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STUDIES IN *CACALIA* SPECIES

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Abstract—Cacalol (Ia), cacalone (Ic) and decompostin (II) were isolated from the roots of *Cacalia ampullacea*. Extraction of *C. decomposita* gave known compounds and the new acetal V, which appears to be an artifact of isolation.

THE CHEMICAL constitution of the roots of *Cacalia decomposita* (A. Gray) has been well established.[1–5] Recent chemical correlation of the main constituent, cacalol,[1,2] with eremophylane derivatives[6] led to the definitive structure of cacalol as 9-hydroxy-3,4,5-trimethyl-5,6,7,8-tetrahydronaphtho(2,3-b)furan (Ia). This was confirmed by the total synthesis[6] of maturinone (IIIa) which had also been correlated[2,3] with cacalol (Ia). Another synthesis of maturinone (IIIa) was developed by Thomson,[7] who claimed spectroscopic (i.r. and NMR) anomalies for cacalone (Ic). However, the published spectral data[2] are in accordance with the structure, since the o.r.d. curves[8] of both compound Ic) and its acetate (Id) demonstrated the presence of inherently disymmetric chromophores, thus prohibiting the formation of the expected hydrogen bond and shifting the i.r. carbonyl frequency. This is due to the fact that the conformation of the alicyclic ring of cacalone (Ic), as deduced from 100 MHz NMR experiments,[9] is such that there are no appreciable steric interactions between the two methyl groups located in the *peri*-position.

Careful chromatography of the hexane extract of the roots of *C. ampullaceae* (Green) afforded cacalol (Ia, 0·88 per cent), cacalone (Ic, 0·012 per cent) and decompostin (II, 0·038 per cent). The benzene extract gave an additional sample of decompostin (II, 0·014 per cent). It is interesting to note that none of the fully aromatic compounds previously found in *C. decomposita* were isolated from *C. ampullaceae.*

A sample of *C. decomposita* was also extracted, and from the fractions we isolated a new very insoluble compound, m.p. 231–233°. Its elemental composition, $C_{30}H_{22}O_7$, and complex u.v. spectrum (see Experimental) suggested an aromatic structure. The i.r. spectrum of this compound shows quinonoid carbonyl groups (1668 cm^{-1}) and C=C double bonds (1621, 1612, 1601 and 1558 cm^{-1}). The NMR spectrum (Fig. 1) was very informative and characteristic: singlets at 7·20, 7·06 and 5·56 τ (3H each) are attributable to two aromatic methyl

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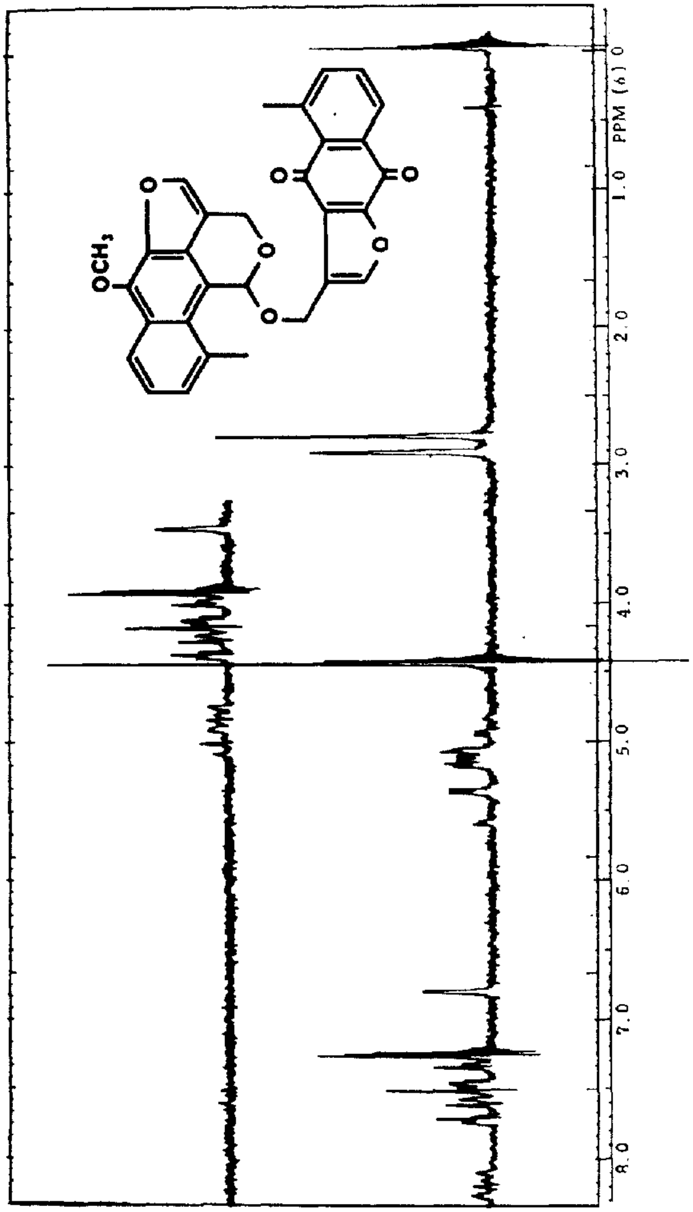


FIG. 1. THE 60 MHz PMR SPECTRUM OF THE ACETAL V.

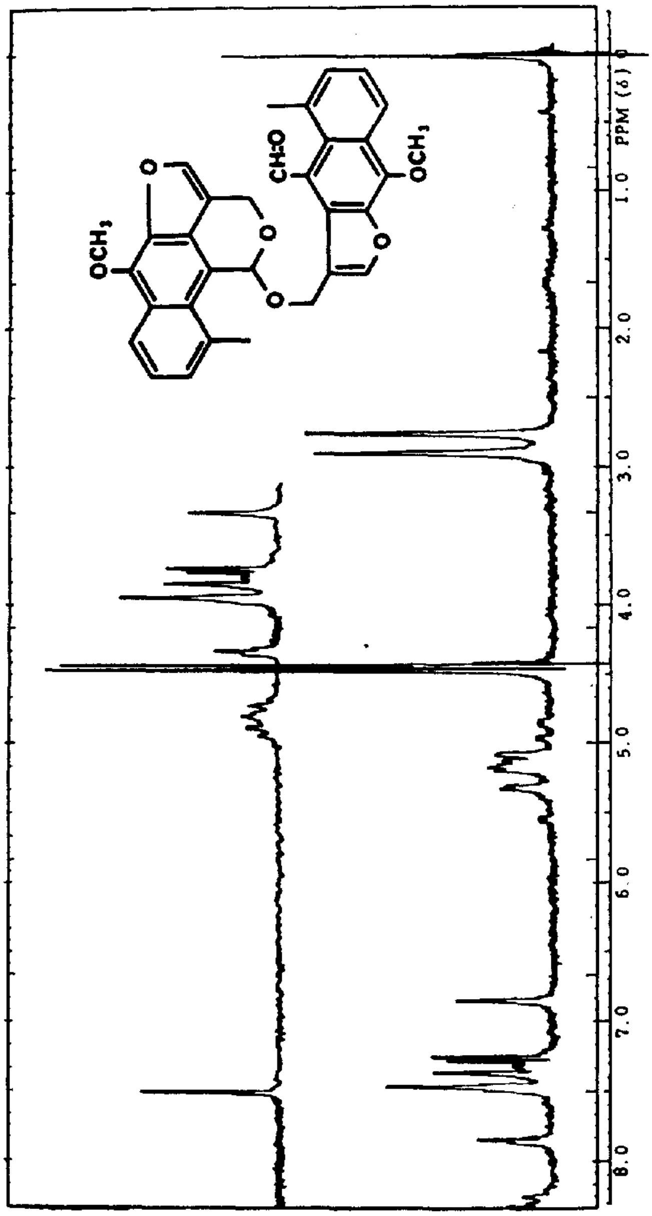
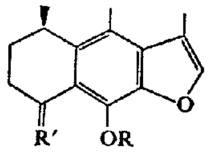
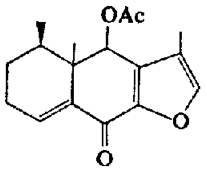


FIG. 2. THE 60 MHz PMR SPECTRUM OF DIMATURIN (VI).

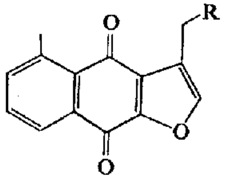
groups and one methoxyl. A complex signal centered at 4·85 τ (4H) is due to the AB part of two superimposed ABX systems arising between the methylene groups forming the acetal and the corresponding furan proton through allylic coupling. The acetal proton is responsible for a sharp singlet (1H) at 3·23 τ whereas the aromatic hydrogens originate complex signals at 1·82 τ (2H) and 2·62 τ (5H) and a singlet at 2·33 τ (1H).



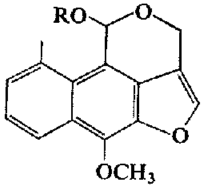
(Ia) R = H; R' = H_2
(Ib) R = Ac; R' = H_2
(Ic) R = H; R' = O
(Id) R = Ac; R' = O



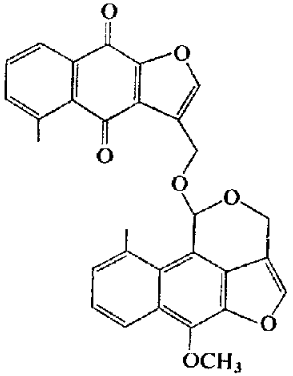
(II)



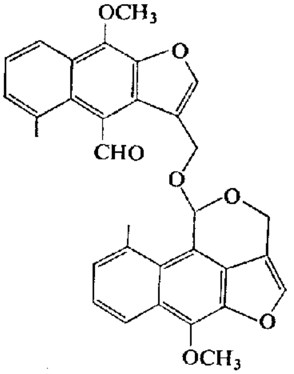
(IIIa) R = H
(IIIb) R = OH



(IVa) R = Me
(IVb) R = Et



(V)



(VI)

This spectrum is closely similar to that of dimaturin (VI, Fig. 2). The unique important differences are the absence of sharp singlets at 5·58 τ (3H) and –0·97 τ (1H) which correspond to a methoxyl group and the aldehydic proton[3] of dimaturin (IV).

The difference in elemental composition between the new compound and dimaturin (VI) combined with spectral properties, suggests assignment of structure V to the former. This was confirmed by acid hydrolysis of V in both methanolic and ethanolic solutions. From the reaction mixtures we isolated maturone (IIIb) identified by standard methods with an authentic specimen. However, neither IVa nor IVb could be obtained, but they may undergo further transformations which preclude their isolation.

The acetal (V), though obtained from the extracts of the roots, appear to be an artifact formed during the process of isolation rather than a product found in the plant. This was also argued[3] for compounds IVa, IVb and VI, since biogenetically[7] these naphthofuran compounds derive from decompostin (II).

EXPERIMENTAL

Melting points are uncorrected; i.r. spectra were determined in $CHCl_3$ with a Perkin–Elmer 421 spectrophotometer and u.v. spectra measured using a Unicam SP-800 instrument. NMR spectra were obtained with a Varian A-60 spectrometer, using tetramethylsilane as internal standard ($\tau = 10{\cdot}00$ ppm) and $CDCl_3$ as solvent. Microanalysis were performed by Dr. A. Bernhardt, Elbach über Engelskirchen, West Germany. Chromatographic separations were made using alumina (Alcoa F-20) deactivated with ethyl acetate.

Extraction of Cacalia Ampullaceae (*Green*)

The plant was collected* on the Cerro de las Ventanas near Pachuca, Hgo, in August 1966. The ground, dried roots (549 g) were extracted twice with hexane (4 l) under reflux for 12 hr. The combined extracts were evaporated to dryness (31 g wt.), treated with pentane and left overnight at 4°. The crystalline product was separated by decantation and recrystallized from acetone–hexane, yielding 1·25 g of cacalol (Ia), m.p. 86–90° identical with an authentic sample.[1,2]

The mother liquors from the recrystallization were acetylated (pyridine–acetic anhydride, 1 hr on the steam bath) and worked up as usual. The residue was chromatographed on alumina (50 g). Several fractions, eluted with hexane and hexane–benzene (4:1), gave crystalline products. These were combined and recrystallized from acetone–hexane, yielding 1·5 g of cacalol acetate (Ib), m.p. 107–108°, identical with an authentic specimen.

The decanted liquors left after the isolation of cacalol were evaporated to dryness (25 g wt.) and the solid chromatographed on alumina (300 g). Various fractions eluted with hexane and hexane–benzene (4:1) crystallized. They were combined, yielding a further 875 mg of cacalol, m.p. 87–90°, which were identified as above.

Several other fractions eluted with hexane–benzene mixtures also crystallized. After combination and recrystallization from ether, 210 mg of decompostin (II), m.p. 185–186°, were obtained and identified† by standard methods.

The mother liquors left from the isolation of decompostin (II) were concentrated, and the product crystallized from ether–hexane, yielding 65 mg of cacalone (Ic) identified as usual.

Further elution from the column gave only oily fractions. After acetylation and repeated chromatography of the various oily residues, an additional 1·7 g of cacalol acetate (Ib) was obtained.

After the extraction of the roots with hexane, the material was heated twice under reflux with benzene (4 l) for 10 hr. The combined extracts were evaporated to dryness (7·1 g) and chromatographed on alumina (98 g). Several fractions eluted with hexane–benzene mixtures crystallized, yielding 75 mg of decompostin (II), m.p. 187–188°.

Acetal (*V*)

The hexane extracts obtained from 4·5 kg of *C. decomposita* (A. Gray) were evaporated to dryness (329 g wt.) and the residue chromatographed on alumina (1 kg). Among the previously isolated compounds[1–5] from the fractions eluted with hexane–benzene (1:1, 1:2, 1:3, 1:4) and benzene a new crystalline compound was obtained. After recrystallization from ethyl acetate, 1·63 g of V, as orange needles, m.p. 231–233°, were obtained, λ_{max} ($CHCl_3$): 248 (s), 252, 268 (s), 304 (s), 325 (s), 340, 352 nm; ϵ, 72,200, 75,750, 13,000, 8500, 11,000, 13,400, 12,700; ν_{max} 1668 (quinonoid carbonyl) and 1621, 1612, 1601 and 1588 cm^{-1} (C=C double bonds). (Found: C, 72·71; H, 4·48; O, 22·89. $C_{30}H_{22}O_7$ required: C, 72·87; H, 4·48; O, 22·65%.)

Dimaturin (VI) showed λ_{max} ($CHCl_3$): 247 (s), 252, 326 (s), 340, 353, 380 nm; ϵ, 63,750, 69,350, 11,200, 13,400, 13,400, 6700.

Acid Hydrolysis of V

A solution of 200 mg of V in 15 ml of EtOH (or MeOH) and 0·5 ml of conc. HCl was heated under reflux during 3 hr. The solvent was evaporated to dryness under reduced pressure and the residue dissolved in ethyl

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* We are grateful to Dr. Jirzy Rzedowsky (Departamento Botánico de la Escuela Nacional de Ciencias Biológicas, IPN) for the recollection and classification of the material (Voucher Number: Rzedowsky 17029).

† We are in debt to Dr. J. Romo (Instituto de Química, UNAM) for the comparison.

acetate, washed with water, dried Na_2SO_4 (Na_2SO_4), filtered and evaporated to dryness. The brown oily residue was chromatographed on 10 g of alumina. The fractions eluted with hexane–benzene (2:3) crystallized. They were combined and recrystallized yielding 50 mg of yellow crystals, m.p. 164–168°. Successive recrystallizations from acetone–ether gave pure maturone (IIIb), m.p. 169–170°, no depression in admixture m.p. with an authentic sample[3] and superimposable i.r. and NMR spectra.