 mμ; ε, 3900; ν max 3500 cm^{-1} (hydroxyl groups); 1630 cm^{-1} (hydrogen bonded, α,β-unsaturated carbonyl group). It was observed also a weak band at 1710 cm^{-1}. (Found: C, 71·62; H, 7·80; O, 20·38. Calc. for $C_{14}H_{18}O_3$: C, 71·77; H, 7·74; O, 20·49%).

The methyl derivative (IIIb), was obtained by treatment of a methanolic solution of the dihydroxyketone (IIIa; 250 mg), with an ethereal solution of diazomethane, (prepared from 2 g of N-nitrosomethylurea). After 24 hr, the excess diazomethane was destroyed with a few drops of acetic acid, the ethereal solution washed with water and concentrated. Crystallization from ether–pentane, afforded the methoxy derivative (IIIb; 70 mg), m.p. 133–135°. The analytical sample showed m.p. 138–139°, (needles from ether–pentane), negative $FeCl_3$ test; $[\alpha]_D$ −14°; ν max 3500 cm^{-1} (hydroxyl group); 1690 cm^{-1} (α,β-unsaturated carbonyl group) and weak bands at 1600 and 1575 cm^{-1}. (Found: C, 72·33; H, 7·96; O, 19·50. Calc. for $C_{15}H_{20}O_3$: C, 72·55; H, 8·12; O, 19·33%; OCH_3, 12·85. Calc. for one OCH_3 12·49%).

Methylcacalol (Ic). Cacalol (800 mg), was dissolved in methanol (20 ml) and treated with an ethereal solution of diazomethane (prepared from 3 g of N-nitrosomethylurea). After 24 hr, the

excess diazomethane was destroyed with acetic acid and the solution evaporated to dryness. The oily residue, (730 mg) did not crystallize after chromatography; $[\alpha]_D$ +7°; λ max 218, 256 mμ; ε, 31000, 11200. (Found: C, 77·93; H, 8·35; O, 13·89. Calc. for $C_{16}H_{20}O_2$: C, 78·65; H, 8·25; O, 13·10%).

Clemmensen reduction of the dihydroxy-ketone (IIIa). To a solution of the dihydroxyketone (IIIa; 250 mg), in ethanol (20 ml), 3 g amalgamated Zn and 10 ml conc. HCl were added. The mixture was refluxed for 2 hr, conc. HCl (5 ml) added and the reflux continued for 2 hr. The Zn was filtered off and the solution diluted with water and extracted with ether. The ethereal extract was washed with water, dried on (Na_2SO_4) and evaporated to dryness. The colourless oily residue (210 mg) was purified by distillation *in vacuo* but failed to crystallize. This *o*-diphenol (IV), gave a green colour with $FeCl_3$, it is soluble in strong alkali; $[\alpha]_D$ −19°; λ max 284 mμ; ε, 1780; ν max 3500 cm^{-1} (hydroxyl groups) and weak bands at 1710 and 1620 cm^{-1}. (Found: C, 76·15; H, 8·74; O, 15·10. Calc. for $C_{14}H_{20}O_2$: C, 76·32; H, 9·15; O, 14·53%).

Quinoxaline derivative (V). The colourless oily diphenol (IV; 200 mg) was dissolved in anhydrous ether (30 ml). Freshly prepared Ag_2O (4 g) and Na_2SO_4 (4 g) were added and the mixture shaken at room temp for 30 min. The precipitate was then filtered off and the red solution evaporated at room temp *in vacuo*. The oily residue was dissolved in acetic acid (6 ml), *o*-phenylenediamine (300 mg) added, the solution refluxed for 30 min and evaporated to dryness *in vacuo*. The residue was dissolved in ether, the extract washed with dil. HCl, 5% NaOH aq and water then decolourized with activated charcoal and evaporated to dryness. The residue crystallized from acetone–methanol, yielding yellow needles (90 mg), m.p. 110–112°. Further crystallizations, raised the m.p. to 115°. (Found: C, 82·87; H, 7·78; N, 9·51. Calc. for $C_{20}H_{22}N_2$: C, 82·72; H, 7·64; N, 9·64).

Chromium trioxide oxidation of cacalol (Ia). A solution of cacalol (Ia; 1 g), in acetic acid (25 ml), was mixed with CrO_3 (900 mg) dissolved in water (3 ml) and acetic acid (7 ml) with mechanical stirring. The temp was kept below 15°. After the addition, the mixture was left at room temp for 1 hr; diluted with water and extracted with ether. The ethereal solution was washed with water, 5% NaOH aq and water again, dried (Na_2SO_4) and evaporated to dryness. The oily residue (370 mg) was dissolved in hexane, 20% benzene and chromatographed on 10 g alumina. The quinone (V) crystallized in the first fractions. They were combined and recrystallized from ether–pentane, yielding (80 mg), m.p. 84–85°; $[\alpha]_D$ +28°; λ max 283 mμ; ε, 8300; ν max; strong band at 1655 cm^{-1} (α,β-unsaturated carbonyl groups), at 1615 and 1590 cm^{-1} (C—C double bonds). (Found: C, 72·88; H, 6·07; O, 21·00. Calc. for $C_{14}H_{14}O_3$: C, 73·02; H, 6·13; O, 20·85).

Diacetylhydroquinone (VII). The quinone (V; 80 mg), was dissolved in acetic anhydride (6 ml;) powdered Zn (100 mg) and anhydrous sodium acetate (100 mg) added and the mixture refluxed for 90 min and then evaporated to dryness *in vacuo*. The residue was dissolved in $CHCl_3$ and the solution washed with water, 5% NaOH aq and water again. The chloroform extract was dried (Na_2SO_4) and evaporated to dryness. The oily residue, crystallized from pentane, yielding 75 mg of the diacetylhydroquinone (VII), m.p. 126–127°. The analytical sample showed m.p. 129–130° (prisms from ether–pentane), $[\alpha]_D$ −19°, λ max 253 mμ; ε, 26000; ν max; band at 1760 cm^{-1} (acetyl groups). (Found: C, 68·46; H, 6·51; O, 25·32. Calc. for $C_{18}H_{20}O_5$: C, 68·34; H, 6·37; O, 25·29).

Chloranil aromatization of cacalol acetate (Ib). To a solution of cacalol acetate (Ib; 500 mg), in xylene (60 ml), chloranil (1·5 g) was added, refluxed for 20 hr and the solvent evaporated to dryness *in vacuo*. The solid residue was refluxed in hexane (300 ml) and the insoluble material filtered off. The solution was chromatographed on alumina (15 g). The fractions eluted with benzene–hexane 2:1, 3:1 and 4:1 left crystalline residues after evaporation. The combined crystalline fractions were recrystallized from acetone–methanol. The acetate (VIII), was obtained as light yellow prisms m.p. 155°, yield 120 mg; λ max 244, 250, 320, 330 and 346 mμ; ε, 34800, 38000, 8750, 8200 and 7300. ν max (KBr) 1770 cm^{-1}, (acetyl group) and weak bands at 1660, 1620 and 1580 cm^{-1}. (Found: C, 76·03; H, 5·97; O, 18·14. Calc. for $C_{17}H_{16}O_5$: C, 76·10; H, 6·01; O, 17·89).

Ozonolysis of cacalol (Ia) *in acetic acid.* A solution of cacalol (1 g) in acetic acid (40 ml) was ozonized at 10–15° for 2 hr. Water (10 ml) was added and the yellow solution evaporated *in vacuo* to dryness. The residue was dissolved in ether and extracted with 20% NaOH aq. The aqueous extract was acidified with dil. H_2SO_4 and extracted with ether. The ethereal extract was washed with water and evaporated to dryness. The residue (210 mg) was esterified with an ethereal solution of diazomethane. After 3 hr, the solution was washed with water and evaporated leaving an oily

residue (190 mg). Gas chromatography on a column (1·84 m × 0·635 cm diam.) using Apiezon L 30% on chromosorb W 60/80 at 180°, showed 3 components (in 25, 23 and 52% yield), whose retention times were identical to those of authentic dimethyl methyl-succinate, dimethyl β-methyl-glutarate and dimethyl β-methyladipate. Addition of the authentic dimethyl β-methyladipate, increased the height of the peak corresponding to the product obtained from the ozonolysis of cacalol (Ia).

Clemmensen reduction of cacalone (IX). Cacalone (IX; 150 mg), was dissolved in ethanol (20 ml); 3 g amalgamated Zn and 10 ml HCl were added. After refluxing 2 hr, 5 ml conc. HCl were added and the reflux continued for 2 hr. The Zn was decanted, off the solution diluted with water and extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4) and evaporated to dryness. Crystallization from pentane yielded 30 mg cacalol (Ia) m.p. 85–87°. It was identified with authentic cacalol (Ia) by the standard methods.

The mother liquors were evaporated to dryness (90 mg); acetylation afforded cacalol acetate (Ib) m.p. 99–101°, 50 mg), identified by the standard methods with authentic cacalol acetate (Ib).

Lithium aluminium hydride reduction of cacalone (IX). To a solution of cacalone (IX; 300 mg), in anhydrous ether (50 ml), powdered $LiAlH_4$ (300 mg), was added, the mixture refluxed for 1 hr, ethyl acetate added first and then water. The mixture was acidified with dil. HCl aq and extracted with ether. The ethereal extract was washed with water, dried (Na_2SO_4) and evaporated to dryness. The oily residue crystallized from pentane, yielding cacalol (Ia) m.p. 86–88°, (50 mg) and identified with an authentic specimen. Acetylation of the mother liquors, afforded cacalol acetate (Ib) m.p. 100–102° (65 mg).

Reaction of hydrazine with cacalone (IX). Cacalone (IX; 100 mg), was dissolved in ethylene glycol (8 ml); 95% hydrazine (1 ml) was added and the solution refluxed for 20 min. After a few min a sublimate began to crystallize on the condenser. The solid material was collected and crystallized from acetone aq, yielding 9 desoxycacalol (XI), as long needles m.p. 131° (40 mg), $[\alpha]_D$ −2·8°; λ max; 216, 258, 284 and 294 mμ; ε, 35000, 11800 ,2800 and 2800; ν max a weak band at 1615 cm^{-1}. (Found: C, 83·83; H, 8·36; O, 7·50. Calc. for $C_{15}H_{18}O$: C, 84·07; H, 8·47; O, 7·46).

Hydrogenation of cacalone (IX). A solution of cacalone (IX; 300 mg) in ethyl acetate (25 ml), was hydrogenated with 10% Pd-C (50 mg). The uptake of hydrogen ceased after the absorption of one equiv. The catalyst was filtered off and the solution evaporated to dryness. The oily residue which did not crystallize was dissolved in benzene–hexane 1:3 and chromatographed on alumina (8 g). A crystalline substance m.p. 151° was obtained by evaporation of the fractions eluted with benzene–hexane 1:3 and 1:2. Crystallization from acetone–hexane yielded dihydrocacalone (X) m.p. 151° (45 mg), $[\alpha]_D$ +52°, λ max 278 mμ; ε, 13200; ν max 3400 (hydroxyl group) 1680 cm^{-1} (α,β-unsaturated ketone). (Found: C, 73·12; H, 7·36; O, 19·58. Calc. for $C_{15}H_{18}O_3$: C, 73·14; H, 7·37; O, 19·49%).

The last fractions eluted with benzene–hexane (1:2) yielded an isomeric dihydrocacalone (X) m.p. 167° (60 mg). The analytical sample was obtained by crystallization from acetone–ether, as leaflets m.p. 167°, $[\alpha]_D$ + 83°, λ max 278 mμ; ε, 13500; ν max 3400 and 1680 cm^{-1}. (Found: C, 73·33; H, 7·53; O, 19·70. Calc. for $C_{15}H_{18}O_3$: C, 73·14; H, 7·37; O, 19·49%).