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THE SESQUITERPENES OF CACALIA SPECIES. II. THE STRUCTURE OF CACALAL AND THE INTERCONVERSIONS OF THE CONSTITUENTS

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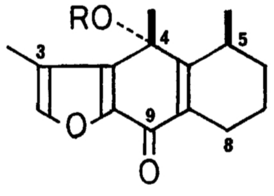
Two known sesquiterpenes, cacalone (I) and decompostin (II), and one new, named cacalal (III), have been isolated from Cacalia delfiniifolia Sieb. et Zucc. The structure of III and cacalolide (XIVa) have been established by selective oxidation of cacalol (IV). The interconversions of the constituents were also investigated.

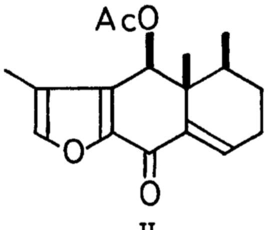
In connection with our investigation,$^{1)}$ we have isolated further three sesquiterpenes from Cacalia delfiniifolia Sieb. et Zucc. ("Momijigasa" in Japanese). These components were cacalone (I),$^{1,2,3)}$ decompostin (II)$^{4)}$ and a new substance named cacalal (III). Recently, the structure of cacalone$^{2)}$ was again revised to the formula I.$^{3)}$ The compound I was identical with a p-quinol, which was already prepared by us upon autoxidation of cacalol (IV) and characterized as the acetate (V).$^{1)}$ We have found that cacalone (I) can also be derived from cacalol (IV) in 21% yield by submitting IV to dye(Rose Bengal)-sensitized photooxygenation in methanol.$^{5)}$

Cacalal (III), $C_{15}H_{16}O_3$, mp 155-156°, $[\alpha]_D$ +136° (c, 0.92, $CHCl_3$), showed the following spectra; UV: λ_{max}^{MeOH} 219 (17900), 245 (34100), 316 nm (ε, 23200); IR($CHCl_3$): 3540, 3400-3000 (br), 1660, 1620, 1590, 1560, 1235, 1140, 1120 cm^{-1}; NMR($CDCl_3$): δ 10.60 (br s, CHO), 7.40 (q, J=1.5 Hz, 2-H), 5.47 (br s, OH), 4.0 (m, 5-H), 2.80 (m, 8-CH_2), 2.38 (d, J=1.5 Hz, 3-Me), 1.80 (m, 6- and 7-CH_2), 1.30 (d, J=7.0 Hz, 5-Me). The above data consist with the structure III, and this assignment was ascertained by the chemical correlation with cacalone (I). Thus, cacalal (III) was treated with $NaBH_4$ in dioxane followed by acetylation with Ac_2O-pyridine to afford the diacetate (VIII), a colorless oil, which was identical with the product obtained by refluxing a solution of cacalone (I) in Ac_2O for 36 hr.$^{6)}$ The structure of the diacetate (VIII) was characterized by the following spectral data; IR(CCl_4): 1770, 1735 (OAc) cm^{-1}; NMR(CCl_4): δ 7.19 (q, J=1.2 Hz, 2-H), 5.30 (d, J=2.0 Hz, 4-CH_2), 3.35 (m, 5-H), 2.67 (m, 8-CH_2), 2.29 (s, 9-OAc), 2.24 (d, J=1.2 Hz, 3-Me), 1.99 (s, 4-OAc), 1.78 (m, 6- and 7-CH_2), 1.20 (d, J=7.0 Hz, 5-Me).

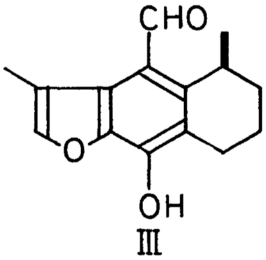
It has been reported[7)] that the methyl group of a substituted p-cresol is oxygenated to furnish exclusively the corresponding p-hydroxybenzaldehyde in an excellent yield by base-catalyzed autoxidation using a large excess of t-BuOK in DMF. In an attempt to directly correlate cacalal (III) with cacalol (IV), the latter was oxidized by this procedure to yield no aldehyde (III). Instead, a pair of α,β-epoxyketones (IXa and IXb) were obtained, each of which was separated by column chromatography (SiO_2; C_6H_6-AcOEt, 10:1). Both IXa, mp 178-179°, and IXb, a colorless oil, showed similar spectra to those of cacalone (I); IR($CHCl_3$): 3550, 3450 (OH), 1670 (C=O) cm^{-1} for IXa and 3560, 3460 (OH), 1680 (C=O) cm^{-1} for IXb; NMR($CDCl_3$): δ 7.34 (q, J=1.2 Hz, 2-H), 3.21 (s, 4-OH), 2.73 (m, 5-H), 2.15 (d, J=1.2 Hz, 3-Me), 1.64 (s, 4-Me), 1.28 (d, J=7.0 Hz, 5-Me) for IXa and 7.34 (q, J=1.2 Hz, 2-H), 2.71 (s, 4-OH), 2.62 (m, 5-H), 2.12 (d, J=1.2 Hz, 3-Me), 1.60 (s, 4-Me), 1.25 (d, J=7.0 Hz, 5-Me) for IXb. The structure and stereochemistry of the two epoxides were tentatively assigned to the formulas, IXa and IXb, from consideration of a possible mechanism[8)] for the base-catalyzed autoxidation of p-alkylated phenols, and their CD maxima[9)]



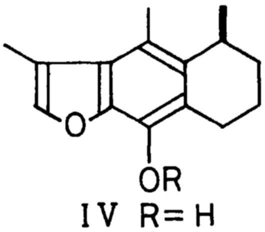
I R=H
V R=Ac



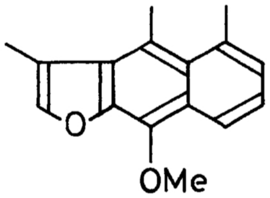
II



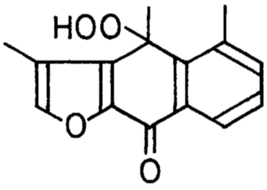
III



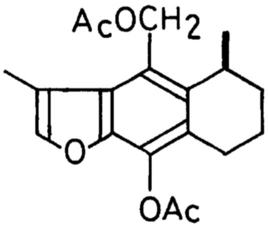
IV R=H
XV R=Ac



VI



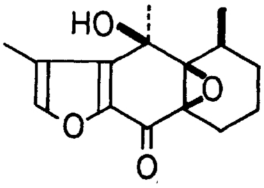
VII



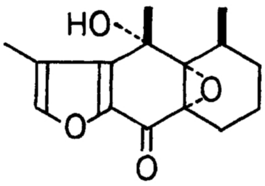
VIII

($[\theta]_{330}$ -2170 for IXa and $[\theta]_{336}$ +3050 for IXb). In this connection, it is worth mentioning that a similar base-catalyzed oxygenation of O-methylcacalodienol (VI), a p-methylanisole, gave exclusively a p-methoxybenzylalkohol (X), $C_{16}H_{16}O_3$, mp 125.5-126°. Its IR and NMR spectra support the assignment to the structure X as follows; 3600, 3440 (OH), 1635, 1600 (C=C) cm^{-1}; δ 5.25 (d, J=1.2 Hz, 4-CH_2O), 4.26 (9-OMe), 1.68 (br s, 4-OH). The acetate (XI) also provides a further support for the structure X; IR($CHCl_3$): 1730 (OAc) cm^{-1}; NMR($CDCl_3$): δ 5.27 (s, 4-CH_2O), 2.13 (4-OAc). The subsequent allylic oxidation of X with DDQ afforded quantitatively the corresponding aldehyde (XII), $C_{16}H_{14}O_3$, mp 96.5-97.5°, which was identical in all respects with the natural maturinin.10) In addition, the compound X gave easily a dimeric product (XIII), $C_{32}H_{30}O_5$, mp 177-178°, through dehydration upon heating or by dissolving in an acidic medium. It exhibits the absence of OH band in the IR spectrum, and shows UV maxima and NMR signals closely similar to those of X. The structure XIII was finally drawn from the results of the elemental analysis and MS: m/e 254, M^+-240, $(RCH_2)_2O$ - RCH_3 = RCHO.

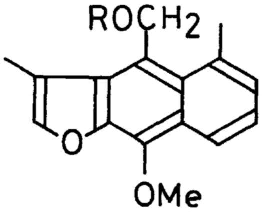
Previously the structure of cacalolide (XIVa) was reported1) except for the C-3 orientation. Now its stereochemistry can be concluded to be as in the formula XIVa on the basis of the following evidence. Oxidation of cacalol acetate (XV) with m-chloroperbenzoic acid gave a crystalline product, which was observed as a mixture of two crystalline forms and separated mechanically to furnish a pair of stereoisomers, (XVIa), mp 193-194°, $[\alpha]_D$ +9.6° (c, 1.02, $CHCl_3$) and (XVIb), mp 110-111°, $[\alpha]_D$ -38.4° (c, 0.995, $CHCl_3$). XVIa was identical with the acetate, mp 194-195°, derived from natural cacalolide (XIVa) by mixed-melting point determination. Both isomers, (XVIa and XVIb), have the same molecular formula, $C_{17}H_{20}O_4$, and showed identical properties (TLC, UV, IR and NMR spectra) except for mps and specific rotations; UV: λ_{max}^{MeOH} 215.5 (16200), 274 (1300), 282 nm (ε, 1300); IR($CHCl_3$): 1800 (γ-lactone), 1760, 1190 (OAc), 1630 (C=C) cm^{-1}; NMR($CDCl_3$): δ 3.70 (q, J=7.5 Hz, 3-H), ca. 3.0 (m, 5-H), ca. 2.6 (m, 8-CH_2), 2.30 (s, 9-OAc), 2.23 (s, 4-Me), 1.76 (m, 6- and 7-CH_2), 1.57 (d, J=7.5 Hz, 3-Me), 1.13 (d, J=7.0 Hz, 5-Me). By a comparison of the specific rotations between the epimeric acetates (XVIa,b) and α-phenylpropionic acids with the known absolute configurations,11) cacalolide (XIVa) and epicacalolide (XIVb) were assigned to the (3S)- and (3R)-configurations, respectively.



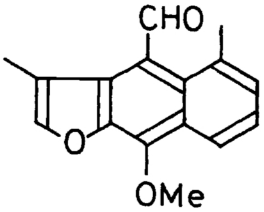
IXa



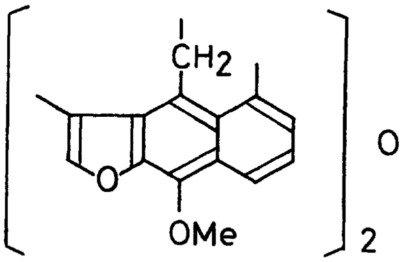
IXb



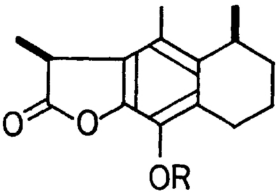
X R = H
XI R = Ac



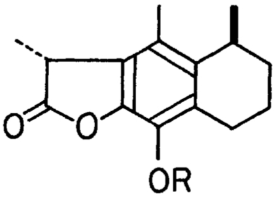
XII



XIII



XIVa R = H
XVIa R = Ac



XIVb R = H
XVIb R = Ac

References and Notes

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5) A similar treatment of O-methylcacalodienol (VI)[1] afforded peroxycacalonol (VII),[1] mp 198° (dec), in a moderate yield (47%).

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