

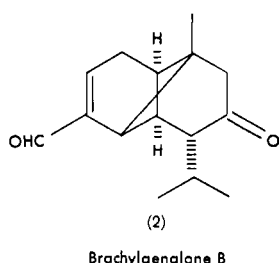
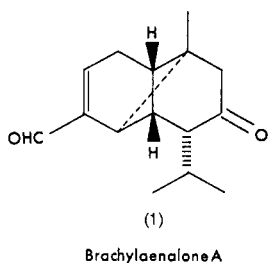
## Structure of Brachyl Oxide

Erich Klein\* and Wolfgang Schmidt

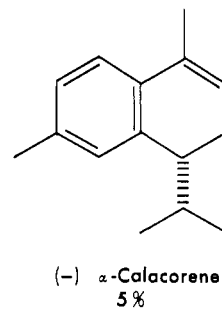
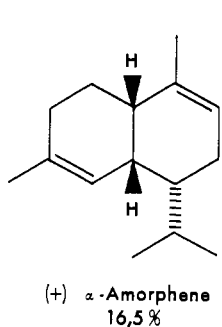
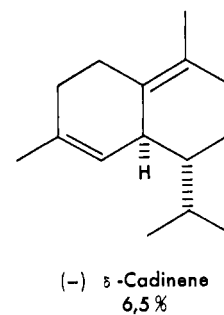
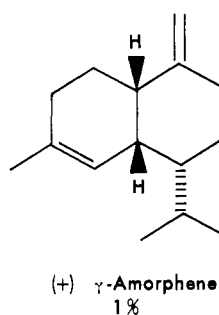
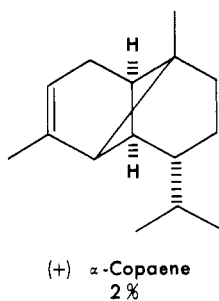
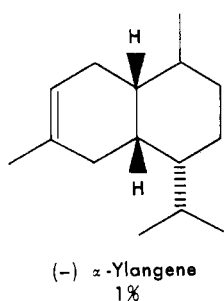
The volatile constituents of the wood of *Brachylaena hutchinsii* Hutch. have been investigated. The main constituents are  $\alpha$ -amorphene and brachyl oxide, along with a number of other sesquiterpenes.

The structure of brachyl oxide has been elucidated. All these sesquiterpenoids belong to the enantiomeric series.

**M**uhuhu is a large tree belonging to the family of Compositae under the name *Brachylaena hutchinsii* Hutch. Its wood was imported for many years from East Africa to Europe and the United States. This hard and heavy yellow timber was exclusively used for flooring blocks. Only recently has the steam volatile oil of this wood become available commercially. The first elementary analysis of this oil was carried out by Naves and Ardizio (1955) and by Van den Dool (1955). Fifteen years later Brooks and Campbell (1969) isolated two keto aldehydes from this oil and suggested structures (1) and (2) for brachylaenalone A and B.



The preliminary investigation revealed that this oil contained only sesquiterpenoids. Therefore, a detailed investigation was undertaken to determine how these sesquiterpenes are interrelated. By fractional distillation, column chromatography using silver nitrate-impregnated silica gel and preparative gas-liquid chromatography, it was possible to isolate and identify almost all the sesquiterpenes.



Besides the small quantities of  $\alpha$ -ylangene,  $\alpha$ -copaene, and  $\gamma$ -amorphene, this oil contains 16.5% of  $\alpha$ -amorphene, which is identical with zizanene, until now an unidentified sesquiterpene of vetiver oil (Klein and Schmidt, 1970). In addition,  $\alpha$ -calacorene,  $\delta$ -cadinene, calamenene, and cadaline (which normally appear in all the oils which are distilled at high temperatures) were also isolated. The most interesting feature was that all of these sesquiterpenes belong to antipodal series. The fact that until now enantiomeric cadinenes were found only in some kinds of vetiver oil is highly interesting from the biogenesis point of view. From the oxygenated products two aldehydes, ylangenal and copaenal, and two primary alcohols, ylangenol and copaenol, were also characterized.

While fractionating the sesquiterpene hydrocarbons by simple chromatography over silica gel and using petroleum ether, a fraction, found to be an oxide, appeared immediately after the hydrocarbons in large quantities (10% of the total oil). The structure of this oxide is presented here.

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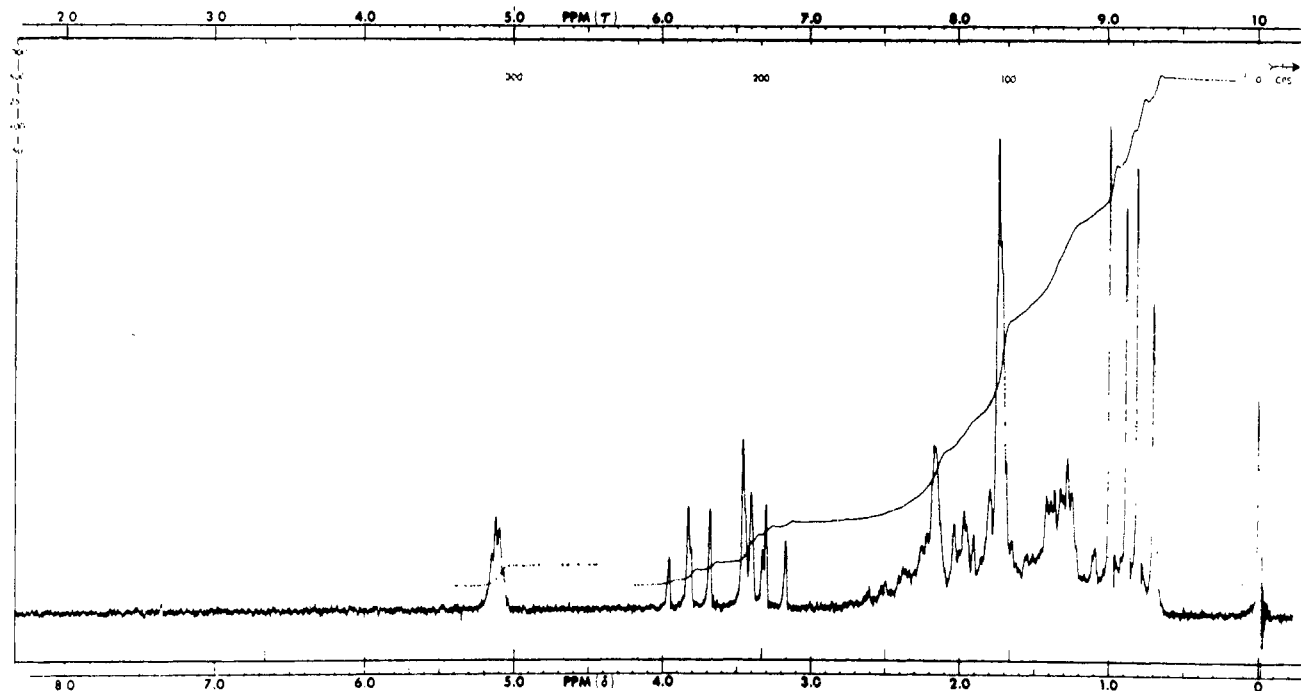


Figure 1. Nmr spectrum of brachyl oxide

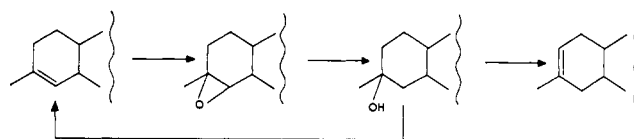
The crude oxide was repeatedly chromatographed over silica gel using 1–10% ether in petroleum ether. The oxide was isolated as a colorless liquid ( $D_{20}^{20}$ : 0.9983;  $n_{20}^{20}$ : 1.4992;  $[\alpha]_D^{20}$ : +28° C) with a faint odor. A molecular ion at 220 in the mass spectrum indicated only C, H, and O. From this the elemental formula,  $C_{15}H_{24}O$ , was deduced.

The nmr spectrum (Figure 1) showed signals for a vinyl proton (1 H, 5.12 multiplet) and three oxide protons (2 H, 3.31, and 3.82; AB part of an  $AB_X$  system,  $J_{AB} = 8.5$ ; 1 H, 3.42 doublet,  $J = 4$ ), the protons of the methyl group on a double bond (3 H, 1.74 singlet) as well as two doublets for two secondary methyl groups (3 H, 0.74 doublet,  $J = 6$ ; 3 H, 0.94 doublet,  $J = 6$ ).

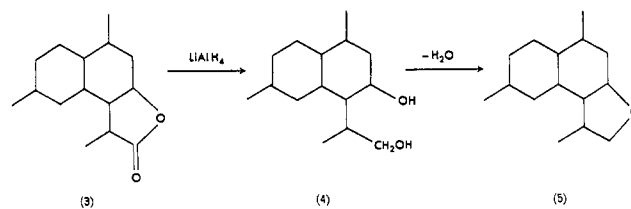
The ir spectrum supported the nmr interpretation and shows absorptions at 3029, 1658, and 824  $cm^{-1}$  for a trisubstituted double bond and three strong bands in the region between 1000–1050  $cm^{-1}$  for the oxide linkage.

Hydrogenation over platinum oxide in acetic acid resulted in the uptake of calculated amount of hydrogen for one double bond. The oxidation with peracetic acid furnished a crystalline monoepoxide (mp 70–71° C). This monoepoxide could not be reduced with  $LiAlH_4$  in ether or in tetrahydrofuran to the corresponding alcohol, but treatment with lithium in ethylamine (Hallsworth and Henbest, 1957) resulted in the opening of the epoxide ring to a tertiary alcohol.

From the above results and the empirical formula of the starting oxide, it was necessary to deal with a compound containing three rings, one with an oxygen atom as a ring member and a trisubstituted double bond. If the isoprene rule is applied to the above findings for the oxide, only two skeleton structures, cadinene and guajane, can be arrived at. A distinction between these classes in favor of the cadinene skeleton can be made by the dehydration of tertiary alcohol of the monoepoxide with potassium bisulfite. During this process two substances appeared which were separated by preparative gas chromatography. One was original oxide, the brachyl oxide; the other was an isomeric oxide but with a trisubstituted double bond.

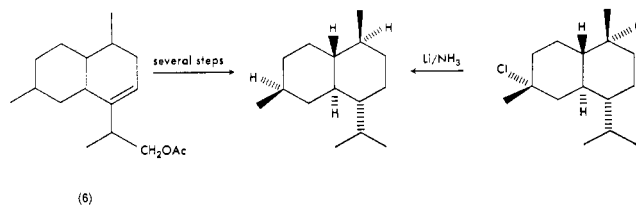


If brachyl oxide has the guajane skeleton, one of the two reaction products must possess a tetrasubstituted double bond. In order to examine the position at which the oxygen ring is attached, the hydrogenated brachyl oxide was oxidized with chromium trioxide in acetic acid (Woodward and Eastman, 1950). The main product was a crystalline five-membered ring lactone (3) (mp 137–38° C; ir spectrum 1762  $cm^{-1}$ ) with a methyl group in  $\alpha$  position to the carbonyl group. Therefore an isopropyl group is involved in the oxide formation of the brachyl oxide.

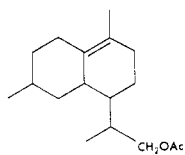


To study the stereochemistry of the brachyl oxide, the saturated lactone was reduced with  $LiAlH_4$  to the primary-secondary diol (4) (mp 73–74.5° C). Tosylation of the diol and removal of the tosyl groups with  $LiAlH_4$  resulted in the formation of dihydrobrachyl oxide (5). Another method was undertaken which included treating the dihydrobrachyl oxide (5) with  $BF_3$  in acetic anhydride at  $-10^\circ C$  (Baggaley *et al.*, 1968). Under these conditions the tetrahydrofuran ring opened completely with the formation of two acetates (6 and 7) which were separated by preparative gas-liquid chromatography.

The nmr spectrum of the acetate (6) showed a trisubstituted double bond, while that of the acetate (7) showed a methyl group on a tetrasubstituted double bond. Hence structure 7



(6)

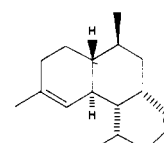


(7)

indicates that this compound could have been derived from  $\Delta^8$ -dihydro cadinene with a cis double bond since migration of such an unsaturated system to the  $\delta$  position is well known. Hydrogenation of the acetate **6**, saponification of the saturated acetate, and tosylation and reduction of the tosylate with  $\text{LiAlH}_4$  gave a saturated hydrocarbon whose ir spectrum was superimposable with the ir spectrum of the authentic cadinane which was obtained by the reduction of cadinene dihydrochloride with lithium in ammonia (Pliva *et al.*, 1960). The cadinane formed by the reduction of cadinene dihydrochloride with lithium in ammonia was uniform and a single product. The rotation of the cadinane from the acetate **6** was in opposition to the rotation given in the literature. Therefore, our brachyl oxide must belong to the antipodal cadinane series.

With the above data and the small value of the coupling constant ( $J = 4$  cps) for the single oxide proton, a cis juncture

of the tetrahydrofuran ring to the rest of the system must be assumed, and brachyl oxide has the following configuration.



Brachyl oxide

The brachyl oxide is the first tetrahydrofuran derivative of the cadinane series and is worth studying from the biogenesis point of view. At this time it is known that antipodal sesquiterpenes are present only in Muhuhu oil and in the oil of Khus variety of vetiver. In both cases a very similar or the same enzyme system seems to be present which also brings about oxidation of the skeleton's carbon atoms which are normally extremely stable against chemical attack.

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