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# CONTRIBUTION TO THE CHEMISTRY OF CACALOL[1,2]

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**Abstract**—The sequence of reactions described in this paper confirm that cacalol is a furotetralin derivative. The position of the methyl group, previously ascribed at C-7 has been shown to be attached at C-8.

CACALOL (Ia) and cacalone (IIa), constituents of *Cacalia decomposita* A. Gray[3] have been shown to be the first representatives of a new class of compounds possessing the furotetralin ring system.[4]

This paper reports additional results of our investigations concerning the structural features of cacalol (Ia) and its ketonic derivative cacalone (IIa). The evidence obtained, permits to assign the C-8 position in the furotetralin nucleus, for the methyl group previously ascribed at C-7.[4]

Recently, it has been reported that benzofurans react with acetic anhydride and phosphoric acid, acetyl derivatives at C-2[5] are formed. In a similar fashion cacalol acetate (Ib) afforded in good yield 2-acetylcacalol acetate (Id). Its IR spectrum showed an $\alpha,\beta$-unsaturated carbonyl band at 1670 $cm^{-1}$. The NMR spectrum[6] did not show the vinyl proton present in cacalol. The new methyl group exhibits a singlet in the acetyl region. 2-acetylcacalol acetate (Id) furnished readily a dark red 2,4-dinitrophenylhydrazone. Alkaline hydrolysis of Id afforded the phenol (Ic).

Treatment of cacalol acetate (Ib) with *m*-chloroperbenzoic acid yielded a product ($C_{17}H_{20}O_4$) whose spectroscopic data showed that the furan ring was oxidized to a five membered lactone (IIId). The IR band at 1800 $cm^{-1}$ corresponds to a $\beta,\gamma$-unsaturated-$\gamma$-lactone. The NMR spectrum of IIId did not exhibit the signals due to the furan proton and the methyl group. A new doublet centered at 8·4 $\tau$ (J = 7 c/s, intensity three protons) indicated the presence of a methyl group on the secondary carbon atom of the lactone ring. Basic hydrolysis of IIId afforded the phenolic lactone (IIIc). A similar derivative was obtained when the dimethoxyketone (IVb), obtained by methylation of the dihydroxyketone (IVa) (previously reported[4]) was oxidized with iodine in an alkaline medium. The presence of iodoform was detected

[1] Taken in part from a thesis to be submitted by J. J. Morales.
[2] Contribution No. 186 from the Instituto de Química de la Universidad Nacional Autónoma de México.
[3] In the preceding paper (Ref. 4) due to an error the term Cacalia was misspelled and written Cacalea.
[4] J. Romo and P. Joseph-Nathan, *Tetrahedron* **20**, 2331 (1964).
[5] N. P. Buu Hoi, N. D. Xuong and N. V. Bach, *J. Chem. Soc.* 173 (1964).
[6] The NMR spectra were determined by Mr. Eduardo Díaz of this Institute, using a Varian A-60 spectrometer, in $CDCl_3$ solution, tetramethylsilane was used as an internal *standard* (t = 10·00).

in this reaction, however, after demethylation only the norlactone (IIIa) was isolated in low yield. The formation of this lactone could be explained by a Favorskii rearrangement of the monoiodinated intermediary product. The norlactone (IIIa) showed an IR band at 1800 $cm^{-1}$ ($\beta,\gamma$-unsaturated, five membered lactone). The methylene group of the lactone is responsible for a sharp singlet at 6·38 $\tau$ (intensity two protons) in the NMR spectrum. The lactone (IIIa) afforded the acetate (IIIb).

In the preceding paper,[4] we described the aromatization of cacalol acetate (Ib) with chloranil, which afforded the naphthofuran (Va). When Ib was treated in a similar manner with 2,3-dichloro-5,6-dicyanobenzoquinone in xylene solution, the phenolic ring of cacalol acetate (Ib) was oxidized. A yellow product ($C_{15}H_{12}O_2$) ($\lambda_{max}$ 211, 234, 250, 290 and 340 m$\mu$) was isolated. This derivative was shown to have the quinonemethide structure (VIa) according to the following data. Its IR spectrum had bands at 1670 $cm^{-1}$ ($\alpha,\beta$-unsaturated carbonyl group) and at 1590 $cm^{-1}$ (C=C double bonds). The NMR spectrum showed two singlets at 7·7 and 7·3 $\tau$ (intensity three protons each) corresponding to the furan and aromatic methyl groups. A sharp signal at 3·76 $\tau$ (intensity two protons) is ascribed to the C-4 methylene group. A complex signal centered at 2·58 $\tau$ (intensity three protons) and a quadruplet at 1·75 $\tau$ (intensity one proton) correspond to the four aromatic protons. Reductive acetylation of the quinonemethide (VIa) yielded the acetate (Va), and chromium trioxide oxidation of VIa afforded the naphthofurandione (VIb), ($C_{14}H_{10}O_3$) ($\lambda_{max}$ 210, 250, 290 and 352 m$\mu$). Its IR spectrum had bands at 1670 $cm^{-1}$ (quinonoid carbonyl groups) and at 1590 $cm^{-1}$ (C=C double bonds). The NMR spectrum of this quinone is very similar to that of the quinonemethide (VIa), but the sharp signal ascribed to the exocyclic methylene group of the latter is not observed in the spectrum of the quinone (VIb). Reductive acetylation of the quinone (VIb) yielded the hydroquinone diacetate (Vb). Several napththofurandiones, substituted at C-2, have been previously described.[7,8] The quinone (VIb) appears to be the first reported without a substituent at C-2.

Alkaline hydrogen peroxide oxidation of the napththofurandione (VIb) yielded 3-methylphthalic acid, characterized as the anhydride (VII). This result shows that the methyl group of the alicyclic ring of cacalol (Ia) is attached at C-8 and is not at C-7, as was previously assigned.[4] The C-5 position was discarded when the properties of cacalone (IIa) were discussed.[4,9]

A shift of the methyl group from $C_7$ to $C_8$, in the treatment of cacalol acetate (Ib) with DDQ (or with chloranil) is not likely to occur. Furthermore, when the dimethoxytetrahydronaphthalene (VIIIb), prepared from the diphenol (VIIIa),[4] was pyrolyzed with 10% Pd–C, it yielded a monomethoxynaphthalene (IXb), characterized as its picrate. Potassium permanganate oxidation of the free phenol (IXa) afforded 3-methylphthalic and hemimellitic acids,[10] isolated as the corresponding anhydrides.

As it is well known, pyrolyses with Pd–C are not accompanied by migration of the substituents. In model compounds we found that the methyl group of the alicyclic

[7] E. F. Pratt and R. G. Rice, *J. Amer. Chem. Soc.* **79**, 5489 (1957).

[8] M. F. Sartori, *Chem. Rev.* **63**, 279 (1963).

[9] We have isolated from the roots of *Cacalia decomposita*, a product m.p. 140–143°, whose properties are in accord with those of IIa (m.p. 119–120°). The difference in m.p. may be attributed to an impurity, tenaciously retained by the product previously reported[4] (Experimental).

[10] We are grateful to Dr. Ernest Wenkert for a sample of hemimellitic acid.

ring did not migrate on aromatization and that the methoxyl group vicinal to the ring junction was eliminated. The experiments were carried out in the following way. Condensation of 1-methyl-3,4-dimethoxybenzene with succinic anhydride yielded β-(2-methyl-4,5-dimethoxybenzoyl) propionic acid, which on Clemmensen reduction afforded γ-(2-methyl-4,5-dimethoxyphenyl) butyric acid. Cyclization of the latter with polyphosphoric acid gave the monomethoxytetralone (Xa). Methylation of Xa furnished the dimethoxytetralone (Xb). Treatment of Xb with methylmagnesium bromide followed by pyrolysis with 10% Pd–C yielded the monomethoxynaphthalene (XIb). The β-naphthol (XIa) was obtained by demethoxylation of XIb. Both products were identical with authentic samples, prepared according to the method of Ruzicka and Sternbach.[11]

The dimethoxytetralone (Xb) was condensed with diethyl oxalate in the presence of sodium hydride and then treated with methyl iodide; basic hydrolysis of the product afforded the tetralone (Xc). Clemmensen reduction of Xc, yielded the oily dimethoxytetrahydronaphthalene (XIIc), characterized as the free phenol (XIIa), and its diacetate (XIIb). Pyrolysis of the dimethoxy derivative (XIIc) yielded the methoxynaphthalene (XIIIb). Demethoxylation of XIIIb furnished the β-naphthol (XIIIa). The latter compounds proved to be identical with those prepared from the tetralone (XIVa)[11] by methylation at C-2, followed by Clemmensen reduction and dehydrogenation with palladium on charcoal of the resulting tetrahydronaphthalene.

We repeated the previously described[4] ozonolysis of cacalol (Ia) and isolated in small amount R-(+)-β-methyladipic acid $[\alpha]_D$ +14·4° identical with an authentic sample. Therefore the absolute configuration of the asymmetric center of cacalol (Ia) and cacalone (IIa), is established (methyl β).

## EXPERIMENTAL[12]

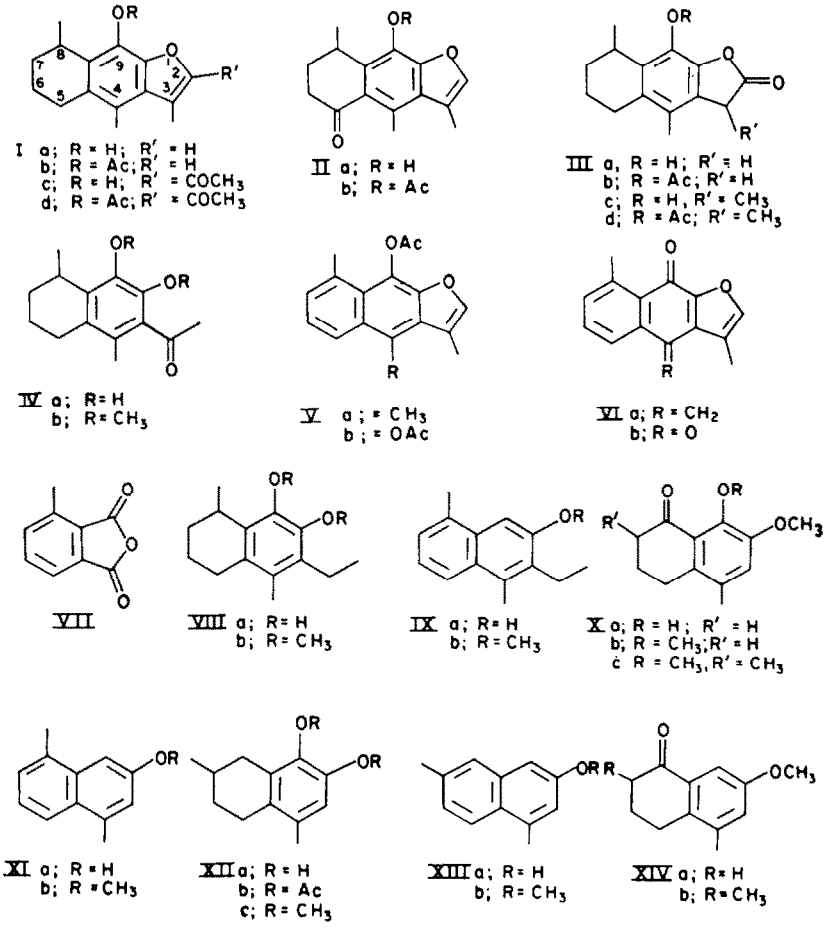
*2-Acetylcacalol acetate* (Id). To a solution of Ib (500 mg) in acetic anhydride (8 ml) 86% $H_3PO_4$ (1 ml) was added. The mixture was heated under reflux for 15 min and left at room temp for 1 hr. It was poured in cold water and the oily precipitate extracted with ether. The organic layer was washed with $NaHCO_3$aq and water, dried and evaporated to dryness. Crystallization of the solid residue from acetone–hexane yielded long needles (400 mg), m.p. 136–138°. Further crystallizations from acetone–hexane raised the m.p. to 142°, $[\alpha]_D$ +18°; $\lambda_{max}$ 242, 308 mμ; ε, 14800, 24500; IR bands at 1760 $cm^{-1}$ (acetate), 1670 $cm^{-1}$ (α,β-unsaturated ketone). (Found: C, 72·48; H, 7·24; O, 20·54. Calc. for $C_{19}H_{22}O_4$: C, 72·57; H, 7·06; O, 20·37%.)

The 2,4-dinitrophenylhydrazone showed m.p. 264–265° (dark red small needles from $CHCl_3$–MeOH); $\lambda_{max}$ ($CHCl_3$) 316 and 411 mμ; ε, 15800, 31000. (Found: C, 60·93; H, 5·40; O, 22·75; N, 11·30. Calc. for $C_{25}H_{26}O_7N_4$: C, 60·72; H, 5·30; O, 22·65; N, 11·33%.)

*2-Acetylcacalol* (Ic). A solution of Id (200 mg) in MeOH (15 ml) was mixed with KOH (200 mg) in water (2 ml), heated under reflux for 30 min, diluted with water and acidified with dil HCl. The precipitate was extracted with ether and the ethereal extract washed with water, dried and evaporated. Crystallization of the solid residue from acetone–hexane yielded needles (130 mg), m.p. 166–168°; $[\alpha]_D$ +30°; $\lambda_{max}$ 252 and 316 mμ; ε, 19600, 19000; IR bands at 3600 and 3300 $cm^{-1}$ (hydroxyl group) and 1670 $cm^{-1}$ (α,β-unsaturated ketone). (Found: C, 74·91; H, 7·36; O, 17·68. Calc. for $C_{17}H_{20}O_3$: C, 74·97; H, 7·40; O, 17·63%.)

[11] L. Ruzicka and L. Sternbach, *Helv. Chim. Acta* **23**, 355 (1940).

[12] M.ps are uncorrected, rotations were determined at 20° in $CHCl_3$. The IR spectra were run in $CHCl_3$ on a Perkin–Elmer 21 double beam spectrophotometer. The UV absorption spectra were determined in 95% EtOH, using a Beckman DK2 spectrophotometer. The microanalyses were performed by Dr. Franz Pascher, Bonn, Germany. We are grateful to Syntex, S. A. for the determination of the rotations and UV spectra.




*Oxidation of cacalol acetate* (Ib) *with* m-*chloroperbenzoic acid.* Compound Ib (500 mg) and *m*-chloroperbenzoic acid (400 mg) were dissolved in anhydrous $CHCl_3$ (25 ml), heated under reflux for 2 hr, washed with $NaHCO_3$aq, dried and evaporated. Crystallization of the residue from acetone–hexane, yielded prisms (225 mg), m.p. 181–183°. Several crystallizations from $CHCl_3$–MeOH raised the m.p. to 190–191°, $[\alpha]_D$ +18·7°; $\lambda_{max}$ 274 and 281 m$\mu$; $\varepsilon$, 1150, 1180; IR bands at 1800 $cm^{-1}$ ($\beta,\gamma$-unsaturated five membered lactone), at 1765 $cm^{-1}$ (acetyl group) and at 1635 $cm^{-1}$ (C=C double bonds). (Found: C, 70·81; H, 6·95; O, 21·89. Calc. for $C_{17}H_{20}O_4$: C, 70·81; H, 6·99; O, 22·20%.)

*Lactone* (IIIc). Compound IIId (500 mg) was dissolved 2% methanolic KOH (20 ml) and heated under reflux for 20 min, diluted with water, acidified with dil HCl and extracted with ether. The ethereal extract was washed with water and evaporated to dryness. The oily residue was sublimed under high vacuum and the solid material so obtained, was crystallized from acetone–hexane; this yielded prisms (220 mg), m.p. 160°; $[\alpha]_D$ ±0°; $\lambda_{max}$ 288 m$\mu$; $\varepsilon$, 2300; IR bands at 3600 and 3250 $cm^{-1}$ (hydroxyl group), 1800 $cm^{-1}$ ($\beta,\gamma$-unsaturated, five membered lactone) and at 1640 $cm^{-1}$ (C=C double bonds). (Found: C, 73·00; H, 7·33; O, 19·62. Calc. for $C_{15}H_{18}O_3$: C, 73·14; H, 7·37; O, 19·49%.)

*Dimethoxyketone* (IVb). A solution of IVa[4] (2 g) in acetone (60 ml) containing anhydrous $K_2CO_3$ (16 g) and dimethyl sulfate (8 g) was heated under reflux for 8 hr, diluted with water and extracted with ether. The ethereal extract was washed with water, dried and evaporated. The oily residue (wt. 1·935 g) did not crystallize even after chromatography on alumina. A small sample was distilled in high vacuum; $[\alpha]_D$ −17°. The NMR spectrum showed 2 singlets at 6·27 and 6·22 $\tau$

(intensity three protons each) ascribed to 2 methoxyl groups. (Found: C, 73·35; H, 8·61; O, 17·91. Calc. for $C_{16}H_{22}O_3$: C, 73·25; H, 8·45; O, 18·30%.)

*Norlactone* (IIIa). Compound IVb (550 mg) in MeOH (40 ml) was treated dropwise and simultaneously with 25% KOHaq (20 ml) and a solution of $I_2$ (6·8 g) and KI (6·8 g) in water (40 ml) with mechanical stirring, at room temp. The mixture was heated under reflux for 1 hr and the MeOH removed *in vacuo*. The alkaline solution was filtered off (the neutral material with a strong odour of iodoform was discarded), acidified with 10% $H_2SO_4$ and extracted with ether. The ethereal extract was washed with 5% $Na_2SO_3$aq and evaporated to dryness. The oily residue was dissolved in 2 ml acetic anhydride, treated with 3 ml 47% HI, heated under reflux for 1 hr, poured into water and extracted with ether. The organic layer was washed with water, dried and evaporated. Crystallization of the residue from acetone–hexane, yielded plates (60 mg), m.p. 156–158°; $[\alpha]_D$ +4·4°; $\lambda_{max}$ 287 m$\mu$; $\varepsilon$, 2150; IR bands at 3580 and 3200 cm$^{-1}$ (hydroxyl group), at 1800 cm$^{-1}$ ($\beta,\gamma$-unsaturated, five membered lactone), and at 1633 cm$^{-1}$ (C=C double bonds). (Found: C, 72·28; H, 7·18; O, 20·50. Calc. for $C_{14}H_{16}O_3$: C, 72·39; H, 6·94; O, 20·65%.)

*Norlactone acetate* (IIIb). Acetylation of IIIa with acetic anhydride and pyridine for 1 hr on the steam bath and crystallization of the product from acetone–hexane afforded prims, m.p. 182°; $\lambda_{max}$ 272 and 280 m$\mu$; $\varepsilon$, 980, 980; IR bands at 1810 cm$^{-1}$ ($\beta,\gamma$-unsaturated, five membered lactone), at 1770 cm$^{-1}$ (acetyl group) and at 1640 cm$^{-1}$ (C=C double bonds). (Found: C. 70·12; H, 6·48; O, 23·51. Calc. for $C_{16}H_{18}O_4$: C, 70·05; H, 6·61; O, 23·33%.)

*Quinonemethide* (VIa). A solution of cacalol acetate (3 g) and DDQ (18 g) in anhydrous xylene (250 ml) was heated under reflux for 12 hr. The solution was filtered off, the precipitate washed with ether and discarded. The combined xylene and ethereal solutions were extracted with 10% NaOHaq, washed with water and the volatile components eliminated by steam distillation. The oily residue was dissolved in benzene–hexane 1:1 and chromatographed on 60 g of slumina. The crystalline fractions eluted with benzene–hexane 1:1, 2:1, 3:1 and benzene, were combined and recrystallized from acetone–hexane, yield 565 mg, m.p. 153–155°. Further crystallizations from acetone–ether, afforded yellow needles, m.p. 160–161°; $\lambda_{max}$ 211, 234, 250, 290 and 340 m$\mu$; $\varepsilon$, 17600, 13500, 13200, 13200, 10000; IR bands at 1670 cm$^{-1}$ ($\alpha,\beta$-unsaturated ketone) and at 1590 cm$^{-1}$ (C=C double bonds). (Found: C, 79·90; H, 5·16; O, 14·62. Calc. for $C_{15}H_{12}O_2$: C, 80·33; H, 5·39, O, 14·27%.)

*Reductive acetylation of the quinonemethide* (VIa). A solution of VIa (100 mg) in acetic anhydride (3 ml), containing anhydrous sodium acetate (300 mg) and powdered Zn (300 mg) was heated under reflux for 1 hr diluted with water and extracted with ether. The organic layer was washed with 5% NaOHaq, water and evaporated to dryness. Crystallization from acetone–hexane yielded Va (40 mg), m.p. 154–155°. Identified by the standard methods with the product obtained by aromatization of Ib with chloranil.[4]

*Furonaphthoquinone* (VIb). A solution of VIa (565 mg) in acetic acid (12 ml) was allowed to stand at room temp with 0·5 g of $CrO_3$ in 2 ml water and 6 ml acetic acid for 1 hr. The mixture was diluted with water, the precipitate collected and washed with water. Crystallization from acetone yielded yellow prisms (300 mg), m.p. 161–163°; $\lambda_{max}$ 210, 250, 290 and 352 m$\mu$; 16200, 23500, 5600, 4400; IR bands at 1670 cm$^{-1}$ (quinonoid carbonyl groups) and at 1590 cm$^{-1}$ (C=C double bonds). (Found: C, 74·02; H, 4·30; O, 21·26. Calc. for $C_{14}H_{10}O_3$: C, 74·33; H, 4·46; O, 21·22%.)

*Hydroquinone diacetate* (Vb). Reductive acetylation of VIb was carried out as in the case of VIa. Crystallization from acetone–hexane yielded Vb as fluffy needles, m.p. 200°: $\lambda_{max}$ 246, 319 and 328 m$\mu$; log $\varepsilon$, 56000, 8500, 7250; IR band at 1770 cm$^{-1}$ (acetyl groups). (Found: C, 68·96; H, 5·34; O, 25·72. Calc. for $C_{18}H_{16}O_5$: C, 69·22; H, 5·16; O, 25·62%.)

*Hydrogen peroxide oxidation of the furonaphthoquinone* (VIb). To a solution of VIb (250 mg) in MeOH (20 ml), 35% $H_2O_2$ (6 ml) and KOH (4 g) in water (8 ml) were added. The solution was heated under reflux for 40 min, concentrated to a small volume, acidified with dil HCl and extracted with ether. The ethereal extract was evaporated and the crystalline residue sublimed at 130–140° in high vacuum. The anhydride (VII; 120 mg), showed m.p. 115°; IR bands at 1845 and at 1775 cm$^{-1}$. It proved to be identical with an authentic specimen. (Found: C, 66·64; H, 3·84; O, 29·43. Calc. for $C_9H_6O_3$: C, 66·67; H, 3·73; O, 29·60%.)

*Aromatization of the dimethoxyderivative* (VIIIb). Compound VIIIa[4] (3·5 g) was methylated, as described for the preparation of IVb. The distilled VIIIb (3·45 g) did not crystallize. The NMR spectrum showed two singlets at 6·29 and 6·32$\tau$ (intensity three protons each), corresponding to 2 methoxyl groups. A mixture of the crude product (3 g) and 10% Pd–C (8 g) was heated at 310–320°

for 40 min, followed by extraction with benzene. The benzene solution was evaporated to dryness and the oily residue (800 mg) treated with a methanolic solution of picric acid, furnishing the picrate of IXb (wt. 920 mg). Crystallization from MeOH yielded red needles, m.p. 98°. Its NMR spectrum showed one singlet at 6·16$\tau$ (intensity three protons) corresponding to 1 methoxyl group. (Found: C, 56·87; H, 4·76; O, 28·67; N, 9·36. Calc. for $C_{21}H_{21}O_8N_3$: C, 56·88; H, 4·77; O, 28·87; N, 9·48%.)

Extraction of an ethereal solution of the picrate (850 mg) with dil $NH_4OH$, afforded oily IXb. It was dissolved in 6 ml of acetic anhydride, treated with 4 ml of 47% HI, heated under reflux for 3 hr, poured in cold water and extracted with ether. The ethereal extract was washed with $NaHCO_3$aq, dried and evaporated. The oily IXa (280 mg) did not crystallize.

*Potassium permanganate oxidation of the napthhol* (IXa). A solution of IXa (500 mg) in acetone (500 ml) with 12 g powdered $KMnO_4$ was heated under reflux for 24 hr and diluted with water (100 ml). A stream of $SO_2$ was passed until the precipitate was dissolved. The solution was concentrated *in vacuo* to a small volume and extracted with ether. From the oily residue left after evaporation of the extract, 3-methylphthalic and hemimellitic anhydrides were obtained by fractional sublimation under high vacuum. Crystallization of VII from ether–pentane yielded 10 mg, m.p. 110–112°. Hemimellitic anhydride crystallized from acetone–hexane, yield 15 mg, m.p. 194–196°. Both compounds were identified with authentic samples by the standard methods.

*β-(2-Methyl-4,5-dimethoxybenzoyl) propionic acid.* A solution of 1-methyl-3,4-dimethoxybenzene (10 g) in $CS_2$ (150 ml) was mixed with succinic anhydride (9 g) dissolved in nitrobenzene (150 ml); $AlCl_3$ (9 g) were added with mechanical stirring and external cooling. The mixture was left at room temp overnight, heated under reflux for 30 min, poured in 300 ml of ice cold 10% HCl and steam distilled until the volatile components were eliminated. The oily residue was dissolved in ether, and the ethereal solution extracted with 10% NaOHaq. The alkaline extract was acidified with dil HCl, the precipitate collected and washed with water. Crystallization of the dried product from benzene–hexane, yielded 8·7 g, m.p. 128–130°. (Found: C, 61·73; H, 6·34; O, 31·71. Calc. for $C_{13}H_{16}O_5$: C, 61·89; H, 6·39; O, 13·71%.)

Alkaline $KMnO_4$ oxidation of a small sample, afforded after sublimation, 4,5-dimethoxyphthalic anhydride m.p. 175°. (Reported,[13] m.p. 175°)

*γ-(2-Methyl-4,5-dimethoxyphenyl) butyric acid.* Clemmensen reduction of β-(2-methyl-4,5-dimethoxybenzoyl) propionic acid (10 g) in acetic acid (140 ml) with amalgamated Zn (16 g), yielded γ-(2-methyl-4,5-dimethoxyphenyl) butyric acid (7·7 g), prisms from ether–hexane, m.p. 82°. (Found: C, 65·23; H, 7·74; O, 26·84. Calc. for $C_{13}H_{18}O_4$: C, 65·53; H, 7·61; O, 26·86%.)

*5-Methyl-7-methoxy-8-hydroxy-1-tetralone* (Xa). A solution of γ-(2-methyl-4,5-dimethoxyphenyl) butyric acid (10 g) in polyphosphoric acid (100 ml) was heated at 150° for 15 min, poured into ice and the precipitate extracted with ether. The ethereal extract was washed with water, $NaHCO_3$aq and evaporated to dryness. Crystallization of the residue from acetone–hexane, yielded 6·7 g m.p. 114–116°; IR band at 1630 $cm^{-1}$ (hydrogen bonded tetralone carbonyl group). Its NMR spectrum exhibited a sharp singlet at 6·11 $\tau$ (intensity three protons) ascribed to 1 methoxyl group. The chelated phenolic proton is responsible for a singlet at −2·75 $\tau$ (intensity one proton). (Found: 69·57; H, 7·00; O, 23·70. Calc. for $C_{12}H_{14}O_3$: C, 69·88; H, 6·84; O, 23·27%.)

*5-Methyl-7,8-dimethoxy-1-tetralone* (Xb). Methylation of Xa (8 g) with dimethyl sulfate, yielded Xb (7·2 g), m.p. 82–83° (yellow prisms from ether–hexane); IR band at 1680 $cm^{-1}$ (tetralone carbonyl group). The NMR spectrum showed a singlet at 6·12 $\tau$ (intensity 6 protons) ascribed to 2 methoxyl groups. (Found: C, 71·11; H, 7·25; O, 21·76. Calc. for $C_{13}H_{16}O_3$: C, 70·89; H, 7·32; O, 21·79%.)

*2,5-Dimethyl-7,8-dimethoxy-1-tetralone* (Xc). A mixture of Xb (7 g), anhydrous benzene (120 ml), freshly distilled dimethylformamide (30 ml) and NaH (1·8 g), was heated under reflux for 20 min. Diethyl oxalate (8 g) was added and the reflux prolonged for 30 min. The solution was then treated with MeI (20 g) and heated under reflux for a further 6 hr. The cold solution was washed with water and evaporated *in vacuo*. The oily residue was dissolved in 10% methanolic NaOH (150 ml), heated under reflux for 30 min, acidified with dil HCl, concentrated *in vacuo* to a small volume and diluted with water. The oily precipitate was extracted with ether, washed with water and evaporated to dryness. The residual gum (3·1 g) dissolved in hexane was chromatographed on alumina. Crystallization from pentane yielded pale yellow prisms (2·1 g), m.p. 52°. The NMR spectrum exhibited a

[13] A. W. Gilbody, W. H. Perkin Jr. and J. Yates, *J. Chem. Soc.*, 79, 1396 (1901).

doublet at 8·8 $\tau$ (J = 7 c/s, intensity three protons) corresponding to the >CH—$CH_3$ group. (Found: C, 71·63; H, 7·59; O, 20·62. Calc. for $C_{14}H_{18}O_3$: C, 71·77; H, 7·74; O, 20·49%.)

*Clemmensen reduction of* 2,5-*dimethyl*-7,8-*dimethoxy*-1-*tetralone* (Xc). Compound Xc (7 g) in EtOH (80 ml) was reduced with amalgamated Zn (15 g) and conc. HCl (25 ml). The oily XIIc did not crystallize after chromatography on alumina, yield 4·2 g.

2,5-*Dimethyl*-7,8-*dihydroxy*-1,2,3,4, *tetrahydronaphthalene* (XIIa). Compound XIIc (2 g) was hydrolyzed with 47% HI (5 ml) and acetic anhydride (10 ml) as described above. The diol (XIIa) was purified by sublimation under high vacuum, yield 1·4 g, m.p. 134–135°. (Found: C, 74·77; H, 8·31; O, 16·86. Calc. for $C_{12}H_{16}O_2$: C, 74·97; H, 8·39; O, 16·65%.)

Its diacetate (XIIb) showed m.p. 104–106° (prisms from acetone–hexane). (Found: C, 69·54; H, 7·30; O, 23·16. Calc. for $C_{16}H_{20}O_4$: C, 69·34; H, 7·43; O, 23·58%.)

*Aromatization of* 2,5-*dimethyl*-7,8-*dimethoxy*-1,2,3,4-*tetrahydronaphthalene* (XIIc). Dehydrogenation of XIIc (1·2 g) with 10% Pd–C (3 g) at 310–320° for 20 min was followed by extraction with benzene. The benzene solution was evaporated to dryness and the residue sublimed under high vacuum. This yielded XIIIb (420 mg), m.p. 44°. (Found: C, 83·51; H, 7·50; O, 8·60. Calc. for $C_{12}H_{14}O$: C, 83·83; H, 7·58; O, 8·59%.)

The picrate showed m.p. 123–125° (red prisms from MeOH). (Found: C, 54·74; H, 4·36; O, 30·67; N, 9·98. Calc. for $C_{19}H_{17}O_8N_3$: C, 54·94; H, 4·13; O, 30·82; N, 10·12%.)

Hydrolysis of XIIIb with acetic anhydride and HI, afforded XIIIa m.p. 124–125° (prisms from ether–pentane). The product decomposes in a few days and an accurate analysis could not be obtained.

1,5-*Dimethyl*-7-*methoxynaphthalene* (XIb). A solution of Xb (2·5 g) in anhydrous benzene (40 ml), was treated with a 6N MeMgBr solution (10 ml), heated under reflux for 8 hr and decomposed with $NH_4Cl$ solution. The organic layer was washed with water and evaporated, the residual oil (2 g) was mixed with 10% Pd–C (4·6 g) and heated at 310–320° for 20 min. The methoxyderivative (XIb) was isolated as previously described for similar cases. Crystallization from MeOH furnished needles m.p. 83–84°. This product was identical with an authentic sample of 1,5-dimethyl-7-methoxynaphthalene prepared according to the directions described by Ruzicka and Sternbach.[11] (Found: C, 83·55; H, 7·60; O, 8·82, Calc. for $C_{12}H_{14}O$: C, 83·83; H, 7·58; O, 8·59%.)

Hydrolysis of XIb yielded XIa, needles from acetone–hexane, m.p. 151–153°.

2,5-*Dimethyl*-7-*methoxytetralone* (XIVb). Compound XIVa[11] (2 g) was methylated at C-2 as described for the preparation of Xc. The tetralone (XIVb) did not crystallize. The alicyclic methyl group is responsible for a doublet centered at 8·83$\tau$ (J = 7 c/s, intensity three protons) in the NMR spectrum. Its 2,4-dinitrophenylhydrazone showed m.p. 235° (red needles from $CHCl_3$–MeOH, $\lambda_{max}$ ($CHCl_3$) 392 m$\mu$; $\varepsilon$, 27000. (Found: C, 59·27; H, 5·36; O, 21·06; N, 14·38. Calc. for $C_{19}H_{20}O_5N_4$: C, 59·37; H, 5·24; O, 20·81; N, 14·58%.)

2,5-*Dimethyl*-7-*methoxynaphthalene* (XIIIb). Clemmensen reduction of XIVb (1·5 g) yielded the corresponding tetralin (1·1 g). It was pyrolized with 10% Pd–C, yielding XIIIb, m.p. 44°. It proved to be identical with the product obtained by aromatization of XIIc.

*Cacalone* (IIa). The hexane extract of the ground roots of Cacalia decomposita (3 Kg) was chromatographed on alumina. Elution with benzene afforded IIa (2·4 g), m.p. 119–120°, identified by the standard methods with an authentic specimen.[4] Several fractions eluted with benzene and increasing proportions of ether yielded a product (1·2 g), m.p. 140–143° (prisms from acetone–hexane), $[\alpha]_D$ +90°; $\lambda_{max}$ 212, 250 and 320 m$\mu$; $\varepsilon$, 6200 10500, 7800. Its IR spectrum was nearly identical with that of IIa and thin layer chromatography of both products showed the same $R_f$. This higher melting product gave all the reactions, previously described for cacalone.[4]

The acetate (IIb) showed m.p. 168–169° (needles from acetone–hexane); $\lambda_{max}$ 212, 254 and 316 m$\mu$; $\varepsilon$, 5300, 9900, 7400; IR bands at 1760 $cm^{-1}$ (acetyl group) and at 1660 $cm^{-1}$ ($\alpha,\beta$-unsaturated ketone). (Found: C, 71·53; H, 6·30; O, 22·41. Calc. for $C_{17}H_{18}O_4$: C, 71·31; H, 6·34; O, 22·35%.)

R-(+)-$\beta$-*methyladipic acid.* A solution of Ia (4 g) in acetic acid (150 ml) was ozonized.[4] The acidic fraction was purified through the cyclohexylamine salt. Decomposition with dil HCl followed by extraction with ether, washing of the ethereal extract with $Na_2SO_4$aq removal of the solvent and crystallization of the residue from benzene, yielded 20 mg of R-(+)-$\beta$-methyladipic acid, m.p. 85–87°, $[\alpha]_D$ +14·4°, undepressed on admixture with an authentic specimen, IR spectra superimposable.