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THE SESQUITERPENES OF CACALIA SPECIES

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Twelve sesquiterpenes including six new compounds have been isolated from Cacalia delphiniifolia Sieb. et Zucc. and C. hastata L. var. tanakae (Franch. et Savat.) Kitam., and their structures have also been determined by their physical and chemical properties.

Since 1964 Romo and his co-workers have isolated a number of the components from the root of Cacalia decomposita A. Gray.1) These compounds can be grouped into two general types of sesquiterpene,2) namely, furanonaphthalene and furanonaphthoquinone derivatives, and it has been postulated that these types may be biogenetically2,3) related to the eremophilane type on the basis of their co-occurring and chemical correlation with decompostin.4,5)

We have investigated the constituents of two Cacalia species native to Japan--Cacalia delphiniifolia Sieb. et Zucc. (Japanese name 'Momijigasa') and C. hastata L. var. tanakae (Franch. et Savat.) Kitam. (Japanese name 'Inudona'). Recently the constituents of the two other domestic Cacalia species have been reported.6,7)

The present paper will report the isolation and the structural elucidation of twelve sesquiterpenic components, i. e., the six (I-IV, V-a, and VI-a) from the methanol extract of the root of the former plant and the other six (VII-IX, X-a, XI, and XII) from the acetone extract of the latter whole plant. They were isolated by repeated column chromatography with silica gel and by recrystallization, and they consisted of six known and six new substances. The known compounds were identified as cacalol (I),1-a,b) maturinone (IV),1-c) O-methyldehydrocacalol (VII),6,7) O-methylcacalodienol (VIII),6,7) cacalonol (IX),7) and fukinanolide (XII).8)

The six new compounds were named as described below, and their structures were elucidated as follows.

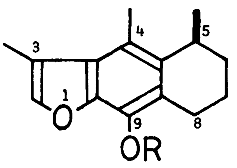
Cacalol acetate (II), $C_{17}H_{20}O_3$, mp 103.5-104.5°, colorless prisms, $[\alpha]_D$ -96.5° (c, 0.995, $CHCl_3$) was identical in all respects with the acetate1-a) prepared from cacalol I with Ac_2O-pyridine.

Tetrahydromaturinone (III), $C_{14}H_{14}O_3$, mp 88.0-88.5°, yellow needles, $[\alpha]_D$ +34.7° (c, 1.0, $CHCl_3$) showed UV: λ_{max}^{MeOH} 220 (14200), 261 (13200), 307 nm (ε, 4100); IR(CCl_4): 1660, 1610 (α,β-unsaturated ketone), 1585, 1530 cm^{-1} (furan), and δ^{CCl_4}: 1.12 (d, J=7.0 Hz, 5-Me), 1.64 (m, 6- and 7-CH_2), 2.22 (s, 3-Me), 2.48 (m, 8-CH_2), 2.87 (m, 5-CH), 7.35 (q, J=1.0 Hz, 2-CH). Dehydrogenation of III with Pd-C afforded maturinone IV. Thus this can be assigned to the formula III.

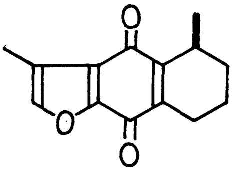
Cacalolide (V-a), $C_{15}H_{18}O_3$, mp 158.0-159.5°, pale yellow prisms, $[\alpha]_D$ +18.0° (c, 1.03, MeOH) showed IR($CHCl_3$): 3545 (OH), 1790 (γ-lactone), 1635 cm^{-1} (C=C), and δ^{CDCl_3}: 1.12 (d, J=7.0 Hz, 5-Me), 1.55 (d, J=7.5 Hz, 3-Me), 1.74 (m, 6- and 7-CH_2), 2.17 (s, 4-Me), 2.70 (m, 8-CH_2), 3.10 (m, 5-CH), 3.70 (q, J=7.5 Hz, 3-CH), 5.22 (br s, 9-OH). Its acetate (V-b), $C_{17}H_{20}O_4$, mp 194.0-195.0°, colorless prisms, was identical with the acetate prepared by oxidation with m-chloroperbenzoic acid of cacalol acetate II.

Senecioyloxycacalol (VI-a), $C_{20}H_{24}O_4$, mp 112.5-113.5°, colorless prisms, $[\alpha]_D$ +17.8° (c, 0.998, $CHCl_3$) exhibited the similar UV absorption[1-a)] as that of cacalol I, and its IR spectrum indicated the presence of an ester group; IR($CHCl_3$): 3550 (OH), 1750, 1230 (ester), 1630 (C=C), 1595, 1575 cm^{-1}. Hydrolysis of VI-a gave hydroxycacalol (VI-b), $C_{15}H_{18}O_3$, mp 180.0-181.0°. colorless needles, $[\alpha]_D$ +31.5° (c, 0.995, MeOH) and an acid as expected. The acid was identified as senecioic acid by the preparation of the p-phenylphenacyl ester, mp 143.0-144.0°. The presence and the location of the $-OCH_2-$ group at C-3 in VI-a, VI-b, and its diacetate (VI-c), a colorless oil, were drawn from the comparison of the chemical shifts with those of the protons at C-2, C-3, and C-4 in the related furanonaphthalene components in their NMR spectra. The substituent effects in VI-a,b,c could be expected for the electronegative group on the C-3 carbon atom adjacent to the 2-CH[9)] as the following assignments; δ^{CDCl_3}:1.15 (d, J=7.0 Hz, 5-Me), 1.80 (m, 6- and 7-CH_2), 1.87 (s, a vinyl Me in the ester), 1.99 (d, J=2.0 Hz, a vinyl Me in the ester), 2.46 (s, 4-Me), 2.80 (m, 8-CH_2), 3.15 (m, 5-CH), 5.11 (s, 9-OH), 5.34 (s, 3-CH_2O-), 6.04 (m, a vinyl proton in the ester), 7.50 (s, 2-CH) in VI-a; δ^{DMSO-d_6}: 2.43 (s, 4-Me), 3.85 (2xOH), 4.67 (s, 3-CH_2O-), 7.14 (br s, 2-CH) in VI-b, and δ^{CDCl_3}: 2.05 (3-OAc), 2.36 (9-OAc), 2.49 (s, 4-Me), 5.25 (s, 3-CH_2O-), 7.52 (s, 2-CH) in VI-c. Thus the senecioate can be represented as in the formula VI-a.

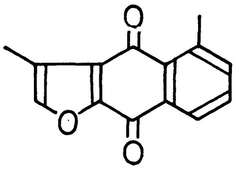
Peroxycacalonol (X-a), $C_{15}H_{14}O_4$, mp 204.0-205.0° (dec), pale yellow plates, showed the similar UV absorption as that of cacalonol IX,[7)] i. e., λ_{max}^{MeOH} 231sh (4100), 255 (6000), 312 nm (ε, 9500). The following spectral data also suggested the structure X-a for this peroxide-- MS: m/e 258 (M^+), 242 (M^+-16), 227 (M^+-31), 226 (M^+-32), 225 (M^+-OOH, base peak); IR(KBr): 3150 (H-bonded OH), 1670 (C=O), 1620 cm^{-1} (C=C); $\delta^{acetone-d_6}$: 1.81 (s, 4-Me), 2.28 (d, J=1.2 Hz, 3-Me), 2.75 (s, 5-Me), 7.46 (m, 6- and 7-CH), 7.72 (q, J=1.2 Hz, 2-CH), 8.05 (m, 8-CH). After deuteration of X-a with MeOD-D_2O, it showed MS: m/e 259 (M^+), 243 (M^+-16), 228 (M^+-31), 227 (M^+-32), 226 (M^+-33), 225 (M^+-OOD, base peak). Furthermore, X-a gave the acetate (X-b), mp 140.5-141.5° by treatment with Ac_2O-pyridine at room temp. Treatment of X-a with $(C_6H_5)_3P$ in methanol yielded cacalonol IX, mp 198.0-199.0°. In addition, heating of X-a up to 270° (bath temp) gave maturinone IV, mp 156.0-158.0°, which was identical with the natural specimen.



I R=H
II R=Ac



III



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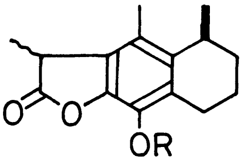
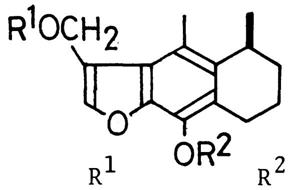
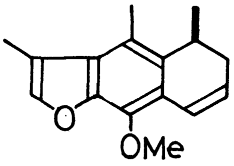


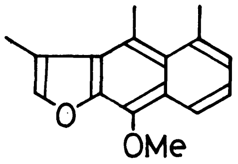
V-a R=H
V-b R=Ac



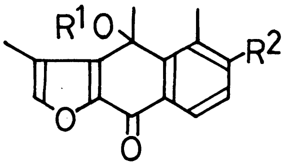
	R^1	R^2
VI-a	Me_2C=CHCO	H
VI-b	H	H
VI-c	Ac	Ac



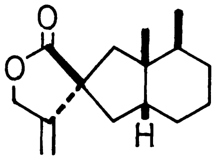
VII



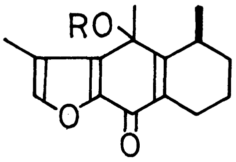
VIII



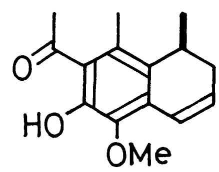
	R^1	R^2
IX	H	H
X-a	OH	H
X-b	OAc	H
XI	H	OMe



XII



XIII-a R=H
XIII-b R=Ac



XIV

6-Methoxycacalonol (XI), $C_{16}H_{16}O_4$, mp 94.0-95.0°, yellow prisms, showed UV: λ_{max}^{MeOH} 226 (20300), 261 (14900), 367 nm (ε, 15400); IR($CHCl_3$): 3440 (OH), 1650 (C=O), 1610 (C=C), 1580 cm^{-1} (furan); δ^{CDCl_3}: 1.57 (s, 4-Me), 2.39 (d, J=1.5 Hz, 3-Me), 2.90 (s, 5-Me), 3.73 (s, 4-OH), 4.17 (s, 6-OMe), 6.13 (d, J=10 Hz, 7-CH), 7.36 (q, J=1.5 Hz, 2-CH), 8.03 (d, J=10 Hz, 8-CH). The ortho-coupling ($J_{7,8}$=10 Hz) and their chemical shifts suggest the position of the MeO group. Thus the above data lead to the formula XI for this compound.

The compounds IX, X-a, and XI having no rotation might be artefacts. In order to find their intermediates, we have examined the following oxygenation methods.

Autoxidation of cacalol I gave an oily ketol (XIII-a), IR(CCl_4): 3370 (OH), 1650 cm^{-1} (C=O); MS: m/e 246 (M^+), which was transformed into the acetate, $C_{17}H_{20}O_4$, mp 164.0-165.5°, colorless needles. This product can be represented by the formula (XIII-b) from the following data; IR($CHCl_3$): 1735, 1240 (OAc), 1650, 1610 (α,β-unsaturated ketone), 1530 cm^{-1} (furan); δ^{CCl_4}: 1.26 (d, J=7.0 Hz, 5-Me), 1.56 (m, 6- and 7-CH_2), 1.65 (s, 4-Me), 2.03 (s, OAc), 2.07 (d, J=1.2 Hz, 3-Me), 2.43 (m, 5-CH and 8-CH_2), 7.25 (q, J=1.2 Hz, 2-CH).

Sensitized photooxygenation of O-methyldehydrocacalol VII with Rose Bengal in methanol afforded a ketol (XIV), $C_{15}H_{18}O_3$, mp 162.0-163.5°, colorless prisms, $[\alpha]_D$ +80.5° (c, 1.0, $CHCl_3$), which should be identical with the natural O-methyldehydronorcacalol[7)] by comparison of the both spectral data. Further investigation for the selective oxygenation of furan and benzenoid rings is in progress.

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