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ALLO-CEDROL: A NEW TRICARBOCYCLIC SESQUITERPENE ALCOHOL*

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Key Word Index—*Juniperus rigida*; Cupressaceae; sesquiterpenes; *allo*-cedrol; degradation to prezizaene enantiomer.

Abstract—The structure of a new tricarbocyclic sesquiterpene alcohol, named *allo*-cedrol, was determined by relation with β-acoradiene. The enantiomer of prezizaene and several compounds were obtained from the *p*-bromobenzenesulfonate of *allo*-cedrol.

INTRODUCTION

IN THE preceding papers,[1–3] we have reported on the stereostructures of α- and β-acoradiene (I) and (II), γ- and δ-acoradiene† (V) and (VI), α- and β-acorenol (III) and (IV), all of which were isolated from the wood of *Juniperus rigida* Sieb. et Zucc., and on the transformation of α-acoradiene (I) to (−)-α-cedrene. Simultaneously we have proposed the probable biogenetic pathway from β-acoradiene (II) to the new tricarbocyclic sesquiterpenes.

In this paper we describe the stereostructure of a new tricarbocyclic sesquiterpene alcohol, named *allo*-cedrol,‡ and its relation with β-acoradiene (II), and further its degradation to the enantiomer of prezizaene (XXVIII), which has been isolated from vetiver oil.[4]

RESULTS AND DISCUSSION

During the course of analysis of sesquiterpenic constituents of the wood of *Juniperus rigida*, we have isolated a new sesquiterpenic alcohol. Physical and spectral properties of this compound were identical with those of the alcohol isolated from *Biota orientalis* by the authors.[5,6] This alcohol, $C_{15}H_{26}O$, $[\alpha]_D$ +68°, m.p. 81·5°, had three tertiary methyl groups, a secondary methyl group in its NMR spectrum. From its IR spectrum (3300, 1040 cm^{-1}) the presence of a secondary hydroxyl group was suggested, that was confirmed by the signals of a proton (δ 3·87, octet, J 9, 6, 2 Hz) corresponding to the proton on the carbon atom bearing the alcoholic hydroxyl group. Since it could not be hydrogenated over PtO_2 in AcOH, showed no signals in the appropriate region to the olefinic protons in its NMR spectrum and gave a negative tetranitromethane test, it was determined to be a saturated tricarbocyclic sesquiterpene of a secondary alcohol.

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* Part XXX in the series "Terpenoids". For Part XXIX see *Mokuzai Gakkaishi* **17**, 306 (1971).

† γ-Acoradiene and δ-acoradiene are identical with α- and β-araskene reported by Andersen. [ANDERSEN, N. H. and SYRDAL, D. D. (1970) *Tetrahedron Letters* 2277].

‡ The name "*allo*-cedrane" was proposed in the previous report.[3]

[1] TOMITA, B., HIROSE, Y. and NAKATSUKA, T. (1969) *Mokuzai Gakkaishi* **15**, 48.

[2] TOMITA, B. and HIROSE, Y. (1970) *Tetrahedron Letters* 143.

[3] TOMITA, B., ISONO, T. and HIROSE, Y. (1970) *Tetrahedron Letters* 1371.

[4] ANDERSEN, N. H. and FALCONE, M. S. (1971) *Chem. & Ind.* No. 2, 61.

[5] TOMITA, B. and HIROSE, Y. (1969) *Mokuzai Gakkaishi* **15**, 377.

[6] TOMITA, B., HIROSE, Y. and NAKATSUKA, T. (1968) *Tetrahedron Letters* 843.

On CrO_3–pyridine oxidation it afforded a ketone which was transformed to a saturated hydrocarbon by Wolff–Kishner reduction. Comparison of its IR spectrum with those of known synthesized sesquiterpenic skeletons indicated that this alcohol has a new tricarbocyclic skeleton. This alcohol was named *allo*-cedrol, related to acoradiene and cedrol.

TABLE 1. THE PRODUCTS FROM β-ACORADIENE AND *p*-BROMOBENZENESULFONATE OF *allo*-CEDROL AND THEIR PROPERTIES

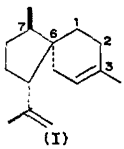
Product	β-Acoradiene HCOOH, 90°	*p*-Bromobenzenesulfonate of *allo*-credol Silica gel	HCOOH, 70°	Retention time*	MS M^+	NMR (δ) in CCl_4
A		18%	5%	0·78	204	*t*-Me 0·88, 1·10 *s*-Me 0·92 *ally*-Me 1·6 olefin 5 11(1H, *m*)
α-Cedrene	10%			1·00		
B	Trace	5	15	*ca.* 1	204	*t*-Me 0·76, 0·84, 1·03 *s*-Me 0·97 5·74, 6·19 (each 1H, *d*, *J* 8 Hz)
C	Trace			*ca.* 1	204	*t*-Me 1·02, 1·08 *s*-Me 0·89 *ally*-Me 1·64 olefin 5·25 (1H, *m*)
D	15	5	15	*ca.* 1	204	*t*-Me 0 965, 0·99, 1·43 *s*-Me 0·83
E	4	1	15	1·11	204	*t*-Me 0·95, 0·98, 1·40 *s*-Me 0·90
F	2	7	10	1·24		
G		15	5	1·37	204	*t*-Me 1·05, 1·08 *s*-Me 0·87 4·59 (2H, *m*)
H	20		3		†222	†*t*-Me 0·76, 0·08, 0·92 *s*-Me 0·83 3·87 (1H, octet)
J		20			222	*t*-Me 0·93 (6H), 1·15 *s*-Me 0·95
K	30				†222	† *t*-Me 0·80, 0·85 *s*-Me 0 78, 0·94
Others	Trace	29	27			

* Ratio of relative retention time is based on α-cedrene. Column: polyethylene glycol 20 M, temp. 125°, carrier gas: H_2, flow rate 10 ml/min.

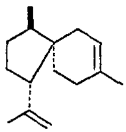
† The properties of the alcohol obtained by hydrolysis of formates are shown

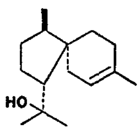
Heating of β-acoradiene (II) with formic acid at 90° gave several products analyzed by GLC as shown in Table 1. One of those products (H) was thought to be a formate of a secondary alcohol. This was hydrolyzed with 10% alcoholic KOH to afford *allo*-cedrol (by IR, NMR, m.p. and specific rotation).

The *p*-bromobenzenesulfonate of allo-cedrol was treated with formic acid at 70° or with silica gel; many products were detected by GLC (Table 1). Since the common products, B, D, E, F and H, were obtained from both β-acoradiene and brosylate of *allo*-cedrol, and since the formate of *allo*-cedrol was formed from β-acoradiene, we wish to propose the structure (XII) for *allo*-cedrol. The tertiary cation (VIII) from α-acoradiene (I) has been related to (—)-α-cedrene.[2] On the other hand as the cyclization of the tertiary cation (IX) from β-acoradiene to C-2 is sterically hindered, the cyclization to C-3 seems to be favorable and gives the cation (XI), whose hydroxylation product is considered to be *allo*-cedrol.

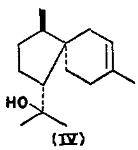


(I)

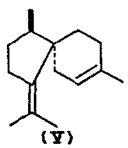

(II)

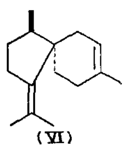


(III)



(IV)


(V)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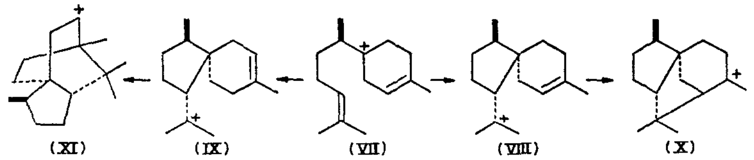
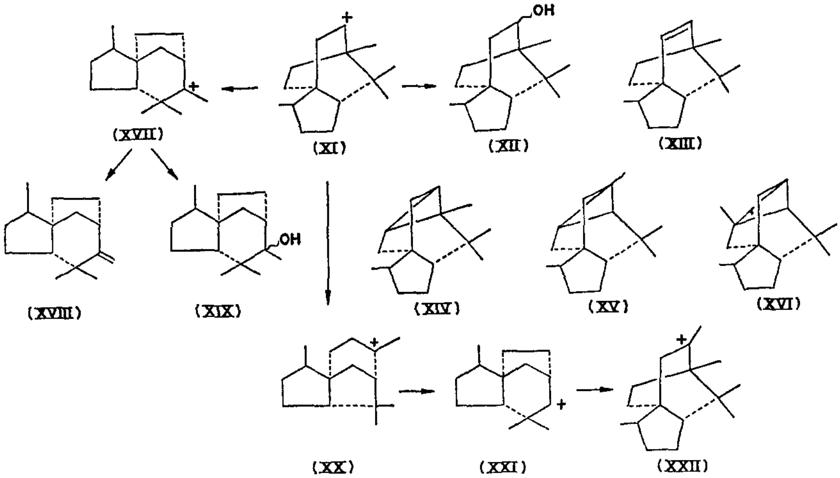


In the NMR spectrum of *allo*-cedrol, an octet signal due to the proton on the carbon atom bearing the hydroxyl group was significant. This proton was coupled with two adjacent protons (J 9 and 6 Hz), and further weakly coupled (J 2 Hz). This long-range coupling was explained in the stereostructure (XII′), in which the carbon atom bearing the hydroxyl group had a S-configuration and the protons H_A and H_D existed in a coplanar W-configuration from observation of a Dreiding Model. The dihedral angle of H_A and H_B was *ca.* 145°, and that of H_A and H_C was *ca.* 25°. The calculated coupling constants from these values based on reported equations were consistent with those of the experimental data.



SCHEME 1

The configuration at the carbon atom in question was further confirmed by applying the benzoate rule.[7] p-Nitrobenzoate was prepared from *allo*-cedrol and its $\Delta[M]_D$ value

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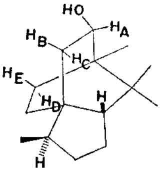
[7] BREWSTER, J. H. (1961) *Tetrahedron* 13, 106.

($=[M]_D^{p\text{-nitrobenzoate}}-[M]_D^{allo\text{-cedrol}}$) was measured. From this value (+96°) the carbon atom was concluded to have a *S*-configuration. Thus the stereostructure (XII′) was proposed for *allo*-cedrol.



(XII′)

Among the solvolytic reaction products of brosylate of *allo*-cedrol, the hydrocarbon (G), $C_{15}H_{24}$, $[\alpha]_D$ −40°, was exclusively obtained from the alcohol (J), $C_{15}H_{26}O$, $[\alpha]_D$ −46·2°, by dehydration with pyridine-modified alumina[8] at 200°. The alcohol had a secondary methyl group and three tertiary methyl groups, one of which was attached to the carbon on a tertiary hydroxyl group. In the NMR spectrum of the hydrocarbon (G) the signal of one tertiary methyl group in (J) disappeared and the signals corresponding to the protons of a terminal methylene group appeared.

We considered that these two products were formed from the cation (XVII) which was derived from the cation (XI). Thus the hydrocarbon (G) and the alcohol (J) were supposed to be represented by (XVIII) and (XIX) respectively. The structure (XVIII) is the enantiomer of prezizaene (XXVIII) which has been recently isolated from vetiver oil and related to zizaene.[4] The IR and NMR spectra of our hydrocarbon were in good agreement with those of prezizaene from vetiver oil.* Prezizaene has the specific rotation of $[\alpha]_D$ +55°, the hydrocarbon has $[\alpha]_D$ −40°. Therefore we concluded that the hydrocarbon (G) is the enantiomer of prezizaene.

Though the precise work on each product was not completed, we could easily achieve the structural assignment of the product (B). Since the NMR spectrum of this hydrocarbon displayed the presences of two olefinic protons coupled with each other and three tertiary methyl groups and a secondary methyl group, the structure (XIII) was proposed. The product (B) seemed to be formed from the cation (XI) by deprotonation.

Both the products (D) and (E) were suggested to be tetracyclic saturated hydrocarbons, because their NMR spectra showed no signals owing to the olefinic protons and methyl groups on a double bond, and because the presence of cyclopropane ring was considered from the chemical shifts of one of tertiary methyl groups (δ 1·43 of IV, 1·40 of V). Moreover their saturated nature was supported by the TLC of total products on silica gel impregnated with silver nitrate which showed these two to be the most nonpolar. The IR spectrum of (D) was very similar to that of (E). The probable structures (XIV, XV, XVI), which seemed to be formed from the cation (XI) by deprotonation and 1,3-cyclization or by the rearrangement of carbonium ion involving 1,2-shift of methyl group, were suggested for the hydrocarbon (D) and (E).

Two kinds of tertiary cation (VIII) and (IX) can be biogenetically derived from γ-bisabolene by protonation, and give the compounds of Δ^3 double bond (I, III, V) and those of Δ^2 double bond (II, IV, VI), respectively. The ion (VIII) has been considered as the

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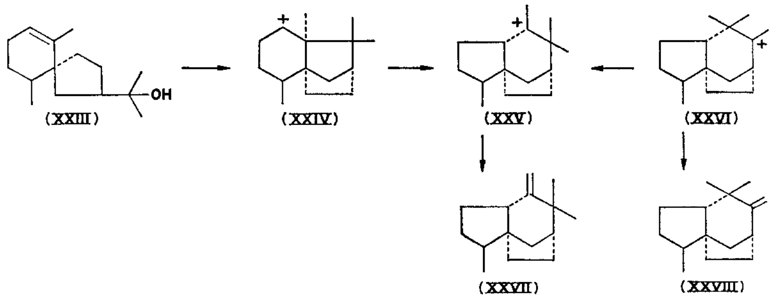
* Direct comparison was made by the kindness of Prof. Andersen.

[8] von Rudloff, E. (1961) *Can. J. Chem.* **38,** 1860.

precursor of cedrane-typed sesquiterpenes.[9] Recently Corey *et al.*[10] and Crandall and Lawton[11] have succeeded in synthesis of *dl*-α-cedrene from the synthetic acorane-typed alcohol by acid treatment. The authors have also obtained (—)-α-cedrene from α-acoradiene (I).[2] Though it has been reported that the cation corresponding to (XI) can be derived by Wagner–Meerwein rearrangement from the cedrane cation (X),[12] α-cedrene and cedrol have shown no skeletal rearrangement by acid treatment.[3]

On the other hand a new tricarbocyclic skeleton involving bicyclic [2,2,2] octane system (XI) has been obtained from β-acoradiene by acid treatment.



SCHEME 2

The Wagner–Meerwein rearrangement of the cation (XI) would produce the two kinds of cations (XVII) and (XX). The former gives the enantiomer of prezizaene. The formation of zizaene (XXVII) in the plant has been postulated as Scheme 2.[13] In this case the cyclized cation (XXIV) from hinesol (XXIII) gives the further rearranged cation (XXV) which leads to zizaene (XXVII). Andersen and Falcone have isolated prezizaene (XXVIII) from vetiver oil and related it to zizaene by their acid treatment.[4]

It has been reported that the gross structure of zizaene can be biogenetically related to an intermediate in cedrene genesis.[14] It is relevant that both β-acoradiene and the related allo-cedrol have been found in the wood of *Juniperus rigida* and that the enantiomer of prezizaene has been derived from the latter. We propose that the cation (XXI) and further rearranged (XXII) are formed from the probable cation (XX), and anticipate the occurrence of their hydroxylated and deprotonated products in nature.

EXPERIMENTAL

Isolation of allo-*cedrol.* The milled wood (air dried, 23 kg) of the wood of *Juniperus rigida* from Yamanashi district was extracted with MeOH. The extract (1·7 kg) was treated with *n*-hexane and its soluble portion (1·1 kg) was shaken with 5% NaOH to remove an acidic fraction (250 g). The neutral fraction (850 g) was distilled *in vacuo.* A part of the fraction of b.p. 115–130°/5 mmHg was chromatographed on alumina (2 kg) using *n*-hexane and EtOAc solvent system. The eluate (*ca.* 1 g) after the fraction containing cedrol consisted of five compounds by GLC analysis (polyethylene glycol 20 M column, H_2 carrier gas). Each component was isolated by preparative GLC. One of these (retention time ratio to cedrol, 1·73 at 170°, carrier gas H_2, flow rate 20 ml/min) was identified as the unknown alcohol from *Biota orientalis* by comparison of IR and NMR spectra. This alcohol crystallized from *n*-hexane had the following properties: m.p. 81·5°, $[\alpha]_D + 68°$, $[M]_D + 151°$, MS. *m/e* 222 (M^+), 177, 149 (base peak), ν^{KBr} 3300, 1040, 1008 cm^{-1}, δ^{CCl_4} 0·76, 0·88, 0·92

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[9] RUZICKA, L. (1953) *Experimentia* **9,** 357.

[10] COREY, E. J., GIROTRA, N. N. and MATHEW, C. T. (1969) *J. Am. Chem. Soc.* **91,** 1557.

[11] CRANDALL, T. G. and LAWTON, R. G. (1969) *J. Am. Chem. Soc.* **91,** 2127.

[12] PARKER, W., ROBERTS, J. S. and RAMAGE, R. (1967) *Quart. Rev.* **21,** 331.

[13] MACSWEENEY, D. F. RAMAGE, R. and SCATTER, A. (1970) *Tetrahedron Letters* 557.

[14] KIDO, F., UDA, H. and YOSHIKOSHI, A. (1967) *Tetrahedron Letters* 2815.

(each 3H, *s*), 0·83 (3H, *d*, *J* 6 Hz), 3·87 (1H, octet, *J* 9, 6, 2 Hz), (*Anal.* Found: C, 80·79; H, 11·92. Calc. for $C_{15}H_{26}O$: C, 81·02; H, 11·79%). *p*-Nitrobenzoate was synthesized by the usual method: m.p. 137–139°, $[\alpha]_D + 66{\cdot}6°$, $[M]_D + 247°$ (*Anal.* Found: C, 70·92; H, 8·05; N, 3·79. Calc. for $C_{22}H_{29}O_4N$: C, 71·13; H, 7·87; N, 3·77%.)

p-Bromobenzenesulfonate of allo-cedrol. To *allo*-cedrol (1·3 g) dissolved in anh. pyridine (10 ml), recrystallized and dried *p*-bromobenzenesulfonyl chloride (2·0 g) was added gradually with cooling and stirring. After being left in the ice-box for 12 hr, the reaction mixture was poured on ice, and the separated crystalline solid (1·9 g) was filtered and dried. After two recrystallizations from *n*-hexane, it gave m.p. 66–68°. (*Anal.* Found: C, 56·85; H, 6·90. Calc. for $C_{21}H_{29}BrO_3S$: C, 57·14; H, 6·62%.)

Wolff-Kishner reduction. Allo-Cedrol (200 mg) was added to the complex of anh. pyridine (2 ml) and CrO_3 (200 mg). The reaction mixture was left overnight at room temp. The filtrate was poured into H_2O and extracted with Et_2O. The ethereal solution was washed with dil. HCl and H_2O. After being dried on Na_2SO_4, it was distilled to give an oily ketone. MS. *m/e* 220 (M^+), 177, 135 (base peak), 121, 109. ν^{nujol} 1720, 1415 cm^{-1}, δ^{CCl_4} 0·78, 0·86, 0 92 (each 3H, *s*), 0 85 (3H, *d*, *J* 6 Hz), 2·02 (2H, *s*). $[\alpha]_D + 43{\cdot}4°$, ORD: $[\phi]_{306.5} + 1840°$, $[\phi]_{272} - 850°$. The ketone (80 mg) was heated at 155–160° for 2 hr with diethylene glycol (2 ml) and 100% hydrazine hydrate (1 ml). The mixture was further heated at 200–210° for 2·5 hr. After cooling it was poured into H_2O and extracted with *n*-hexane (100 ml). This solution was directly chromatographed on alumina (20 g). The eluated was a pure hydrocarbon, M^+ 206, by GLC analysis (yield 20 mg).

Acid treatment of β-acoradiene. Pure *β*-acoradiene (1·2 g) in formic acid (20 ml) was heated at 90° for 5 hr. After cooling it was added to H_2O and extracted with Et_2O. The ethereal solution was neutralized with $NaHCO_3$ and washed and dried over Na_2SO_4 Evaporation gave *ca.* 900 mg of oil. This was analyzed by GLC as shown in Table 1. Each peak was isolated by preparative GLC to give a practically pure compound, except the first peak, and their spectral properties were measured. The mixture (20 mg) obtained from the first peak was chromatographed on silica gel (2 g) impregnated with $AgNO_3$ (200 mg) using *n*-hexane. The first eluate (10 mg) was (D), followed by *α*-cedrene (5 mg) The products D, E, F were hydrocarbons shown in Table 1, and H and K seemed to be liquid formates by their IR spectra (1720, 1180 cm^{-1}, strong). The product H (100 mg) prepared by GLC was treated with 10% alcoholic KOH (10 ml) at 80° for 30 min. After cooling, it was added to H_2O and extracted with Et_2O. Usual treatment of the solution gave crystals (80 mg), which were recrystallized from *n*-hexane: m.p. 81°, $[\alpha]_D + 66°$. IR and NMR spectra were completely identical with those of *allo*-cedrol. The product K was similarly treated to give a tertiary alcohol.

Treatment of p-bromobenzenesulfonate of allo-cedrol. (*a*) *With silica gel. p*-Bromobenzenesulfonate (1·1 g) was passed through a silica gel column (50 g) at room temp. using benzene (100 ml) and then benzene containing 5% EtOAc (200 ml). The eluates were pooled; they contained *ca.* 500 mg products which were analyzed by GLC. The five peaks corresponding to the hydrocarbons were isolated by preparative GLC and the products (A, E, F, G) were obtained, respectively. The second peak (20 mg) was chromatographed on silica gel (2 g) impregnated with $AgNO_3$ (200 mg). The first eluate (8 mg) with *n*-hexane contained the product D and the last one (8 mg) with Et_2O contained the product B. (*b*) *With formic acid.* To formic acid (10 ml), *p*-bromobenzenesulfonate (300 mg) was added with stirring and heating at 70°. After 5 min, the reaction mixture was poured into H_2O and extracted with Et_2O. The ethereal solution was washed with $NaHCO_3$ and H_2O, and evaporated to give 260 mg of oil. This was investigated by the same method mentioned above to be resulted in Table 1.

Dehydration of (J). The mixture of pyridine-modified alumina (30 mg) and J (30 mg) was heated at 200° for 10 min. After cooling, the reactant was applied to an alumina (1 g) column. The eluate of *n*-hexane (15 mg) was completely identified as the hydrocarbon G (IR spectra).

Acknowledgements—We are indebted to Professor N. H. Andersen for the IR and NMR spectra of zizaene and prezizaene.