Summary

The N-acetyl group of melatonin was replaced with a histidylphenylalanylarginyl moiety. The product, N-(histidylphenylalanylarginyl)-5-methoxytryptamine, reversed the darkening action of α-melanocyte-stimulating hormone (MSH) on frog-skin *in vitro* in contrast to the closely related tetrapeptide, histidylphenylalanylarginyltryptophan which exhibits intrinsic MSH activity. The synthetic intermediates, N-arginyl-5-methoxytryptamine and N-(phenylalanylarginyl)-5-methoxytryptamine also reversed the action of α-MSH. The color lightening potency of these compounds was about one millionth that of melatonin.

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120. Hiroshi Hikino, Keitaro Aota, and Tsunematsu Takemoto : Structure and Absolute Configuration of Cyperotundone.*1

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The tuber of nutgrass (*Cyperus rotundus* LINNÉ (Cyperaceae)), widespread throughout the tropical and temperate zone, has long been used in folk drug and native perfumes. In Japan, it is called "Kō-bushi" and utilized as a Chinese medicine for women's diseases. Although the composition of the essential oil has been studied by a number of workers, it is only known in part.[1] Two oils of Japanese nutgrass were examined by Kimura, *et al.*[2] who described the presence of a hydrocarbon fraction and an alcohol fraction which were termed cyperene and cyperol, respectively. However, no ketonic component was found in this report,[2] though the foreign oils have been shown to contain a large amount (33~54%) of ketones.[3] In order to ascertain the composition of the oil of Japanese origin, we have re-investigated it and isolated besides α-cyperone as one of the main constituents, a sesquiterpenoid ketone of molecular formula $C_{15}H_{22}O$ for which the name cyperotundone is proposed. In a preliminary communication,[4] we have reported the structure and absolute stereochemistry of cyperotundone as shown in formula I. The present paper provides the evidence in full detail.

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*1 This paper constitutes Part Ⅳ in the series on Sesquiterpenoids. Preceding paper, Part Ⅲ, H. Hikino, Y. Takeshita, Y. Hikino, T. Takemoto : This Bulletin, **14**, 735 (1966).

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1) For historical aspects of the research, see E. Gildemeister, F. Hoffmann : "Die Ätherischen Öle," Vol. Ⅳ, 425 (1956). Akademie Verlag, Berlin.

2) Y. Kimura, M. Otani : Yakugaku Zasshi, **48**, 971 (1928).

3) A. E. Bradfield, B. H. Hegde, B. S. Rao, J. L. Simonsen, A. E. Gillam : J. Chem. Soc., **1936**, 667.

4) H. Hikino, K. Aota, T. Takemoto : This Bulletin, **13**, 628 (1965).

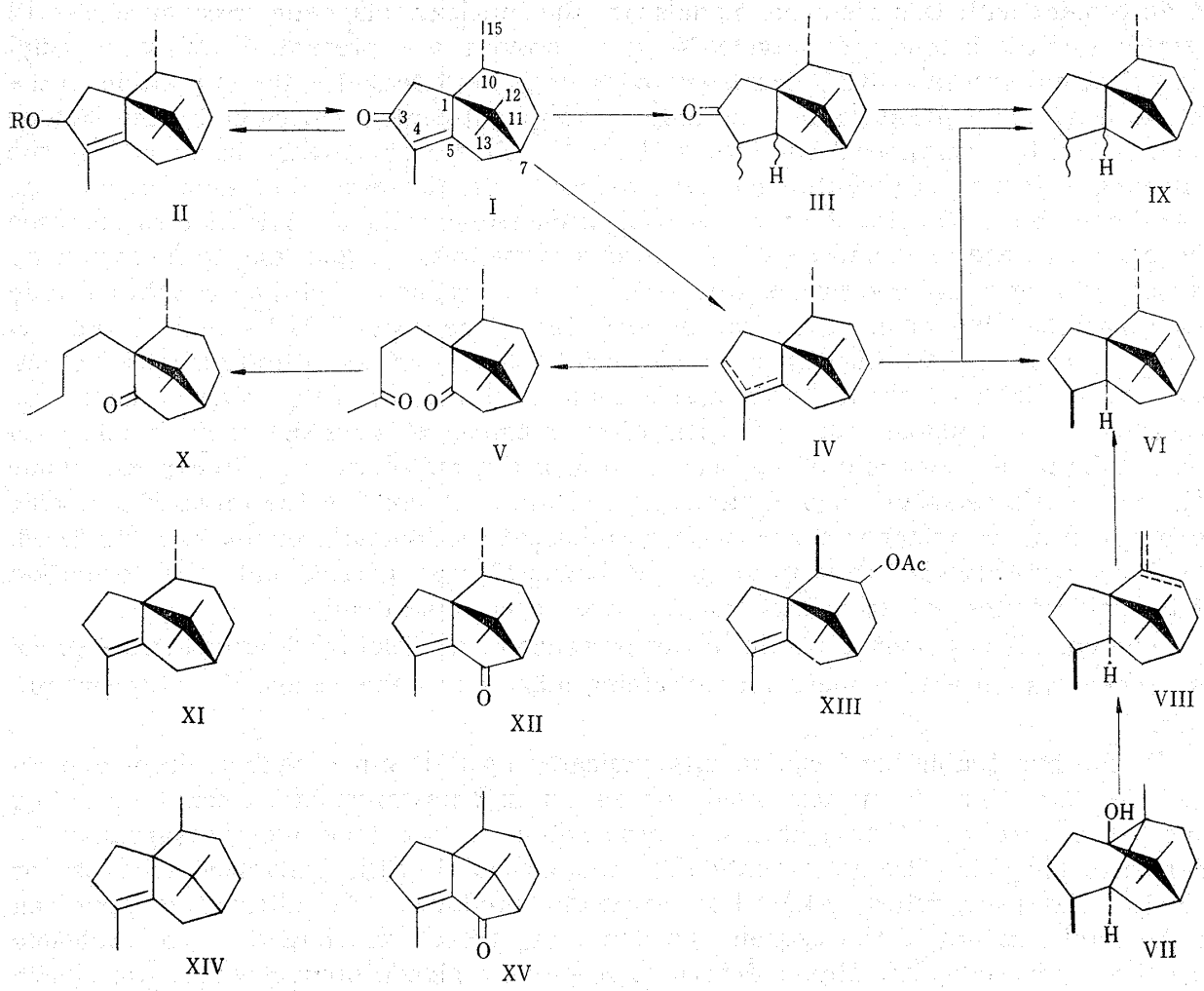

Chart 1.

Meanwhile, Trivedi, *et al.*[5,6] investigated the composition of a Chinese nutgrass oil, separated two new sesquiterpenoids, cyperene and patchoulenone, and proposed structure XIV and XV, respectively (no stereochemistry indicated).

The tubers of Japanese nutgrass on distillation in steam yielded a mobile oil in 0.6 per cent. The oil was chromatographed on alumina affording the ketonic fractions by elution with benzene. α-Cyperone was separated from the ketonic fractions by the semicarbazone method. From the mother liquor of the semicarbazone fraction cyperotundone was obtained which, purified by vapor phase chromatography followed by crystallization, has m. p. 46~47.5°, $[\alpha]_D$ +40.4°. The physical and spectral properties of the ketone did not agree with those of patchoulenone or any hitherto known ketones. Further details of the isolation of the other constituents are not described here as a separate communication will be published.

Cyperotundone has an infrared spectrum which shows two bands of practically equal intensities at 1706 and 1667 cm^{-1} and its ultraviolet spectrum exhibits a maximum at 245 mμ (log ϵ 3.96); both reveal that it is a fully-substituted α,β-unsaturated ketones in a five-membered ring. The ultraviolet maximum of its 2,4-dinitrophenylhydrazone at 396 mμ (log ϵ 4.35) also indicates it to be a tetrasubstituted enone derivative.

5) B. Trivedi, O. Motl, J. Smolíková, F. Šorm : Tetrahedron Letters, **1964**, 1197.
6) O. Motl, B. Trivedi, V. Herout, F. Šorm : Chem. & Ind. (London), **1963**, 1284. B. Trivedi, O. Motl, V. Herout, F. Šorm : Collection Czechoslov. Chem. Communs., **29**, 1675 (1964).

In agreement with this view no signals in the nuclear magnetic resonance (NMR) spectrum of the ketone attributable to vinyl protons are present. Further, a vinyl methyl signal occurs at 8.33τ consistent with its being situated at the α-position on the double bond. The presence of a methylene group adjacent to carbonyl in the ketone is suggested by an infrared band at 1410 cm^{-1}. This was further confirmed by the following evidence. Cyperotundone was reduced with lithium aluminum hydride to give the alcohol (Ⅱ;R=H). Since the alcohol on manganese dioxide oxidation regenerated the parent ketone and, since its NMR spectrum exhibits a signal due to hydrogen on carbon bearing a hydoxyl group, the possibility that reduction with concomitant allylic rearrangement had taken place, can be excluded. The above NMR signal of the hydrogen in the -CH(OR)- moiety of the alcohol (Ⅱ; R=H) or its acetate (Ⅱ; R=Ac) appears as a triplet which indicates it to be coupled with a pair of the adjacent methylene protons. Cyperotundone was hydrogenated over palladized charcoal in methanol, with the uptake of one molecule of hydrogen, to give the saturated dihydrocyperotundone (Ⅲ). Since this compound shows bands at 1736 and 1412 cm^{-1} in the infrared a ketonic carbonyl in a five-membered ring with an adjacent methylene grouping was indicated. Further, base-catalyzed deuteration of the ketone (Ⅲ) was carried out, the formation of the trideuterio-derivative was detected mass spectrometrically.

The combined evidence points to the presence of a 2-methyl-3-substituted 2-cyclopentenone system with a methylene grouping adjacent to the carbonyl in cyperotundone.

Of the five double-bond equivalents indicated by the empirical formula of cyperotundone, two have been accounted for as an α,β-unsaturated carbonyl grouping. Since there are no other points of unsaturation in the molecule the substance is, therefore, tricyclic. Dehydrogenation of the alcohol (Ⅱ) with palladized charcoal or selenium, however, failed to afford any aromatic products. An alternative approach to the establishment of the carbon skeleton was, therefore, sought. Cyperotundone was then reduced by the Huang-Minlon procedure to give a product which was shown to be the deoxo-derivative by the disappearance of the bands in the infrared attributable to the carbonyl group. The heterogeneous nature of this deoxo-derivative, however, was indicated by its vapor phase chromatography giving two peaks in the approximate ratio 3:2 in which the major one corresponded to that of cyperene (isopatchoul-4-ene). This was confirmed by its NMR spectrum in which, in addition to signals associated with cyperene, a signal (equivalent to ~0.4 H) due to vinyl hydrogen appeared, leading to the conclusion that it is a mixture (Ⅳ) of cyperene and its double bond migrated isomer, isopatchoul-3-ene. This conclusion was further verified by the fact that the deoxo-derivative (Ⅳ) on ozonolysis gave, together with an acidic product, a diketone which was identified as the dione (Ⅴ) obtained from cyperene. The above results provide unambiguous evidence that cyperotundone has the same carbon skeleton as cyperene.Although that cyperene has the isopatchoulane skeleton has been reported by Trivedi, *et al.*,[5] the saturated hydrocarbons from cyperene and patchouli alcohol have not been fully characterized. Therefore, in order to confirm the carbon skeleton, we also performed catalytic hydrogenation of deoxocyperotundone (Ⅳ) over platinum oxide in acetic acid to give a saturated hydrocarbon whose physical and spectral prorerties were essentially identical with those of an isopatchoulane (Ⅵ) prepared from patchouli alcohol (Ⅶ) *via* its rearranged dehydration product, α,γ-patchoulene (Ⅷ). The slight difference in properties of both the saturated hydrocarbons is explained by the coexistence of some elements in different ratios. In fact, vapor phase chromatography indicated that the saturated hydrocarbon (Ⅵ) from patchouli alcohol (Ⅶ) was contaminated with minute amount of two hydrocarbons, while the saturated hydrocarbon from cyperotundone consisted of the isopatchoulane (Ⅵ) and a small quantity of a hydro-

carbon. The minor component observed in the latter had the same retention time as that of an isopatchoulane (Ⅸ), the Wolff-Kishner reduction product of dihydrocyperotundone. The isopatchoulane (Ⅸ) is clearly different from the isopatchoulane (Ⅵ) by the optical rotations, behaviors on vapor phase chromatography, and the infrared and NMR spectra but is considered to be a stereo isomer of the isopatchoulane (Ⅵ). On the basis of these results, cyperotundone is shown to have the isopatchoulane skeleton.

Arrangement of the previous partial structure into this skeleton gives formula I but exclusive of stereochemistry as the structure of cyperotundone.

The remaining problem, its stereochemistry, was established by the following evidence. The absolute configuration of patchouli alcohol was bigorously elucidated as shown in formula Ⅶ.[7,8] Accordingly, the correlation of cyperotundone with patchouli alcohol (Ⅶ) *via* the isopatchoulane (Ⅵ) fixed the absolute configuration of the C-11 carbon bridge as β in cyperotundone. This was further confirmed by the fact that the diketone (Ⅴ) on Huang-Minlon reduction afforded the monoketone (Ⅹ) whose optical rotatory dispersion curve gives a positive Cotton effect ($a = +66$) in accord with expectance for the postulated absolute configuration.[9] The absolute configuration of the C-15 methyl group in cyperotundone was deduced on the basis of the NMR data described below. In this molecule, due to anisotropy of the unsaturated system (C-4: C-5 double bond and C-3 carbonyl group), α- and β-methyl groups on C-10 or C-11 cannot be equivalent and a β-methyl is expected to be fairly deshielded while an α-methyl is predicted to be rather shielded. Experimentally, the C-12 (*i.e.*, β-) and C-13 (*i.e.*, α-) methyl protons have their resonance positions at 8.83 and 9.25τ, respectively. On the other hand, the C-15 methyl protons appear at 9.39τ;the high field of the resonance indicates this group to be situated in an α-configuration. Consequently, the absolute stereochemistry of cyperotundone is represented by formula I.

Although the structure of cyperene and patchoulenone have been allocated as formula XIV and XV, respectively, no stereochemistry has been discussed. As we have now established that both compounds possess the same carbon skeleton as cyperotundone, it follows that the absolute stereochemistry of cyperene and patchoulenone must be as indicated in formulae Ⅺ and Ⅻ, respectively.

In the NMR spectra of both compounds, Ⅺ and Ⅻ, similar shielding of the methyl protons to that observed in cyperotundone can be found although the magnitudes of

Table I.

Compounds	Chemical shifts of the methyl protons (in τ-values)			
	C-12	C-13	C-15α	C-15β
Cyperotundone (I)	8.83	9.25	9.39	
Cyperene (Ⅺ)	9.06	9.25	9.20	
The alcohol (Ⅱ; R=H)	9.02	9.21	9.33	
The acetate (Ⅱ; R=Ac)	9.04	9.20	9.25	
Patchoulenone (Ⅻ)[6]	8.97	9.10	9.15	
The intermediate (ⅩⅢ)[8]	8.97	9.20		8.85

the shifts are relatively small (see Table I). In confirmation, the C-15 methyl protons in a β-configuration were found to be strongly deshielded, occurring at 8.85τ, in the intermediate (ⅩⅢ)[8] prepared *en route* for the synthesis of patchouli alcohol.

7) G. Büchi, R. E. Erickson, N. Wakabayashi : J. Am. Chem. Soc., **83**, 927 (1961); M. Dobler, J. D. Dunitz, B. Gubler, H. H. Weber, G. Büchi, J. Pallida O. : Proc. Chem. Soc., **1963**, 383.
8) G. Büchi, W. D. MacLeod, Jr., J. Pallida O. : J. Am. Chem. Soc., **86**, 4438 (1964).
9) W. Klyne : Tetrahedron, **13**, 29 (1961).

Trivedi, *et al.*[5] have assigned the NMR signals of cyperene as follows : a singlet at 9.25τ is due to the C-12 and C-13 dimethyl protons and a doublet at 9.16 and 9.05τ due to the C-15 methyl protons. As has been discussed before, however, it is improbable that the C-12 and C-13 geminal dimethyl protons are equivalent. In fact, precise examinations of the spectrum reveals the propriety of the present assignment.

Of all the physical and spectral data, it is noteworthy that the intensity of the carbon-carbon double bond stretching frequency at 1667 cm^{-1} in the infrared spectrum of cyperotundone is much higher than would be expected for that of a *transoid* enone system. This is certainly due to the strongly strained feature of the conjugated ring.

Quite recently, there came to our attention that, after publication of our preliminary communication,[4] Bhattacharyya[10] and Nigam[11] independently submitted papers which reported the structural elucidation as constitution I (without stereochemistry) of cyperotundone isolated from *Cyperus scarosius* R. Brown of Indian origin; the conclusion being in accordance with our own. Despite of dealing with the same substance, Bhattacharyya[10] and Nigam[11] have newly proposed the different names, isopatchoulenone and cyperenone, respectively.

Experimental*3

Isolation of Cyperotundone——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.

The oil (5.0 g.) was chromatographed over alumina (150 g.). After percolation with light petroleum, elution with benzene afforded ketone fractions which, upon combination and evaporation, gave a yellow oil (1.3 g.). This oil (1.3 g.) was treated with semicarbazide acetate separating a solid semicarbazone (0.4 g.) which was crystallized from EtOH to give α-cyperone semicarbazone, m. p. 209~210°. After separation of the solid semicarbazone, the solvent was removed by evaporation; a liquid semicarbazone remained.

The liquid semicarbazone was hydrolyzed by oxalic acid in acetone solution to yield a ketone contaminated with a small quantity of α-cyperone. This mixture, when purified by preparative VPC followed by crystallization from light petroleum, gave cyperotundone (I) as colorless needles, m. p. 46~47.5°, $[\alpha]_D$ +40.4°(c=3.2), *Anal.* Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found : C, 82.43; H, 10.19. UV λ_{max}^{EtOH} mμ (log ε) : 245 (3.96). IR (KBr) cm^{-1} : 1706, 1667 (cyclopentenone), NMR : doublet (3H) at 9.39 τ (J=6.5, $C\underline{H}_3$-CH<), singlet (3H) at 9.25 τ ($C\underline{H}_3$-C<), singlet (3H) at 8.83 τ ($C\underline{H}_3$-C<), triplet (3H) at 8.33 τ (J=1.1, $C\underline{H}_3$-C=C).

The 2,4-dinitrophenylhydrazone,prepared in the customary manner ($NH_2NHC_6H_3(NO_2)_2$-H_2SO_4-EtOH), crystallized from AcOEt as red needles, m. p. 224~225°, *Anal.* Calcd. for $C_{21}H_{26}O_4N_4$: C, 63.30; H, 6.58; N, 14.06. Found : C, 63.44; H, 6.36: N, 13.93. UV $\lambda_{max}^{CHCl_3}$ mμ (log ε) : 260 (4.12), 297 (3.78), 396 (4.35).

Reduction of Cyperotundone with Lithium Aluminum Hydride——Cyperotundone (125 mg.) was stirred with $LiAlH_4$ (55 mg.) in anhydrous ether (15 ml.) for 3.5 hr. at room temperature. Upon isolation, the product (120 mg.) was crystallized from light petroleum to give the alcohol (II; R=H) as colorless needles, m.p. 136°, $[\alpha]_D$ −37.7°(c=4.8). *Anal.* Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found : C, 81.76; H, 10.80. IR (KBr) cm^{-1} : 3205 (hydroxyl), NMR : doublet (3H) at 9.33 τ (J=5.7, $C\underline{H}_3$-CH<), singlet (3H) at 9.21 τ ($C\underline{H}_3$-C<), singlet (3H) at 9.02 τ ($C\underline{H}_3$-C<), triplet (3H) at 8.33 τ (J=1.6, $C\underline{H}_3$-C=C), triplet (1H) at 5.14 τ (J=6.3, -CH_2-$C\underline{H}$(OH)-C=C).

Acetylation of the Alcohol——The alcohol (II; R=H) (112 mg.) was acetylated (Ac_2O-pyridine) by standing 1 day at room temperature. After isolation, the product was placed on a silica gel column (3 g.). Elution with ether afforded an oil (136 mg.) which was distilled under reduced pressure to give the acetate (II; R=Ac) as a colorless oil, n_D^{25} 1.508, $[\alpha]_D$ −28.3°(c=3.6). *Anal.* Calcd. for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found : C, 77.86; H, 10.22. IR (liquid) cm^{-1} : 1739, 1238 (acetoxyl). NMR : doublet (3H) at 9.25 τ (J=6.0, $C\underline{H}_3$-CH<), singlet (3H) at 9.20 τ ($C\underline{H}_3$-C<), singlet (3H) at 9.04 τ ($C\underline{H}_3$-C<), triplet (3H) at 8.44 τ (J=1.5, $C\underline{H}_3$-C=C), singlet (3H) at 8.06 τ ($C\underline{H}_3$-CO-O-), triplet (1H) at 4.83 τ (J=~7, -CH_2-$C\underline{H}$(OAc)-C=C).

Oxidation of the Alcohol with Manganese Dioxide——The alcohol (II; R=H) (30 mg.) in $CHCl_3$ (5 ml.) was stirred with MnO_2 (100 mg.) at room temperature for 2 days. Upon isolation, the product (29 mg.), shown by TLC to be a mixture of the ketone (I) and the starting material (II; R=H), was separated by preparative

*3 Melting points are uncorrected. Specific rotations were measured in $CHCl_3$ solution. NMR spectra were determined at 60 Mc.p.s. in CCl_4 solution against Me_4Si as internal standard unless otherwise indicated. Chemical shifts are given in τ-values and coupling constants (J) in c.p.s.

10) S. C. Bhattacharyya : private communication (September 16, 1965).

11) I. G. Nigam : *Ibid.* (November 18, 1965).

TLC (silica gel, benzene–AcOEt=10:3) to give cyperotundone (I) (12 mg.), identified by IR comparison.

Oxidation of the Alcohol with Chromic Acid——To a stirred solution of the alcohol (II; R=H) (2.19 g.) in ether (30 ml.) was added $Na_2Cr_2O_7 \cdot 2H_2O$ (1.8 g.) in H_2SO_4 (1.5 ml.) and H_2O (3.5 ml.), stirring was continued for 6 hr. at room temperature. Isolation of the product (2.15 g.) by ether extraction and crystallization from light petroleum yielded cyperotundone (I) as colorless needles, m.p. 46~47.5°, identified by the IR spectrum and mixed melting point.

Hydrogenation of Cyperotundone over Palladized Charcoal in Ethanol——Cyperotundone (244 mg.) was hydrogenated in EtOH (6 ml.) over 10% Pd-C (250 mg.) at room temperature. After the uptake of 1 mole H_2, the solution was filtered and evaporated to give the product (243 mg.) which upon crystallization from light petroleum afforded dihydrocyperotundone (III) as colorless needles, m.p. 83~84°, $[\alpha]_D$ −9.9°(c=5.4), mol. wt. 220 (mass spec.). *Anal.* Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.50; H, 10.82. IR (KBr) cm^{-1}: 1736 (cyclopentanone), 1412 (methylene α to carbonyl). NMR: singlet (3H) at 9.45 τ ($C\underline{H}_3$–C<), doublet (3H) at 9.21 τ (J=6.0, $C\underline{H}_3$–CH<), singlet (3H) at 9.05 τ ($C\underline{H}_3$–C<), doublet (3H) at 8.98 τ (J=7.0, $C\underline{H}_3$CH<).

Base-catalyzed Deuteration of Dihydrocyperotundone——Na (40 mg.) was added to a mixture of D_2O (1 ml.) and dioxane (1 ml.), followed by dihydrocyperotundone (III) (68 mg.). The mixture was refluxed for 10 min. under N_2, the solvent evaporated, and the residue redissolved in D_2O (1 ml.) and dioxane (1 ml.) and again refluxed for 10 min. under N_2. The cycle of operation was repeated twice more, the mixture being protected from outside moisture throughout. After the final evaporation the residue was dissolved in anhydrous ether and acidified with 20% AcOH. The product (67 mg.) from the ether extraction was crystallized from light petroleum to give trideuteriodihydrocyperotundone as colorless needles, m.p. 77~80°, mol. wt. 223 (mass spec.). IR (KBr) cm^{-1}: 1739 (cyclopentanone), no band due to a methylene α to carbonyl.

Wolff-Kishner Reduction of Cyperotundone——Cyperotundone (250 mg.) and 80% $NH_2NH_2 \cdot H_2O$ (200 mg.) in EtOH (2 ml.) were refluxed for 2.5 hr. and then KOH (180 mg.) and triethylene glycol (1.5 ml.) were added. The mixture allowed to stand at 190~200° for 5 hr., poured into H_2O and extracted with ether. The ether extract (242 mg.) was distilled under diminished pressure to yield the deoxo-derivative (IV) as a colorless oil, n_D^{25} 1.499, $[\alpha]_D$ −22.2°(c=4.5), *Anal.* Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.89; H, 11.55, which was shown to be a mixture of isopatchoul-4-ene (cyperene) and isopatchoul-3-ene by behavior upon VPC and by the NMR spectrum. Thus, its VPC (PEG 6000) exhibited two peaks with integrated intensities in the approximate ratio 3:2; the former had the same retention time as that of cyperene. The NMR spectrum showed methyl singlets at 9.26 and 9.06 τ, a methyl doublet at 9.21 τ (J=5), and a methyl triplet at 8.39 τ (J=1) for cyperene as well as a methyl doublet at 9.30 τ (J=5) and a vinyl hydrogen peak at 4.98 τ (broad) for isopatchoul-3-ene.

Ozonolysis of Deoxocyperotundone——Deoxocyperotundone (IV) (272 mg.) was dissolved in AcOEt (16 ml.), cooled in an ice bath, and a stream of ozonized oxygen was passed for 2 hr. H_2O (16 ml.) was added and the mixture was heated under reflux for 2 hr. The product (245 mg.) was separated into a neutral (158 mg.) and an acidic material (87 mg.) in the usual manner. The neutral material was chromatographed over alumina (4 g.). Benzene eluted a crystalline fraction (54 mg.) crystallized from light petroleum to give the diketone (V) as colorless needles, m.p. 77.5~78.5°, $[\alpha]_D$ +39.8°(c=3.6). *Anal.* Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 75.71; H, 10.10. IR (KBr) cm^{-1}: 1724 (broad; cyclopentanone and acetyl), 1412 (methylene α to carbonyl). NMR: doublet (3H) at 9.28 τ (J=6.0, $C\underline{H}_3$–CH<), singlet (3H) at 9.06 τ ($C\underline{H}_3$–C<), singlet (3H) at 8.84 τ ($C\underline{H}_3$–C<), singlet (3H) at 7.93 τ ($C\underline{H}_3$–CO–), which was identified by IR and NMR spectra and mixed melting point as the dione obtained from cyperene.

Hydrogenation of Deoxocyperotundone over Adams' Catalyst in Acetic Acid——Deoxocyperotundone (IV) (185 mg.) in AcOH (8 ml.) was hydrogenated using PtO_2 (100 mg.). The product in light petroleum was filtered through alumina (4 g.). The same solvent eluted an oil (107 mg.) distilled under reduced pressure to give dihydrodeoxocyperotundone as colorless oil, n_D^{25} 1.496, $[\alpha]_D$ −57.7°(c=5.3). *Anal.* Calcd. for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.83; H, 12.67. NMR: doublet (3H) at 9.30 τ (J=6.0, $C\underline{H}_3$–CH<), singlet (3H) at 9.17 τ ($C\underline{H}_3$–C<), singlet (3H) at 9.07 τ ($C\underline{H}_3$–C<), doublet (3H) at 9.04 τ (J=6.5, $C\underline{H}_3$–CH<), identified as the isopatchoulane (VI) obtained from patchouli alcohol (VII) (*vide infra*) by IR and NMR spectra. VPC (PEG 6000) showed one main peak with a minor peak. The retention time of the former was identical with that of the isopatchoulane (VI) and that of the latter identical with that of the isopatchoulane (IX), the deoxo-derivative of dihydrocyperotundone (*vide infra*).

Wolff-Kishner Reduction of Dihydrocyperotundone——Dihydrocyperotundone (II) (224 mg.) and 80% $NH_2 \cdot NH_2 \cdot H_2O$ (170 mg.) in EtOH (1.5 ml.) was refluxed for 2.5 hr. and then KOH (0.3 g.) and triethylene glycol (1.5 ml.) were added. The mixture was kept at 190~200° for 10 hr. The cooled solution was poured into H_2O and extracted with ether. The product was distilled under reduced pressure to give deoxodihydrocyperotundone, the isopatchoulane (IX), as colorless oil, $[\alpha]_D$ −89.9°(c=4.6), n_D^{25} 1.478. *Anal.* Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.47; H, 12.02. NMR: doublet (3H) at 9.21 τ (J=6.2, $C\underline{H}_3$–CH<), singlet (3H) at 9.11 τ ($C\underline{H}_3$–C<), doublet (3H) at 9.07 τ (J=~4, $C\underline{H}_3$–CH<), singlet (3H) at 9.05 τ ($C\underline{H}_3$–C<). The IR and NMR spectra were not identical with those of the isopatchoulane (VI) derived from patchouli alcohol (VII) (*vide infra*). VPC (PEG 6000) showed one peak whose retention time was different from that of the isopat-

choulane (VI) but was identical with that of the minor component of the dihydro-derivative of deoxocyperotundone (*vide supra*).

Wolff-Kishner Reduction of the Diketone——The dione (V) (102 mg.) was refluxed 2.5 hr. in EtOH (1.5 ml.) with 80% $NH_2NH_2 \cdot H_2O$ (80 mg.) and then let stand 5.5 hr. at 190~200° with KOH (240 mg.) in triethylene glycol (1.5 ml.). The mixture was poured into H_2O and extracted with ether. The product was chromatographed on alumina (3 g.). Elution with light petroleum afforded an oil (90 mg.) which on distillation under reduced pressure gave the monoketone (X) as a colorless oil, n_D^{25} 1.489, $[\alpha]_D$ +15.8° (c=4.0), ORD (c=0.134, MeOH): $[M]_{323.5}^{peak}$ +3340°, $[M]_{284}^{trough}$ −3220°. *Anal.* Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.76; H, 11.42. IR (liquid) cm^{-1}: 1736 (cyclopentanone), 1416 (methylene α to carbonyl).

Dehydration of Patchouli Alcohol with Phosphorus Oxychloride in Pyridine——Patchouli alcohol (VII) (320 mg.) in pyridine (5 ml.) was treated with $POCl_3$ (2 ml.) on the steam bath at 100° for 7 hr. The mixture was poured on crushed ice and extracted with ether. The ether extract (303 mg.) was chromatographed on a column of alumina (4 g.). Elution with light petroleum and distillation under diminished pressure afforded α,γ-patchoulene (VIII) as a colorless oil. n_D^{25} 1.504, $[\alpha]_D$ −53.7°(c=6.4). *Anal.* Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.03; H, 12.15. IR (liquid) cm^{-1}: 1639, 881 (vinylidene), 788 (trisubstituted ethylene).

Hydrogenation of α,γ-Patchoulene over Palladized Charcoal in Ethyl Acetate——α,γ-Patchoulene (VIII) (236 mg.) was hydrogenated in AcOEt (8 ml.) over 10% Pd-C (300 mg.). Distillation of the product (220 mg.) gave the isopatchoulane (VI) as a colorless oil, n_D^{25} 1.498, $[\alpha]_D$ −49.2°(c=5.9). *Anal.* Calcd. for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.23; H, 12.60. NMR: doublet (3H) at 9.30 τ (J=6.0, $C\underline{H}_3$-CH<), singlet (3H) at 9.17 τ ($C\underline{H}_3$-C<), singlet (3H) at 9.07 τ ($C\underline{H}_3$-C<), doublet (3H) at 9.04 τ (J=6.5, $C\underline{H}_3$-CH<). The VPC (PEG 6000) showed one main peak with two slight peaks.

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Summary

Cyperotundone, the constituent of nutgrass (*Cyperus rotundus* (Cyperaceae)), has been shown to have the stereostructure I as follows: Spectral determinations of it and its derivatives revealed the presence of a 2-methyl-3-substituted cyclopent-2-enone system with a methylene α to the carbonyl. The carbon skeleton was established by transformation to the isopatchoulane (VI) derived from patchouli alcohol (VII). The absolute configuration of the C-11 bridge was deduced from the above transformation and a positive Cotton effect of the optical rotatory dispersion of the ketone (X) and that of the C-10 methyl from examination of the NMR methyl signals.

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