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172. Hiroshi Hikino, Keitaro Aota, Yukio Maebayashi, and Tsunematsu Takemoto : Structure and Absolute Configuration of Cyperolone.*1

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A sesquiterpenic keto-alcohol, cyperolone, has been isolated from nutgrass (*Cyperus rotundus* (Cyperaceae)) and shown to have the stereostructure I (R=H) of a novel skeleton based on the following evidence. The spectral data showed the presence of a secondary hydroxyl, an acetyl, an isopropenyl, and a tertiary methyl group. Cyperolone gave the saturated dihydro-derivative (II; R=H). Oxidation of the ketols (I & II; R=H) afforded the cyclopentanones (III & IV), respectively. $LiAlH_4$ reduction of cyperolone formed the diol (VI; R=H) whose NMR spectrum indicated the acetyl bearing carbon in cyperolone to be quaternary. Alkali treatment of the dione (IV) gave the monoketone (VII) which was synthesized from 14-noreudesmanone (X). The β-configuration of the C-3 hydroxyl and the C-5 acetyl was deduced from application of the benzoate rule and from a positive Cotton curve of the ketol acetate (VIII; $R=COCH_3$), respectively. The *cis* relationship of the C-3 and C-5 substituents was confirmed by the presence of an intramolecular hydrogen bond in the diol (VI; R=H).

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In our earlier publications[1] on the constituents of nutgrass, *Cyperus rotundus* Linné (Cyperaceae), of Japanese origin, we reported the isolation and structural elucidation of the new sesquiterpenic ketone cyperotundone, a bitter principle, as well as the isolation of α-cyperone. Recently we have further isolated a new sesquiterpenic keto-alcohol as another bitter principle for which the name cyperolone is proposed. The present paper describes evidence for the structure and absolute configuration of cyperolone as represented by formula I (R=H) which has a novel skeleton.*3

Cyperolone analyzed for $C_{15}H_{24}O_2$ and has $[\alpha]_D+31.4°$. It is a colorless oil but with one mole of water crystallized to form colorless needles, m.p. 41~42°, $[\alpha]_D+27.6°$. The infrared and nuclear magnetic resonance (NMR) spectra show the presence of a secondary hydroxyl (3436 cm^{-1},5.70τ), an acetyl (1695 cm^{-1},7.93τ), a vinylidene (3086, 1642, 885 cm^{-1}, 5.32τ), a vinyl methyl (8.25τ), and a tertiary methyl group (9.06τ).

On hydrogenation over palladized charcoal in methanol, cyperolone gave dihydrocyperolone (II; R=H), whose infrared and NMR spectra no longer exhibited the bands due to the vinylidene and the vinyl methyl group, but new bands due to two secondary methyl groups (1381, 1366 cm^{-1}, 9.06τ). This can be explained as the disappearance of the isopropenyl and the formation of the isopropyl group during hydrogenation of cyperolone. Since no other points of unsaturation can be observed in the dihydro-derivative (II), the number of the double bonds in cyperolone is only one, present in the isopropenyl group and hence cyperolone is bicyclic.

The nuclear magnetic resonance (NMR) signal associated with a hydrogen on carbon attached to the hydroxyl group of cyperolone or dihydrocyperolone (II; R=H) appears as a broad peak which does not permit exact analysis of the splitting pattern but the cor-

*1 This paper is Part XII in the series on Sesquiterpenoids. Preceding paper, Part XI, H. Hikino, K. Aota, T. Takemoto : Tetrahedron, **23**, 2169 (1967).

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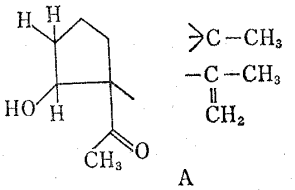
*3 Part of the material contained herein constituted a preliminary communication, H. Hikino, K. Aota, Y. Maebayashi, T. Takemoto : This Bulletin, **14**, 1439 (1966).

1) H. Hikino, K. Aota, T. Takemoto : *Ibid.*, **13**, 628 (1965); **14**, 890 (1966).

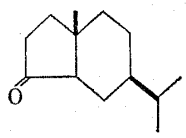
responding signal of cyperolone acetate (I; R=$COCH_3$) or its dihydro-derivative (II; R=$COCH_3$) occurs as a triplet indicating that adjacent carbons have at least two hydrogens. Further, oxidation of cyperolone or dihydrocyperolone (II; R=H) with chromic acid at room temperature afforded a dione (III or IV), respectively, the infrared spectrum of which shows new bands at 1406 and 1742 cm^{-1} or 1406 and 1748 cm^{-1}. The former band (1406 cm^{-1}) shows the presence of a methylene grouping next to the carbon bearing the hydroxyl group in cyperolone. Furthermore, since the latter band indicates the formation of a cyclopentanone moiety, the secondary hydroxyl group in cyperolone is, therefore, situated on a five-membered ring. On oxidation of cyperolone with chromic acid under more vigorous conditions oxidative cleavage of the vinylidene system also took place giving the trione (V) as well as the dione (III).

Cyperolone was reduced with lithium aluminum hydride to yield the diol (VI; R=H), which exhibited NMR signals attributed to the secondary methyl (8.47τ) and to the hydrogen (6.51τ) on carbon attached to the hydroxyl group formed by reduction of the acetyl; both signals are spin-coupled only with each other showing the carbon atom bearing the acetyl group in cyperolone is quaternary.

Alkali treatment of the dione (IV) gave a monoketone of molecular formula $C_{13}H_{22}O$, whose infrared and NMR spectra showed the retention of a cyclopentanone (1742 cm^{-1}), a methylene α to the carbonyl (1408 cm^{-1}), an isopropyl (1383, 1366 cm^{-1}, 9.06, 9.08τ), and a tertiary methyl group (8.75τ). This fact can be understood that on treatment with alkali the dione (IV), a β-diketone, was cleaved to give, with the loss of the acetyl group, the monoketone. The diones (III and IV) have the NMR spectra which disclose no signals attributable to hydrogens on carbons α to both carbonyls of β-diketones, and the ultraviolet spectra which display only weak maxima at 291 mμ and 296 mμ, respectively, the maxima being unchanged upon addition of alkali. These observations indicate that the diones (III and IV) are β-diketones having no α-hydrogens, the features which are in accord with the previous finding that the acetyl group in cyperolone is attached to a quaternary carbon. Therefore, cyperolone must have the partial structure A.

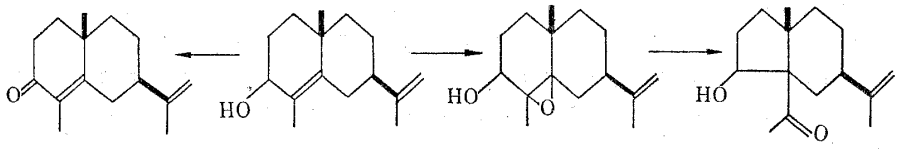


A



B

Now, the fact that cyperolone coexists with α-cyperone in the same plant coupled with the evidence so far obtained suggests that cyperolone having the structure I is biosynthesized from the alcohol corresponding to α-cyperone as depicted in Chart 1. If this biogenetic hypothesis is correct, the above mentioned C_{13}-monoketone must be shown in formula B.



α-cyperone

cyperolone (I)

Chart 1.

It was, therefore, expected that synthesis of the postulated monoketone (B) and identification of it with the monoketone derived from cyperolone could lead to the establishment of the structure of cyperolone. The convenient starting substance 14-noreudesmanone (X), recently prepared from β-eudesmol,[2] was condensed with benzaldehyde in

2) H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro, T. Takemoto: This Bulletin, **13**, 1408 (1965).

the presence of alkali to give the benzylidene-derivative (XI) which was converted into the dicarboxylic acid (XII) by ozonolysis followed by hydrogen peroxide oxidation. Ketonization of the dicarboxylic acid (XII) yielded the ketone (VII) having the molecular formula $C_{13}H_{22}O$. Since the ketone (VII) exhibits a positive Cotton curve (a=+90), the ring fusion, during pyrolysis, is shown to have been transformed from *trans* to *cis*; the latter being more stable junction in this system. Direct comparison of the C_{13}-monoketone derived from cyperolone with the ketone (VII), now synthesized from β-eudesmol, revealed that both the ketones were identical in their physical and spectral properties and the melting points of their semicarbazones and 2,4-dinitrophenylhydrazones. On the basis of the above evidence, the structure of cyperolone is elucidated as I (R=H) but exclusive of stereochemistry.

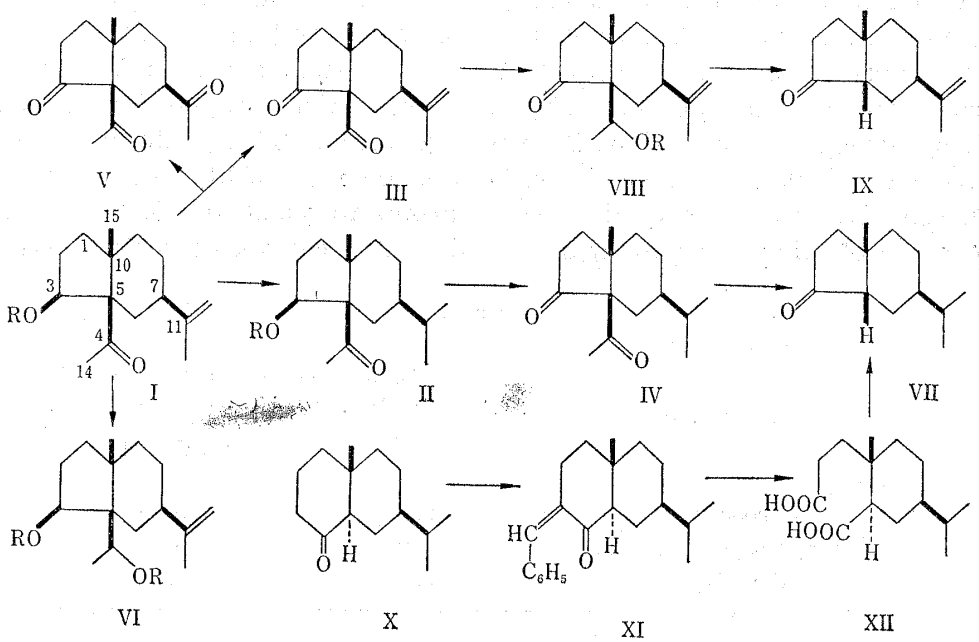


Chart 2.

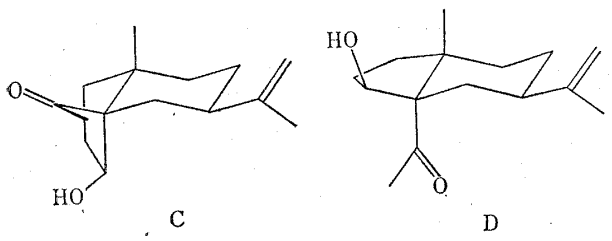
Since the configuration of both the C-7 isopropyl and the C-10 methyl groups of the ketone (X) of the naturally occurring eudesmane series has rigorously been established as β, correlation of cyperolone with 14-noreudesmanone (X) by means of the monoketone (VII) consequently fixed the configuration of the C-7 and C-10 substituents in cyperolone also as β.

Application of the benzoate rule[3] to cyperolone and 3-*epi*-cyperolone, synthesized for this purpose,[4] indicates that the absolute configuration at C-3 of cyperolone is *S* (*i.e.*, the hydroxyl being β) and that of 3-*epi*-cyperolone is *R* (*i.e.*, the hydroxyl being α) as shown in Table I.

Table I.

Compounds	Molecular rotations $[M]_D$		Molecular rotation differences $[M]_D$
	benzoate	alcohol	
Cyperolone	+243	+74	+169
3-*epi*-Cyperolone	−130	+56	−186

3) J. H. Brewster : Tetrahedron, **13**, 106 (1961).
4) H. Hikino, N. Suzuki, T. Takemoto : This Bulletin, **15**, 1395 (1967).



The configuration of both the C-3 hydroxyl and the C-10 methyl having been established as β, two stereostructures C and D are, therefore, possible for cyperolone depending upon the configuration of the acetyl group. If the acetyl group were α-oriented (*i.e.*, the ring junction were *trans*), the C-3 hydroxyl and the C-10 methyl group should be situated in a quasi-1,3-diaxial relationship on a cyclopentane ring. However, in the NMR spectra of cyperolone, dihydrocyperolone (II; R=H), the diol (VI; R=H), and their acetates (I, II, and VI; R=$COCH_3$), the acetylation shift of the C-10 methyl signal, which should be expected if both the functional groups were in such a relation,[5] was not observed as shown in Table II. This fact excludes the possibility D for cyperolone and consequently suggests the acetyl group to be in the β-configuration; *i.e.*, cyperolone has the stereostructure C. In order to verify this assumption, preparation of a ketone having a carbonyl group only at C-3 position was required. Thus, after a few preliminary experiments, treatment of the dione (III) with a quarter mole of lithium aluminum hydride resulted in selective reduction of the acetyl group to yield the keto-alcohol (VIII; R=H), the structure of which was confirmed by the infrared bands showing the retention of

Table II.

Compounds	Chemical shifts of the C-10 methyl groups (in τ values)	
	R=H	R=$COCH_3$
Cyperolone (I)	9.06	9.08
Dihydrocyperolone (II)	9.09	9.08
The diol (VI)	9.01	8.85

the carbonyl on a five membered ring (1726 cm^{-1}) as well as the formation of a hydroxyl (3428 cm^{-1}) and by the NMR signals indicating the formation of a secondary methyl (8.75τ) and a hydrogen (6.21τ), which is on carbon bearing the hydroxyl and coupled only with the methyl protons. This ketol (VIII; R=H) suffered a reverse aldol reaction to give, gradually on standing and rapidly on heating, the ketone (IX) with the loss of the C-2 unit. The *cis* ring junction of the ketone (VIII) was indicated by a positive Cotton curve (a=+153). Therefore, the free ketol (VIII; R=H) was difficult to isolate in the pure condition. It was then acetylated yielding the stable acetate (VIII; R=$COCH_3$). It is predicted that the Cotton effect should be positive if the C-5 substituent were β-situated while negative if α-situated.[6] The observed sign (a=+50) established the orientation of the C-5 substituent to be β, the conclusion being compatible with the previous assumption from the NMR evidence.

Since both the C-3 hydroxyl and the C-5 acetyl group have been shown to be located in the β-configuration, it is, therefore, expected that an intramolecular hydrogen bond is present between both functions. However, examinations of the infrared spectra in carbon tetrachloride in various concentrations revealed the absence of such a bond. This phenomenon can be explained by the following assumption. If the acetyl group were in the conformation favorable for chelation with the C-3 hydroxyl, the C-4 and

5) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, K. Tsuda: This Bulletin, **10**, 338 (1962).
6) W. Klyne: Tetrahedron, **13**, 29 (1961).

the C-10 methyl groups should be in the energetically disadvantageous parallel relation. Therefore, the acetyl group must be in a conformation where it is thermodynamically stable but unfavorable for chelation with the 3β-hydroxyl group. A positive Cotton curve observed coupled with inspection of the octant diagrams enables a decision for the most probable conformation to be made in favor of that depicted in perspective C. On the other hand, the diol (Ⅵ; R=H) showed in the infrared an intramolecularly hydrogen-bonded hydroxyl band at 3535 cm^{-1} (concentration independent) confirming that both the C-3 and the C-5 substituents are in the *cis* relationship.

On the basis of the above facts it is concluded that cyperolone is represented by the stereoformula I (R=H).

We propose the name cyperane, with the numbering shown, for the presently found skeleton of cyperolone.

Experimental*4

Isolation of Cyperolone——The crude drug "Kō-bushi", the dried rhizomes of *Cyperus rotundus* LINNÉ (Japanese name: Hama-suge), was steam-distilled to give the essential oil as a pale brown liquid in 0.6% yield.[1]

The oil (5.0 g.) was chromatographed over alumina (150 g.). After percolation with light petroleum followed by benzene, elution with benzene–AcOEt (10:3) afforded ketol fractions which, upon combination and evaporation, gave a yellow oil (0.6 g.). The oil (0.6 g.) was crystallized from light petroleum containing H_2O to give cyperolone hydrate as colorless plates, m.p. 41~42°, $[\alpha]_D$ +27.6°(c=5.2). This monohydrate, when dried at room temperature *in vacuo* (pressure 0.1 mm. Hg) for 7 days, lost 7.02% of its weight (theoretically 7.08%) to give the anhydrous cyperolone (I; R=H) as a colorless oil, $[\alpha]_D$ +31.4°(c=6.9). ORD (c=0.108, MeOH): $[M]_{310}^{peak}$ +1950°, $[M]_{270}^{trough}$ +640°, CD (c=0.108, MeOH): $[\theta]_{293}$ +1200. *Anal.* Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.24; H, 10.00. IR (liquid) cm^{-1}: 3086, 1642, 885 (vinylidene), 3436 (hydroxyl), 1695 (acetyl). IR (0.1*M*, CCl_4) cm^{-1}: 3562 (free hydroxyl), 3455 (intramolecularly assoc. hydroxyl). IR (0.02*M*, CCl_4) cm^{-1}: 3563 (free hydroxyl), NMR: singlet (3H) at 9.06 τ (CH_3–C<), triplet (3H) at 8.25 τ (J=1, CH_3–C=CH_2), singlet (3H) at 7.93 τ (CH_3–CO–), broad peak (1H) at 5.70 τ (H–C<OH), quadruplet (2H) at 5.32 τ (J=1, CH_2=C–CH_3).

Hydrogenation of Cyperolone——Cyperolone (130 mg.) in MeOH (8 ml.) was hydrogenated over 10% Pd-C (150 mg.) at room temperature. Distillation of the product (130 mg.) under reduced pressure gave dihydrocyperolone (Ⅱ; R=H) as a colorless oil, $[\alpha]_D$ +24.7°(c=7.1). *Anal.* Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.83; H, 10.71. IR (liquid) cm^{-1}: 3460 (hydroxyl), 1689 (acetyl), NMR: singlet (3H) at 9.09 τ (CH_3–C<), doublet (6H) at 9.06 τ (J=5, $(CH_3)_2$CH–), singlet (3H) at 7.93 τ (CH_3–CO–), broad peak (1H) at 5.68 τ (H–C<OH).

Acetylation of Cyperolone——Cyperolone (200 mg.) was allowed to stand overnight at room temperature in pyridine (1 ml.) containing Ac_2O (0.5 ml.). Isolation of the product (214 mg.) and distillation under reduced pressure afforded cyperolone acetate (I; R=$COCH_3$) as a colorless oil, $[\alpha]_D$ +60.2°(c=6.7). *Anal.* Calcd. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.57; H, 9.44. IR (liquid) cm^{-1}: 3096, 1647, 888 (vinylidene), 1742, 1235 (acetoxyl), 1701 (acetyl), NMR: singlet (3H) at 9.08 τ (CH_3–C<), triplet (3H) at 8.27 τ (J=1, CH_3–C=CH_2), singlet (3H) at 8.06 τ (CH_3–CO–O–), singlet (3H) at 7.96 τ (CH_3–CO–), unresolved band (2H) at 5.30 τ (CH_2=C–CH_3), triplet (1H) at 4.47 τ (J=9, H–C<$OCOCH_3$).

Acetylation of Dihydrocyperolone——Dihydrocyperolone (Ⅱ; R=H) (90 mg.) in pyridine (1 ml.) was treated overnight with Ac_2O (0.5 ml.). Upon isolation, the product (101 mg.) was distilled under diminished pressure to give dihydrocyperolone acetate (Ⅱ; R=$COCH_3$) as a colorless oil, $[\alpha]_D$ +69.6°(c=5.5). *Anal.* Calcd. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.24; H, 9.74. IR (liquid) cm^{-1}: 1742, 1238 (acetoxyl), 1704 (acetyl), NMR: singlet (3H) at 9.08 τ (CH_3–C<), doublet (6H) at 9.08 τ (J=7, $(CH_3)_2$CH–), singlet (3H) at 8.06 τ (CH_3–CO–O–), singlet (3H) at 7.96 τ (CH_3–CO–), triplet (1H) at 4.54 τ (J=8, H–C<$OCOCH_3$).

Oxidation of Cyperolone with Chromic Acid——a) Cyperolone (530 mg.) in ether (10 ml.) was stirred with $Na_2Cr_2O_7 \cdot 2H_2O$ (400 mg.) in dil. H_2SO_4 (1:2; 4 ml.) at room temperature for 10 hr. Isolation of the product (512 mg.) and distillation under reduced pressure yielded the dione (Ⅲ) as a colorless oil, $[\alpha]_D$ +38.7° (c=4.1). *Anal.* Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.80; H, 9.27. UV λ_{max}^{EtOH} mμ (log ε): 291 (2.00), $\lambda_{max}^{0.01N\,NaOH\text{-}EtOH}$ mμ (log ε): 291 (2.14), IR (liquid) cm^{-1}: 3096, 1642, 886 (vinylidene), 1742 (cyclo-

*4 Melting points are uncorrected. Specific rotations were measured in $CHCl_3$. NMR spectra were recorded at 60 Mc.p.s. in CCl_4 solution using Me_4Si as internal standard. Chemical shifts are reported in τ units and coupling constants (J) in c.p.s.

pentanone), 1692 (acetyl), 1406 (methylene α to carbonyl), NMR : singlet (3H) at 8.84 τ ($C\underline{H}_3$-C$\lessdot$), triplet (3H) at 8.26 τ (J=1, $C\underline{H}_3$-C=CH_2), singlet (3H) at 7.97 τ ($C\underline{H}_3$-CO-), quadruplet (2H) at 5.31 τ (J=1, $C\underline{H}_2$=C-CH_3).

b) Cyperolone (1.00 g.) in ether (30 ml.) was stirred with $Na_2Cr_2O_7 \cdot 2H_2O$ (4.0 g.) in dil. H_2SO_4 (1:2; 45 ml.) at 35° for 3 hr. The product (0.85 g.), isolated as usual was chromatographed over silica gel (15 g.).

Elution with light petroleum–benzene (1:1) gave the dione (Ⅲ) (0.27 g.), identified in the usual criteria.

Elution with benzene and distillation *in vacuo* afforded the trione (Ⅴ) (0.31 g.), $[\alpha]_D$ +20.4° (c=4.3). *Anal.* Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found : C, 71.33; H, 8.52. IR (liquid) cm^{-1} : 1745 (cyclopentanone), 1712, 1692 (acetyls), 1408 (methylene adjacent to carbonyl), NMR : singlet (3H) at 8.77 τ ($C\underline{H}_3$-C$\lessdot$), singlet (6H) at 7.84 τ ($C\underline{H}_3$-CO-).

Oxidation of Dihydrocyperolone with Chromic Acid——Dihydrocyperolone (Ⅱ) (1.00 g.) in ether (20 ml.) was stirred with $Na_2Cr_2O_7 \cdot 2H_2O$ (1.2 g.) in dil. H_2SO_4 (1:2; 8 ml.) at room temperature for 6 hr. Isolation and distillation under diminished pressure gave the dione (Ⅳ) as a colorless oil, $[\alpha]_D$ +48.5° (c=5.3). *Anal.* Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found : C, 76.38; H, 10.48. UV λ_{max}^{EtOH} mμ (log ε) : 296 (1.95). $\lambda_{max}^{0.01N\,NaOH\text{-}EtOH}$ mμ (log ε) : 296 (2.02). IR (liquid) cm^{-1} : 1748 (cyclopentanone), 1695 (acetyl), 1418 (methylene α to carbonyl), NMR : doublet (3H) at 9.07 (J=7, $C\underline{H}_3$-CH$\diagup$), doublet (3H) at 9.01 τ (J=7, $C\underline{H}_3$-CH$\diagup$), singlet (3H) at 8.83 τ ($C\underline{H}_3$-C$\lessdot$), singlet (3H) at 7.93 τ ($C\underline{H}_3$-CO-).

Reduction of Cyperolone with Lithium Aluminum Hydride——Cyperolone (200 mg.) in ether (6 ml.) was stirred with an excess of $LiAlH_4$ at room temperature for 1 hr. After working up in the usual way, crystallization from light petroleum gave the diol (Ⅵ; R=H) as colorless prisms, m.p. 112~112.5°, $[\alpha]_D$ +72.4° (c=4.9). *Anal.* Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found : C, 75.29; H, 10.76. IR (KBr) cm^{-1} : 3077, 1642, 891 (vinylidene), 3448, 3311 (hydroxyl). IR (0.1*M*, CCl_4) cm^{-1} : 3624 (free hydroxyl), 3530 (intramolecularly assoc. hydroxyl), 3330 (intermolecularly assoc. hydroxyl). IR (0.005*M*, CCl_4) cm^{-1}: 3625 (free hydroxyl), 3530 (intramolecularly assoc. hydroxyl), NMR : singlet (3H) at 9.01 τ ($C\underline{H}_3$-C$\lessdot$), doublet (3H) at 8.47 τ (J=7, $C\underline{H}_3$-CH(OH)-), triplet (3H) at 8.24 τ (J=1, $C\underline{H}_3$-C=CH_2), quadruplet (1H) at 6.51 τ (J=7, $\gtrdot$C-$C\underline{H}$(OH)-CH_3), broad peak (1H) at 5.75 τ ($\underline{H}$-C$\lessdot$OH), unresolved band (2H) at 5.33 τ ($C\underline{H}_2$=C-CH_3).

Treatment of the Diketone with Alkali——The dione (Ⅳ) (400 mg.) was refluxed under N_2 with methanolic KOH solution (10%; 4 ml.) for 1 hr. Isolation of the product (367 mg.) followed by distillation under reduced pressure furnished the monoketone (Ⅶ) as a colorless oil, $[\alpha]_D$ +171.4° (c=5.0). ORD (c=0.102, MeOH) : $[M]_{310}^{peak}$ +5180°, $[M]_{276}^{trough}$ −3770°. *Anal.* Calcd. for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.16; H, 11.38. IR (liquid) cm^{-1} : 1742 (cyclopentanone), 1408 (methylene next to carbonyl), NMR : two doublets (3H each) at 9.08 and 9.06 τ (J=6, $(C\underline{H}_3)_2$CH-), singlet (3H) at 8.75 τ ($C\underline{H}_3$-C$\lessdot$), which exhibited identical behavior upon VPC (silicone SE 30). The IR and NMR spectra were indistinguishable from those of the monoketone (Ⅶ) derived from β-eudesmol (see below).

The semicarbazone, prepared in the customary manner ($NH_2NHCONH_2 \cdot HCl$-AcONa-H_2O-EtOH), crystallized from EtOH as colorless plates, m.p. 209~210°. *Anal.* Calcd. for $C_{14}H_{25}ON_3$: C, 66.89; H, 10.03. N, 16.72. Found : C, 66.60; H, 9.76; N, 16.67, which gave no depression in m.p. on admixture with the semicarbazone of the ketone (Ⅶ) derived from β-eudesmol (see below).

The 2,4-dinitrophenylhydrazone, prepared in the usual way ($NH_2NHC_6H_3(NO_2)_2$-H_2SO_4-EtOH), crystallized from AcOEt as orange needles, m.p. 153~154°. *Anal.* Calcd. for $C_{19}H_{26}O_4N_4$: C, 60.94; H, 7.00; N, 14.96. Found : C, 60.87; H, 7.19; N, 15.11, which gave no m.p. depression on admixture with the 2,4-dinitrophenylhydrazone of the ketone (Ⅶ), derived from β-eudesmol (see below).

Reaction of 14-Noreudesmanone with Benzaldehyde——14-Noreudesmanone (Ⅹ) (1.90 g.) in 50% KOH solution (10 ml.) and EtOH (10 ml.) was refluxed with benzaldehyde (3 g.; freshly distilled) under N_2 for 3 hr. Ether extraction in the customary manner gave the brown oily product (3.37 g.) which crystallized partly. Chromatography of the filtrate over alumina (10 g.) and elution with light petroleum afforded a crystalline mass. The combined crystals were crystallized from MeOH to give the benzylidene derivative (Ⅺ) as colorless needles (1.56 g.), m.p. 88~88.5°. *Anal.* Calcd. for $C_{21}H_{28}O$: C, 85.08; H, 9.52. Found : C, 85.10; H, 9.82. UV λ_{max}^{EtOH} mμ (log ε) : 220 (4.33), 285 (4.51). IR (KBr) cm^{-1} : 1684 (enone), 3058, 1605, 1142, 759, 689 (phenyl).

Ozonolysis followed by Hydrogen Peroxide Oxidation of the Benzylidene Derivative——The benzylidene derivative (Ⅺ) (1.43 g.) in AcOEt (50 ml.) was ozonized at 0° until no further color was given with $C(NO_2)_4$. The solvent was removed at room temperature under reduced pressure. After addition of 30% H_2O_2 solution (8 ml.), the mixture was kept overnight at room temperature and then heated at 100° for 10 hr. The product was isolated by ether extraction and separated into a neutral and an acidic portion (1.45 g.). The latter was adsorbed from benzene on silica gel (20 g.). Benzene eluted benzoic acid (0.32 g.). Benzene-AcOEt (1:1) eluted the dicarboxylic acid (Ⅻ) as a colorless viscous oil (1.05 g.). IR (liquid) cm^{-1} : 3500~2300, 1705, 928 (carboxyl).

The dicarboxylic acid (Ⅻ) was treated with CH_2N_2 in ether and distilled under reduced pressure to afford the corresponding di-ester as a colorless oil, $[\alpha]_D$ −4.7° (c=3.8). *Anal.* Calcd. for $C_{16}H_{28}O_4$: C, 67.57; H, 9.93. Found : C, 67.25; H, 9.64. IR (liquid) cm^{-1} : 1736 (ester), NMR : doublet (6H) at 9.12 τ (J=5, $(C\underline{H}_3)_2$CH-), singlet (3H) at 9.09 τ ($C\underline{H}_3$-C$\lessdot$), singlet (6H) at 6.42 τ ($C\underline{H}_3$-O-CO-).

Pyrolysis of the Dicarboxylic Acid——A mixture of the dicarboxylic acid (Ⅻ) (407 mg.), $Ba(OH)_2$ (40 mg.), and Ac_2O (3.5 ml.) was heated at 150° to remove Ac_2O, and then at 300~400° to distill an oil (267 mg.)

which was warmed with H_2O, extracted with ether in the usual manner, and distilled under diminished pressure to furnish the monoketone (Ⅶ) as a colorless oil (82 mg.), $[\alpha]_D$ +157.0°(c=5.8). IR (liquid) cm^{-1}: 1742 (cyclopentanone), 1408 (methylene α to carbonyl), NMR: doublet (3H) at 9.08 τ (J=6, $C\underline{H}_3$-CH<), doublet (3H) at 9.06 τ (J=6, $C\underline{H}_3$-CH<), singlet (3H) at 8.75 τ ($C\underline{H}_3$-C<).

The semicarbazone, prepared in the usual way ($NH_2NHCONH_2 \cdot HCl$-AcONa-H_2O-EtOH), crystallized from EtOH as colorless plates, m.p. 209~210°. *Anal.* Calcd. for $C_{14}H_{25}ON_3$: N, 16.72. Found: N, 16.58.

The 2,4-dinitrophenylhydrazone, prepared in the customary manner ($NH_2NHC_6H_3(NO_2)_2$-H_2SO_4-EtOH), crystallized from AcOEt as orange needles, m.p. 152.5~153.5°. *Anal.* Calcd. for $C_{19}H_{26}O_4N_4$: N, 14.96. Found: N, 15.36.

Benzoylation of Cyperolone——Cyperolone (230 mg.) was treated with BzCl (230 mg.) in pyridine (1 ml.) at room temperature for 8 hr. The mixture was diluted with H_2O and extracted with ether. The residue (489 mg.) was chromatographed on alumina (5 g.). Elution with benzene and distillation *in vacuo* yielded cyperolone benzoate (Ⅰ; R=COC_6H_5) as a colorless oil, $[\alpha]_D$ +71.3°(c=4.0). *Anal.* Calcd. for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.39; H, 8.17. IR (liquid) cm^{-1}: 3096, 1642, 889 (vinylidene),1721, 1272 (ester), 1704 (acetyl), 1605, 1111, 711 (phenyl).

Acetylation of the Diol——The diol (Ⅵ; R=H) was acetylated (AcCl-pyridine) by standing overnight at room temperature to yield the diacetate (Ⅵ; R=$COCH_3$) as a colorless oil, $[\alpha]_D$ +4.2°(c=4.8). *Anal.* Calcd. for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.68; H, 9.31. IR (liquid) cm^{-1}: 3106, 1647, 890 (vinylidene), 1742, 1248 (acetoxyl), NMR: singlet (3H) at 8.85 τ ($C\underline{H}_3$-C<), doublet (3H) at 8.62 τ (J=7, $C\underline{H}_3$-CH-($OCOCH_3$)-), triplet (3H) at 8.26 τ (J=1, $C\underline{H}_3$-C=CH_2), unresolved band (2H) at 5.32 τ ($C\underline{H}_2$=C-CH_3), quadruplet (1H) at 5.08 τ (J=7, >C-C$\underline{H}$($OCOCH_3$)-CH_3), quadruplet (1H) at 4.40 τ (J_1=9, J_2=7, $\underline{H}$-C<$OCOCH_3$).

Partial Reduction of the Diketone with Lithium Aluminum Hydride——The dione (Ⅲ) (310 mg.) in ether (10 ml.) was stirred with $LiAlH_4$ (13 mg.) at room temperature for 1 hr. The mixture was worked up in the customary manner and the product was chromatographed on silica gel (10 g.).

Elution with light petroleum-benzene (1:1) yielded crystalline mass (37 mg.) which on crystallization from light petroleum gave the monoketone (Ⅸ) as colorless needles, m.p. 40.5°, $[\alpha]_D$ +163.6°(c=5.4), ORD (c=0.101, MeOH): $[M]_{311}^{peak}$ +8550°, $[M]_{278}^{trough}$ −6750°. *Anal.* Calcd. for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.24; H, 10.35. IR (KBr) cm^{-1}: 3086, 1642, 885 (vinylidene), 1730 (cyclopentanone), NMR: singlet (3H) at 8.74 τ ($C\underline{H}_3$-C<), triplet (3H) at 8.21 τ (J=1, $C\underline{H}_3$-C=CH_2), quadruplet (2H) at 5.34 τ (J=1, $C\underline{H}_2$=C-CH_3).

Successive elution with the same solvent gave the starting dione (Ⅱ) as a colorless oil (144 mg.), identified in the usual criteria.

Elution with benzene-AcOEt (5:2) afforded the ketol (Ⅷ; R=H) as a colorless oil (57 mg.). IR (CCl_4) cm^{-1}: 3053, 1643, 900 (vinylidene), 3428 (hydroxyl), 1726 (cyclopentanone), 1406 (methylene α to carbonyl), NMR: singlet (3H) at 8.74 τ ($C\underline{H}_3$-C<), doublet (3H) at 8.75 τ (J=6, $C\underline{H}_3$-CH(OH)-), triplet (3H) at 8.25 τ (J=1, $C\underline{H}_3$-C=CH_2), quadruplet (1H) at 6.21 τ (J=6, >C-C$\underline{H}$(OH)-CH_3), singlet (2H) with fine splittings at 5.36 τ ($C\underline{H}_2$=C-CH_3). This ketol (Ⅷ; R=H) gave, gradually on standing at room temperature and rapidly on heating (*e.g.*, distillation), the ketone (Ⅸ).

Acetylation of the Keto-alcohol——The ketol (Ⅷ; R=H) was allowed to react with Ac_2O-pyridine at room temperature overnight to give the keto-acetate (Ⅷ; R=$COCH_3$) as a colorless oil, ORD (c=0.119, MeOH): $[M]_{324}^{peak}$ +2580°, $[M]_{318}^{trough}$ +2340°, $[M]_{314}^{peak}$ +2400°, $[M]_{278}^{trough}$ −2400°. *Anal.* Calcd. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.26; H, 9.33. IR (liquid) cm^{-1}: 3096, 1645, 888 (vinylidene), 1739, 1236 (cyclopentanone & acetoxyl), NMR: singlet (3H) at 8.86 τ ($C\underline{H}_3$-C<), doublet (3H) at 8.86 τ (J=7, $C\underline{H}_3$-CH-(OH)-), triplet (3H) at 8.23 τ (J=1, $C\underline{H}_3$-C=CH_2), singlet (3H) at 7.97 τ ($C\underline{H}_3$=CO-O-), unresolved band (2H) at 5.29 τ ($C\underline{H}_2$=C-CH_3), quadruplet (1H) at 5.03 τ (J=7, >C-C$\underline{H}$-($OCOCH_3$)-CH_3).

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