[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Terpenes. XVI.[1,2] Constitution of Patchouli Alcohol and Absolute Configuration of Cedrene

BY G. BÜCHI, R. E. ERICKSON[3] AND NOBEL WAKABAYASHI[4]

RECEIVED SEPTEMBER 21, 1960

Patchouli alcohol was shown to be 1. Oxidative decarboxylation of norpatchoulidicarboxylic acid monomethyl ester with lead tetraacetate gave 3-carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]oct-8-ene and 3-carbomethoxy-2,2,6-trimethylbicyclo[3.3.0]oct-5(6)-ene. On catalytic reduction both yielded 3-carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]octane. 3-Carbomethoxy-2,2,6-trimethylbicyclo[3.3.0]oct-5(6)-ene is also available by oxidative decarboxylation of norcedrenedicarboxylic acid monomethylester. This correlation establishes the absolute configuration of cedrene (**34**).

Patchouli oil is an article of commerce and an important material in perfumery. Several species of the Labiatae family with patchouli-like odor grow in the tropics, but only one, *Pogostemon patchouli* Pellet is utilized for the commercial distillation of the oil. The scent of the essence is partly due to patchouli alcohol first isolated in crystalline form by Gal (in 1869) and correctly formulated as $C_{15}H_{26}O$, by Montgolfier. Early structural investigation[5] established the presence of a saturated tricyclic tertiary alcohol. More recent work on the structure of patchouli alcohol or, more correctly, on patchoulene by Treibs[6] will be discussed later and we now wish to present our own observations which are in agreement with the complete structure **1**.

Patchouli acetate (**2**) was prepared by the action of ketene on the natural product and its structure confirmed by reduction to **1** with lithium aluminum hydride. Pyrolysis of **2** at 300° afforded a mixture of olefins and acetic acid. The distribution of isomers in the pyrolysate was estimated by gas chromatography and found to be: α-patchoulene (**4**), 52%; β-patchoulene (**17**), 4%; and γ-patchoulene (**3**), 46%.[7] For further degradation this mixture of olefins was oxidized with osmium tetroxide and the resulting products were separated into γ-patchouli diol (**9**), and α-patchoulidiol (**10**). Diol **9** on cleavage with lead tetraacetate gave formaldehyde and norpatchoulione (**12**) whose infrared spectrum (in CCl_4) exhibited a carbonyl band at 1706. cm.$^{-1}$, excluding the presence of a substituted cyclopentanone. Condensation of norpatchoulione (**12**) with isoamyl nitrite afforded an α-oximino ketone (**13**) (λ_{max}^{EtOH} 234 mμ, ε 8400) even under conditions known to yield oximino esters provided the molecule contains the grouping–COCH<.[8] This finding and the low reactivity of **12** with 2,4-dinitrophenylhydrazine tentatively suggested a carbonyl group located next to a fully substituted carbon atom and part structure $-CH_2-C(CH_3)(OH)-<$ follows for patchouli alcohol assuming that acetate pyrolysis proceeded without rearrangement. This was verified by degradation of α-patchoulidiol (**10**) which was oxidized with lead tetraacetate to a ketoaldehyde (**14**) (characterized by a mono-2,4-dinitrophenylhydrazone) and further with air to a ketocarboxylic acid (**15**). The carbonyl group in **15** is again hindered and did not react with 2,4-dinitrophenylhydrazine and no iodoform could be detected after treatment with sodium hypoiodite. Its presence was eventually ascertained by the preparation of an oxime.

Evidence for the size of ring C in patchouli alcohol was secured as follows. Oxidation of a mixture of α- and γ- patchoulenes (**4** and **3**) consecutively with potassium permangamate and with nitric acid gave a dicarboxylic acid $C_{13}H_{20}O_4$ (**5**). Its formation can be rationalized with ease in part structure $-CH_2-CH_2-C(H_3C)(OH)-C-$ was originally present. Treatment of patchoulidicarboxylic acid (**5**) with hot acetic anhydride yielded an anhydride possessing infrared bands (in KBr) at 1786 and 1754 cm.$^{-1}$ attributable to a glutaric anhydride and identical with those present in the spectrum of camphoric anhydride. As anticipated for a six-membered cyclic anhydride it was formed readily from the dicarboxylic acid on sublimation. This behavior is paralleled by camphoric acid (**20**) but not by homocamphoric acid (**19**).[6] If we accept this argument ring C in patchouli alcohol is six membered.

The size of ring B was ascertained by further degradation of norpatchoulidicarboxylic acid (**5**). Treatment of its dimethyl ester (**6**) with phenylmagnesium bromide followed by dehydration of the carbinol with acetic anhydride resulted in the formation of a diphenylene-ester (**11**) (λ_{max}^{EtOH} 227 mμ, ε 11,200) which exhibits maximum light absorption at abnormally short wave lengths.[9] This is caused by the geminal dimethyl group which prevents formation of a planar chromophore. Attempts to oxidize **11** with chromium trioxide using a variety of well established procedures gave little benzophenone but much starting material and it became clear that an oxidizing agent capable of attacking the

(1) Part XV, G. Büchi and R. E. Manning, *Tetrahedron Letters*, in press (1960).

(2) Part of this investigation was published in a Communication to the Editor, G. Büchi and R. E. Erickson, *J. Am. Chem. Soc.*, **78**, 1262 (1956).

(3) Louis Francisco Verges Fellow 1954–1955.

(4) National Institutes of Health Predoctoral Fellow 1957–1960.

(5) Summarized in J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press, London, 1952; and E. Guenther, "The Essential Oils, Vol. III, D. Van Nostrand Co., Inc., New York, N. Y., 1949.

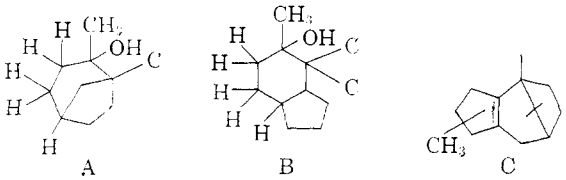
(6) W. Treibs, *Ann.*, **564**, 141 (1949).

(7) The nomenclature adopted here is that used for the designation of the isomeric ionones and irones; H. Schinz, "Die Veilchenriechstoffe" in L. Zechmeister, "Progress in the Chemistry of Organic Natural Products," Vol. VIII, Springer Verlag, Wien, 1951, p. 146.

(8) R. B. Woodward and W. E. Doering, *J. Am. Chem. Soc.*, **67**, 860 (1945).

(9) *E.g.*, Δ^{23}-3α,12β-diacetoxy-24,24-diphenyl-cholene has $\lambda_{max}^{CHCl_3}$ 250 mμ (ε 25,000); Ch. Meystre, H. Frey, A. Wettstein and K. Miescher, *Helv. Chim. Acta*, **27**, 1815 (1944).

benzene rings as well as the hindered double bond should yield the desired ketoester (**16**). Prolonged ozonization in acetic acid solution at 25° eventually led to **16** whose infrared spectrum showed no carbonyl absorption at wave lengths characteristic of cyclobutanones or cyclohexanones. By exclusion, **16** becomes a cyclopentanone. Consequently, one of the carboxyl groups in norpatchoulidicarboxylic acid (**5**) is secondary and that only one of the ester functions did react with Grignard reagent can be rationalized if the other is tertiary. The data so far presented can be summarized in partial structures A and B.



To decide between these alternatives we have to consider the structure of β-patchoulene (**17**). This olefin was available by dehydration of patchouli alcohol with (a) sulfuric acid, (b) iodine and (c) boric acid. The infrared spectra of β-patchoulene samples prepared by these methods were all identical and furthermore superimposable on those of patchoulene obtained by dehydration with formic acid[6] and other acidic catalysts.[10,11] Gas chromatographic analysis demonstrated the identity of β-patchoulene with a third olefin formed in 4% yield on pyrolysis of patchouliacetate (**2**). Hot acetic acid liberated in this conversion must have caused partial isomerization to **17**. Degradation of β-patchoulene (**17**) with ozone yielded (+)-homocamphoric acid (**19**) while oxidation with chromium trioxide afforded **19** and (+)-camphoric acid (**20**) in complete agreement with the findings of Treibs.[6] To establish the position of the double bond in β-patchoulene (**17**) we had to study additional transformations. Osmylation produced a single diol which was oxidized with lead tetraacetate to a diketone that failed to give an iodoform test and exhibited a single carbonyl band in the infrared spectrum (in CCl_4) at 1695 cm.$^{-1}$. Smooth cyclization of this diketone (**18**) to a cyclohexenone (**21**), λ_{max}^{EtOH} 260 mμ, (ε11000), $\gamma_{max}^{CS_2}$ 1656, 1613 cm.$^{-1}$, with either acid or base suggested a δ-diketone. β-Patchoulene consequently is a cyclopentene. Only partial structure C is consistent with the data presented and if we furthermore recall the dehydrogenation of patchouli alcohol to guaiazulene (**22**)[6] we arrive at structure **17**. Incidentally, we have been able to improve this aromatization considerably by dehydrogenating **1** in the gas phase over a palladium catalyst[12] and the presence of a guaiane skeleton in **1** can hardly be questioned. Before returning to a discussion of the structure of patchouli alcohol itself we call attention to the ultraviolet light absorption of the fully substituted cyclohexenone (**21**) (λ_{max}^{calcd} 249 mμ) which occurs at unusually long wave lengths. Such bathochromic displacements have been encountered previously[13] in spectra of molecules containing the double bond in a strained ring and an electronic interpretation has been presented.[13] Clearly, partial formula B cannot be expanded to a complete structure explaining the acid-catalyzed dehydration of the original alcohol to **17**. Expression A, on the other hand, develops into **1** and dehydration consequently is accompanied by Wagner–Meerwein rearrangement, apparently facilitated by release of steric strain present in the original ring system. The possibility of such a rearrangement was first considered by Wallach[14] who felt it might explain his inability to prepare patchouli alcohol by hydration of β-patchoulene. It was overlooked by Treibs[6] when he postulated **23** after having established the correct carbon skeleton of **17**. As anticipated, a mixture of α- and γ-patchoulene (**4**, **3**) was converted quantitatively to **17** on exposure to acids. The transformations discussed are formulated in Table I.

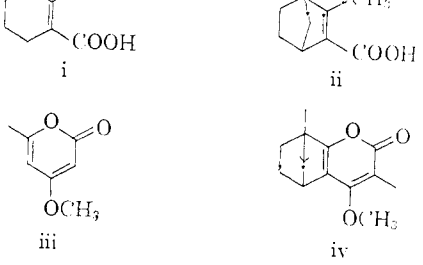
We shall now present arguments concerning the configurations of the five asymmetric centers in patchouli alcohol. As pointed out previously,[15] the absolute configuration at C_7 is established by conversion of **17** to **19** and **20** both related to (+)-camphor of known absolute configuration.[16] The arrangement of substituents at C_{3a} follows and if we assume for the time being that the two cyclopentane rings are *cis* fused we arrive at the ring system shown in **1**. We next investigated the configuration at C_4 and the results are summarized in Table II. For this purpose the reactions of norpatchoulione (**12**) with both methyllithium and methylmagnesium bromide were studied. Instead of the anticipated axial alcohol,[17] unaltered starting material was isolated. Dehydration of **1** with phosphorus oxychloride in pyridine gave a mixture of **4** (78%), **3** (7%) and **17** (7%). This means that the hydroxyl group is axial assuming a chair conformation for ring C.[17,18] Oxidation with peracetic acid produced a mixture of epoxides (**24** and **25**) and *trans*-α-patchouli diol (**26**). Isomerization of the

(10) W. Zimmermann, Ph.D. thesis, E. T. H., Zürich, 1933.

(11) E. Koller, Diplomarbeit, E. T. H., Zürich, 1948.

(12) Method of A. G. Anderson, J. A. Nelson and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4980 (1953).

(13) Compare i, λ_{max}^{EtOH} 225 mμ, with ii, λ_{max}^{EtOH} 234 mμ (E. R. H. Jones, G. H. Mansfield and M. C. Whiting, *J. Chem. Soc.*, 4073 (1956)), and iii, λ_{max}^{EtOH} 280 mμ, with iv, λ_{max}^{EtOH} 320 mμ (E. A. Chandross and P. Yates, *Chemistry & Industry*, 149 (1960).



(14) O. Wallach and W. Walker, *Ann.*, **271**, 285 (1892); O. Wallach and F. E. Tuttle, *ibid.*, **279**, 391 (1894).

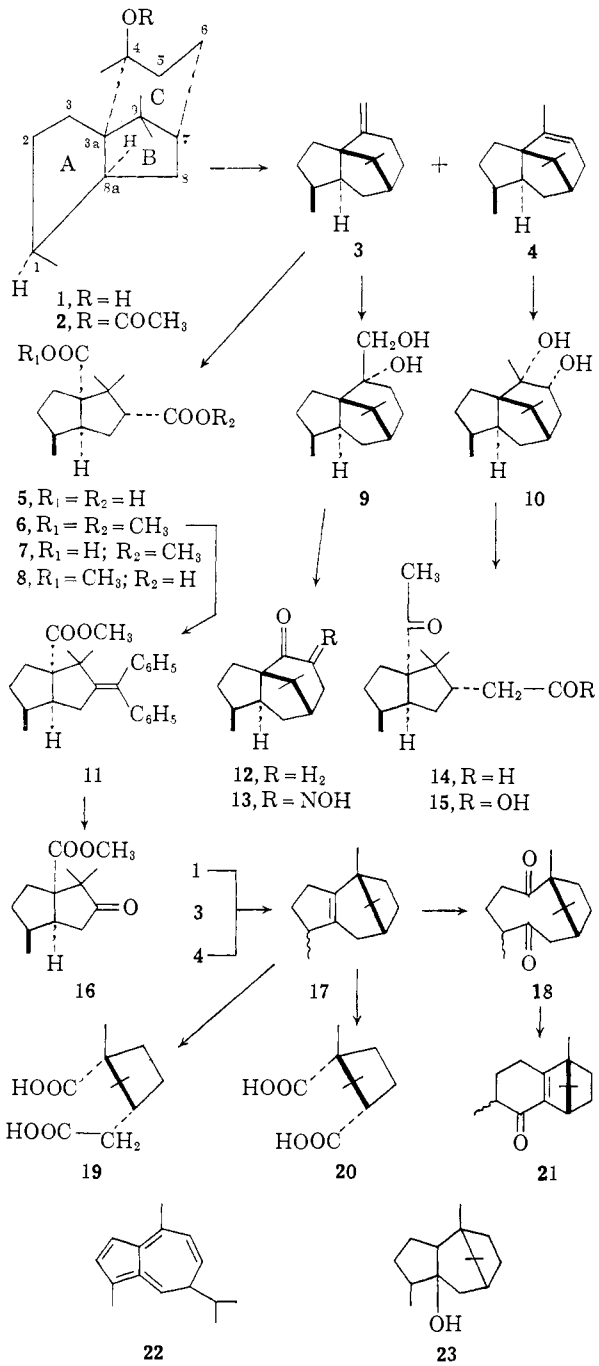
(15) W. Klyne, *Chemistry & Industry*, 725 (1954).

(16) A. Fredga and J. K. Miettinen, *Acta Chem. Scand.*, **1**, 371 (1947); K. Freudenberg and W. Lwowski, *Ann.*, **587**, 213 (1954); **594**, 76 (1955); V. Prelog, O. Ceder and M. Wilhelm, *Helv. Chim. Acta*, **38**, 303 (1955).

(17) G. Büchi, M. Schach v. Wittenau and D. M. White, *J. Am. Chem. Soc.*, **81**, 1968 (1959), and references cited.

(18) D. H. R. Barton, A. da S. Campos-Neves and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956); J. D. Cocker and T. G. Halsall, *ibid.*, 4262 (1956).

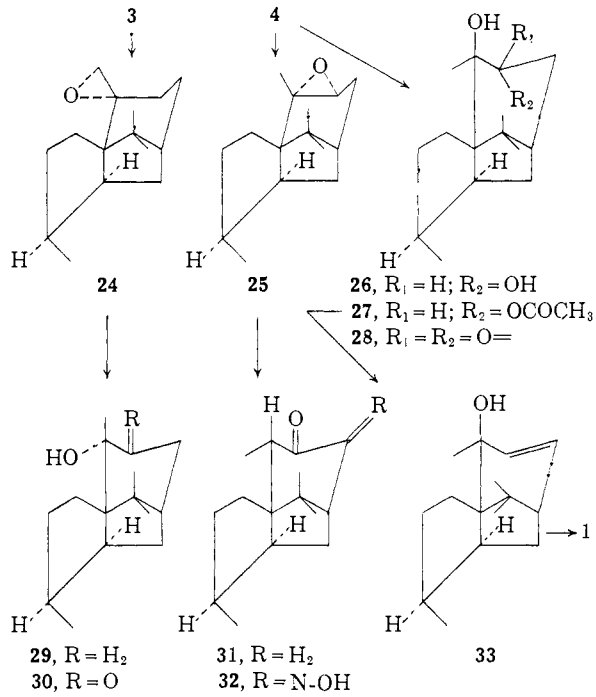
TABLE I



crude epoxides with boron trifluoride[19] afforded products from which a crystalline ketone could be isolated by fractional distillation. In agreement with **31** it exhibited infrared absorption (in CCl_4) at 1700 cm.$^{-1}$ and on equilibration with potassium deuteroxide in deuterioethanol[17] a trideuterioketone was obtained. Surprisingly, condensation with isoamyl nitrite yielded an oximino ketone (**32**), rather than the anticipated oximino ester.[8] Steric hindrance seems to prevent nitrosation of the $\Delta^{4,5}$-enol at C_4. This new ketone (**31**), which we have named patchoulione, can be prepared also by dehydration of **26**[20] or, more directly but not more efficiently, by ozonization of α-patchoulene (**4**). The course of the latter transformation became clear when we found that chromatography over alumina (used for the isolation of **31**) caused isomerization of the epoxide **25** to the ketone **31**. Formation of epoxides directly from unsaturated hydrocarbons and ozone has been observed with other hindered olefins.[21,22] Patchoulione (**31**) has a powerful odor reminiscent of ambergris and is being used in perfumery.[23]

(19) H. O. House, *J. Am. Chem. Soc.*, **78**, 2298 (1956).

TABLE II



Structure **26** for *trans*-α-patchouli diol rests on the following observations. (a) The method of preparation suggests a diaxial glycol and (b) its resistance to lead tetraacetate is also in agreement with the configuration assigned.[24] (c) Oxidation with potassium dichromate in acetic acid solution gave 5-oxopatchouli alcohol (**28**) which possessed infrared bands (in $CHCl_3$) at 3640 (free OH) and 3540 cm.$^{-1}$ (bonded OH). In contrast, 5-oxoepipatchouli alcohol (**30**) prepared from α-patchoulene (**4**) with potassium permanganate or by oxidation of **10** with chromium trioxide had $\gamma_{max}^{CHCl_3}$ 3550 cm.$^{-1}$ (bonded OH). These spectral characteristics[25] support the structures proposed and we now had to correlate patchouli alcohol with one of the epimeric acyloins or with the diol **26**.

(20) H. E. Eschinazi, personal communication.

(21) P. D. Bartlett and M. Stiles, *J. Am. Chem. Soc.*, **77**, 2806 (1955).

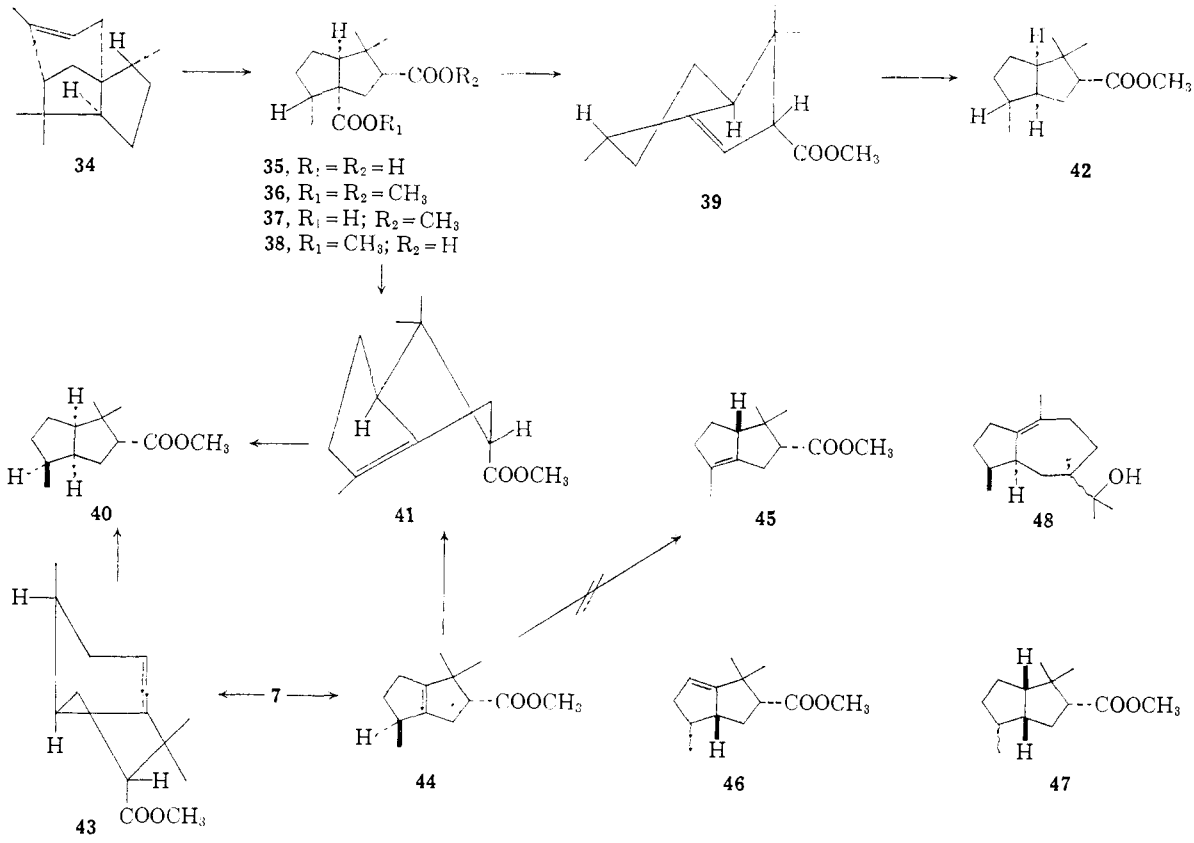
(22) I. A. Kaye, M. Fieser and L. F. Fieser, *ibid.*, **77**, 5936 (1955)

(23) G. Büchi and R. E. Erickson, U. S. Patent 2,942,029 (1960), assignors to the Givaudan Corporation, New York, N. Y..

(24) S. J. Angyal and R. J. Young, *J. Am. Chem. Soc.*, **81**, 5251 (1959), and other examples cited.

(25) N. L. Wendler, D. Taub, S. Dobriner and D. Fukushima, *ibid.*, **78**, 5027 (1956); A. R. H. Cole and G. T. A. Müller, *J. Chem. Soc.*, 1224 (1959).

TABLE III



Wolff–Kishner reduction of **28** yielded only α-patchoulene (**4**),[26] but the epimeric acyloin (**30**) gave some *epi*-patchouli alcohol (**29**) which was also available by reduction of epoxide **24** with lithium aluminum hydride but not from the isomeric epoxide **25** which is stable to this reagent.[27] These transformations show that additions to the double bonds in **3** and **4** occur consistently from the less hindered α-side of the molecule and demand α-configuration of the hydroxyl group in *epi*-patchouli alcohol (**29**). By exclusion the naturally-occurring alcohol must be **1** and this was confirmed as follows. The monoacetate **27** prepared by acetylation of **26**, on pyrolysis produced the allylic alcohol **33** which was reduced to **1**. Furthermore, the mass spectra of the two pairs of epimeric alcohols (**1**/**29**) and (**28**/**30**) are in agreement with the configurations assigned.[28]

We shall now discuss the configuration at C_1 (see Table III). The stereochemistry of cedrene (**34**) has been ascertained by degradative work[29,30] and particularly by a stereospecific total synthesis.[31] Norcedrenedicarboxylic acid (**35**) and norpatchoulidicarboxylic acid (**5**) have similar structures and correlation should be possible by removal of the tertiary carboxyl groups. This would establish the configuration at the remaining center in patchouli alcohol and the absolute configuration of cedrene. Exploratory work was carried out with the known[32,33] and more readily available norcedrenedicarboxylic acid monomethylester (**37**). Hunsdiecker degradation, using a variety of conditions, gave no identifiable products. We next attempted to effect decarboxylation by electrolysis, a method used successfully for the removal of the tertiary carboxyl group in camphoric acid (**20**).[34] In agreement with a report by Ruzicka,[32] electrolysis of **37** in methanol solution gave a complex mixture of products. Gas chromatography indicated the presence of at least seven individual compounds and a mass spectrum[35] showed that none of them had the molecular weight of the anticipated unsaturated ester. After these failures we examined the reaction of the half-ester **37** with lead tetraacetate. This approach was based on the hypothesis that a mixed lead ester (D), formed by transesterification, might decompose to an olefin, lead acetate, acetic acid and carbon dioxide as indicated (arrows). Such oxidative decarboxylations

(26) Other axial α-hydroxycyclohexanones have been found to undergo essentially complete elimination; R. B. Turner, R. Anliker, R. Helbling, J. Meier and H. Heusser, *Helv. Chim. Acta*, **38**, 411 (1955).

(27) Similarly, α-pinene epoxide is not reduced by lithium aluminum hydride; R. N. Moore, C. Golumbic and G. S. Fisher, *J. Am. Chem. Soc.*, **78**, 1173 (1956).

(28) K. Biemann and J. Seibl, *ibid.*, **81**, 3149 (1959).

(29) G. Stork and R. Breslow, *ibid.*, **75**, 3291 (1953).

(30) Pl. A. Plattner, A. Fürst, A. Eschenmoser, W. Keller, H. Kläui, St. Meyer and M. Rosner, *Helv. Chim. Acta*, **36**, 1845 (1953).

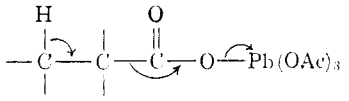
(31) G. Stork and F. H. Clarke, Jr., *J. Am. Chem. Soc.*, **77**, 1072 (1955).

(32) L. Ruzicka and J. A. van Melsen, *Ann.*, **471**, 40 (1929).

(33) Pl. A. Plattner, G. W. Kusserow and H. Kläui, *Helv. Chim. Acta*, **25**, 1345 (1942).

(34) J. Walker and W. Cormack, *J. Chem. Soc.*, **77**, 374 (1900).

(35) We are much indebted to Prof. K. Biemann and Dr. J. Seibl for the mass spectra and their interpretation. They were taken on a CEC 21-103C mass spectrometer equipped with a heated inlet system (135°) using an ionization potential of 70 v.



D

have been accomplished and interpreted in similar terms.[36] When a solution of **37** in benzene was heated with approximately two equivalents of lead tetraacetate, two isomeric unsaturated esters, separable by gas chromatography, were produced. One of these (**39**) had infrared absorption (in CCl_4) at 1732, 1663 and 846 cm.$^{-1}$ and a nuclear magnetic resonance spectrum showed well defined peaks at 8.95 (3H), 8.85 (3H) (CH_3–C–CH_3); a doublet (3H) centered at 8.78, J 8 c.p.s. (CH_3–C–H), 6.16 (3 H, $COOCH_3$) and 4.54 τ (broad) (1H, >C=C<H). The other again was not an α,β-unsaturated ester and both the infrared and the nuclear magnetic resonance spectra,[37] the latter containing significant peaks at 9.17 (3H), 9.07 (3H) (CH_3–C–CH_3), 8.37 (3 H) (CH_3C=C) and 6.40 τ (3H) ($COOCH_3$), were in agreement with structure **41**. Although the preferred conformations of bicyclo[3.3.0]octenes are unknown it seems reasonable that the ring with the exocyclic double bond is a half-chair while the other is forced into an envelope by the endocyclic double bond.[38] The puckering in each cycle is dictated by the angular hydrogen atom which should be axial in the envelope and pseudo-axial in the half chair. Molecular models suggest formation of *cis*-bicyclo[3.3.0]octanes on catalytic reduction of **39** and **41** (see also ref. 31) and in practice both were readily reduced to **42** and **40**, respectively. In agreement with prediction, the mass spectra showed a higher ratio of $(M)^+$ to $(M-15)^+$ in **42** demonstrating greater stability (*exo*-methyl configuration!).[28]

To continue the degradation in the patchouli series we had to prepare the correct monomethyl ester **7**. Esterification of norpatchoulidicarboxylic acid (**5**) with methanol in the presence of sulfuric acid under conditions previously used for the preparation of the corresponding ester **37** yielded the dimethyl ester **6** exclusively. In **35** the tertiary carboxyl group is hindered by both a *cis*-1,2- and a *cis*-1,3-carboxyl → methyl interaction. We can rationalize the higher reactivity of the tertiary carboxyl group in **5** if the 1,3-interaction is missing. Consequently the methyl group in **5** seems to have *endo*-configuration and this agrees with a more rigorous argument to be presented. The desired monoester was eventually prepared by esterification of **5** under much milder conditions and isolated in crystalline form after purification through the benzylammonium salt. Its structure follows from the following observations. Treatment of norpatchoulidicarboxylic acid anhydride with sodium methoxide yielded the same ester **7** and its isomer **8** was available by partial saponification of **6**. Interestingly the frequencies of the C=O stretching vibrations in the tertiary carboxyl groups are lower than anticipated. They occur at 1690 cm.$^{-1}$ in the two acids **7**/**37** and at 1725 cm.$^{-1}$ in the two esters **8**/**38** while the two secondary acids and the corresponding esters absorb normally at 1700 and 1735 cm.$^{-1}$, respectively. Oxidative decarboxylation of **7** with lead tetraacetate produced three isomeric unsaturated esters and a small amount of an unidentified acetoxyester. One (**43**) was isolated by adsorption chromatography and identified as such by the presence of infrared absorption at 1735, 1630 (CCl_4) and 825 cm.$^{-1}$ (pure liquid). It exhibited characteristic peaks in the nuclear magnetic resonance spectrum[37] at 9.00, 8.91 (6H, CH_3–C–CH_3); doublet centered at 8.91, J 6 c.p.s. (3H, CH_3–C(H)–); 6.41 (3H, $COOCH_3$) and 4.97 τ (broad, 1H, >C=C<H). The other two isomers were separated by gas chromatography and one was shown to be identical with **41** which we had previously synthesized from cedrene. It must have been formed by acetic acid-catalyzed isomerization of the primary decarboxylation product **44**. Scale models demonstrate that both rate and thermodynamic control favor **41** over **45** which has the carbomethoxy group in the *endo* configuration. A third isomer formed in the decarboxylation of **7** seemed to be the result of a rearrangement because its nuclear magnetic resonance spectrum no longer showed the peaks characteristic of the geminal dimethyl system. Catalytic reduction of **43** yielded the saturated ester **40**. Identity was established by comparison of infrared and mass spectra, optical rotation and retention time in the gas chromatogram. We have assumed *cis*-fusion of the two cyclopentane rings in patchouli alcohol. If they were *trans*-fused the unsaturated ester and its dihydro derivative would be represented by **46** and **47**, respectively. The identity of the saturated ester with **40** of established configuration clearly contradicts this assumption and the complete structure of patchouli alcohol is **1**. Formula **34** then expresses the absolute configuration of cedrene and agrees with that deduced from the rotatory dispersion curve of norcedranone.[39] Patchouli alcohol (**1**) is a formal cyclization product of bulnesol (**48**)[40] if the latter sesquiterpene has the 7-β isopropyl configuration and this relationship may have biogenetic significance.

Acknowledgment.—We are much indebted to the Givaudan Corporation for financial support and to Dr. Max Luthy for his interest in the problem. The patchouli oil was kindly provided by Dr. E. Guenther.

(36) W. A. Mosher and C. L. Kehr, THIS JOURNAL, **75**, 3172 (1953); L. L. McCoy and A. Zagalo, *J. Org. Chem.*, **25**, 824 (1960).

(37) N.m.r. spectra, made available through the courtesy of Prof. E. J. Corey, were measured on a Varian Associates instrument in carbon tetrachloride with tetramethylsilane as internal reference. Peak positions are in τ values [G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)].

(38) F. V. Brutcher, Jr., T. Roberts, S. J. Barr and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959), and earlier work cited.

(39) Prof. G. Stork, personal communication.

(40) L. Dolejš, A. Mironov and F. Šorm, *Tetrahedron Letters*, **11**, 18 (1960); E. J. Eisenbraun, T. George, B. Riniker and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 3648 (1960).

Experimental

Microanalyses by Dr. S. M. Nagy and associates, M. I. T. Melting points were taken on a Kofler hot-stage microscope and are corrected. Ultraviolet spectra were measured on a Cary recording spectrophotometer, model 11. Infrared spectra, unless otherwise indicated, were determined on a Perkin–Elmer instrument, model 21, by Mrs. N. F. Alvord. High intensity infrared bands and others relevant to the structural arguments are listed textually. The activity of alumina used for chromatograms was controlled using the method of Brockmann.[41]

Patchouli Alcohol (1).—Commercial oil of patchouli was obtained from Fritzche Bros., Inc., New York, and distilled at 15–17 mm. through a short Vigreux column. The fraction (approximately 50–60% of the original oil) boiling at 160–170° solidified on cooling and was recrystallized from *n*-pentane at −70° to yield pure patchouli alcohol, m.p. 55–56°, pure or mixed with a sample prepared in the laboratories of Prof. L. Ruzicka, Zürich, Switzerland. An infrared spectrum was identical with that of the authentic sample. The compound gave no color reaction with tetranitromethane: $[\alpha]^{27}D$ −129° (*c*, 4.02 in $CHCl_3$).

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.99; H, 11.65.

Patchouli Acetate (2).—Patchouli alcohol (30 g., 0.135 mole) was added to a solution of 1 ml. of concentrated sulfuric acid in 300 ml. of anhydrous ether (cooled to −5° under a calcium chloride drying tube) and allowed to react with ketene (approximately 0.22 mole) by bubbling in the reagent directly from the generator for 45 minutes. At the end of the reaction time the ether solution was poured into cold water. The ether layer was separated and washed with water, 5% sodium carbonate solution, water, and dried over anhydrous magnesium sulfate. Removal of the ether yielded 33.7 g. of a colorless oil. The crude product was distilled through a semi-micro column at 17 mm. and separation of material boiling up to 140° afforded a pale yellow oil (8.09 g., 26%), which was separated by redistillation, and β-patchoulene (**17**), b.p. 66.5–67.5° (0.4 mm.), and α,γ-patchoulene (**4,3**), b.p. 74–75° (0.4 mm.), identified by their infrared spectra. Pressure and temperature in the column were then reduced and a second fraction (19.82 g., 56%) was obtained, b.p. 102–130° (0.2 mm.). Careful fractionation of a portion of the product through the same column gave patchouli acetate, b.p. 101–101.5° (0.2 mm.), $n^{25}D$ 1.5010, d^{20}_4 1.043, $[\alpha]^{30}D$ − 71°. The melting point was determined to be approximately 24°. The compound did not give any color reaction with tetranitromethane; infrared spectrum (pure liquid) 2941–2841, 1715, 1460, 1361, 1307, 1250, 1186, 1160, 1105, 1031–1000, 961, 934, 909, 877, 855, 781, 746, 724, 690 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.05; H, 10.64.

In subsequent runs the following modifications were employed. Ketene was bubbled into 200 ml. of anhydrous ether (protected by a calcium chloride drying tube) at −70° for 1 hour. A solution of patchouli alcohol (30.0 g., 0.135 mole) in 50 ml. of dry ether was added followed by a solution of 1 ml. of concentrated sulfuric acid in 50 ml. of dry ether. Ketene was bubbled through for an additional 30 minutes and the reaction was worked up as above. Yields of 60–65% of patchouli acetate were obtained in this manner.

Conversion of Patchouli Acetate (2) to Alcohol (1).—The acetate (**2**) (0.98 g.) was dissolved in anhydrous ether and added slowly to excess lithium aluminum hydride in ether. The mixture was heated under reflux for 6 hours and the excess reagent destroyed with ethyl acetate. The resulting precipitate was dissolved in 10% sodium hydroxide solution, the ether layer separated, washed with water, and dried over anhydrous magnesium sulfate. Removal of the ether afforded a crystalline product which was recrystallized from cold petroleum ether to give 0.62 g. (75%) of patchouli alcohol, m.p. 56.5–58°, pure or mixed with an authentic sample.

Pyrolysis of Patchouli Acetate (2).—Patchouli acetate (8.0 g., 0.03 mole), in a 25-ml. one-neck round-bottom flask with a 20-cm. Vigreux column leading to an ice-cooled receiver, was heated in a Wood metal-bath to 250°. Acetic acid was evolved slowly and collected in the receiver. The temperature was raised slowly to just maintain the evolution of acetic acid and keep the temperature of the vapors at the top of the Vigreux column below 120°. At a bath temperature of 320°, the product began to reflux and was maintained at this temperature for 30 minutes. The weight of the acetic acid was 1.3 g. (72%). After cooling to 27°, product and distillate were combined and dissolved in ether. The ether solution was washed with water, dilute potassium hydroxide solution, water and dried over anhydrous magnesium sulfate. Removal of the ether yielded 6.3 g. of yellow oil which on distillation through a semi-micro column at 17 mm. afforded one major fraction and about 1 g. of a non-distillable residue. Redistillation of the major fraction through the same column afforded α,γ-patchoulene, b.p. 141–142° (17 mm.), $n^{25}D$ 1.5075, d^{20}_4 0.9537, $[\alpha]^{30}D$ −44°. The compound gave a yellow color with tetranitromethane.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.34; H, 11.82.

α,γ-Patchoulene (4,3).—In a 1000-ml. round-bottom flask containing 400 ml. of pyridine was added patchouli alcohol (24 g., 0.11 mole). To this solution 140 ml. of phosphorus oxychloride was added at once and the flask was equipped with a reflux condenser protected with a drying tube. The reaction mixture was allowed to relux for 6 hours and was then cooled to room temperature. Crushed ice was placed in a 10-cm. glass column and the dark purple reaction mixture was poured slowly through the column and more ice added when necessary to prevent overheating. The mixture was extracted with ether and the ether layer washed with 10% hydrochloric acid and then with water until neutral, dried over sodium carbonate, filtered, and the ether removed on a steam-bath. Distillation of the product through a Vigreux column gave 21.8 g. (91%) of α,γ-patchoulene as a colorless liquid, b.p. 53.5–54.5°(0.14 mm.), 141–142° (17 mm.).

cis-α-Patchoulidiol (10).—α,γ-Patchoulene was oxidized with osmium tetroxide by the procedure used for the oxidation of β-patchoulene. In a typical run, 6.65 g. (0.033 mole) of α,γ-patchoulene yielded 5.24 g. (68%) of α,γ-patchoulidiols, m.p. 85–90°. The mixture of glycols (*ca.* 4 g.) was dissolved in petroleum ether and passed through a column containing 130 g. of alumina (IV). Petroleum ether containing increasing concentrations of ethyl acetate was used to elute the glycols. Crystalline α-patchoulidiol (2.04 g.) was eluted with 20% ethyl acetate–petroleum ether and recrystallized from petroleum ether to constant m.p. 107–108°; infrared spectrum (CCl_4, CS_2): 3279, 2941, 2857, 1449, 1370, 1117, 1099, 1064, 1044, 1026, 990, 970, 926 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.61; H, 10.84.

γ-Patchoulidiol (9).—The same column was eluted with 50% ethyl acetate–petroleum ether to give γ-patchouli diol (2.10 g.), recrystallized from petroleum ether to constant m.p. 95–96°; infrared spectrum (CCl_4, CS_2): 3279, 2941, 2857, 1449, 1370, 1333, 1227, 1149, 1036, 990, 980, 961, 943, 930, 888, 855 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.75; H, 11.06.

Patchouliketocarboxylic Acid (15) (Patchouliketoaldehyde, 14).—α-Patchoulidiol (100 mg., 0.42 mmole) in acetic acid was oxidized with lead tetraacetate (220 mg., 0.5 mmole) by the procedure used for the oxidation of β-patchouli diol except that a gentle stream of nitrogen was passed through the reaction mixture into a trap containing a solution of dimedone in 95% ethanol. At the end of the reaction, no formaldehyde derivative had been formed. The product obtained after work up was treated with 2,4-dinitrophenylhydrazine reagent and gave an immediate reaction yielding a yellow derivative, recrystallized from methanol to constant m.p. 161–161.5°.

Anal. Calcd. for $C_{21}H_{28}N_4O_5$: C, 60.56; H, 6.78. Found: C, 60.61; H, 6.79.

The oxidation was repeated on a fourfold scale without the use of nitrogen. After working up the reaction, a practically quantitative yield of crystalline material was obtained which was recrystallized from petroleum ether and cyclohexane to constant m.p. 82.5–83.5°; infrared spectrum (CCl_4, CS_2): 3226–2500, 1695, 1471, 1404, 1389, 1366, 1348, 1295, 1253, 1233, 1212, 1174, 1136, 952–925 cm.$^{-1}$.

(41) H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941).

Anal. Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.30; H, 9.60.

The compound was found to be soluble in sodium carbonate solution, did not give a derivative with 2,4-dinitrophenylhydrazine reagent, and did not give a positive iodoform test. Treatment with hydroxylamine hydrochloride and potassium hydroxide in water in the usual manner afforded an oximino acid, recrystallized from aqueous ethanol to constant m.p. 164–165°.

Anal. Calcd. for $C_{15}H_{25}NO_3$: C, 67.38; H, 9.43. Found: C, 67.39; H, 9.44.

Norpatchoulione (12).—γ-Patchouli diol (100 mg., 0.42 mmole) in acetic acid was oxidized with lead tetraacetate (220 mg., 0.5 mmole) by the procedure used for the oxidation of β-patchouli diol. From the "dimedone trap" there was isolated 35 mg. (30%) of formaldehyde-dimedone adduct, m.p. 191–192°, pure or mixed with an authentic sample. The product obtained after work up was treated with 2,4-dinitrophenylhydrazine reagent and gave no immediate reaction. After a day, there was isolated an orange derivative, recrystallized from aqueous ethanol to constant m.p. 144–145°.

Anal. Calcd. for $C_{20}H_{26}N_4O_4$: C, 62.16; H, 6.78. Found: C, 61.88, 61.90; H, 6.85, 6.60.

In a second preparation norpatchoulione was purified by adsorption on alumina (I). Elution with 10% benzene–hexane gave an oil that could not be crystallized and was distilled for analysis; infrared spectrum in CS_2: 2940, 1706, 1266, 980, 848, 806 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 80.94; H, 10.45.

α-Oximinonorpatchoulione (13).—To a solution of norpatchoulione (200 mg., 1.0 mmole) in 1.3 ml. of dry ethanol was added 0.7 ml. of a solution of sodium ethoxide (60 mg./ml.) in dry ethanol. The mixture was cooled in an ice-bath and freshly distilled isoamyl nitrite (0.16 ml., 1.4 mmoles) was added. After warming to 27° over a period of 15 hours, the reaction mixture was worked up in the usual manner and the crude product dissolved in petroleum ether and passed through a column of 10 g. of silica gel. Solvent mixtures containing increasing concentrations of ethyl acetate in petroleum ether were used until 50% ethyl acetate–petroleum ether eluted a viscous oil which crystallized on trituration with petroleum ether. The product (125 mg., 53%) was recrystallized from petroleum ether to constant m.p. 131.5–132°, λ_{max}^{EtOH} 234 (8400).

Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.45; H, 9.00. Found: C, 71.65; H, 9.04.

Norpatchoulidicarboxylic Acid (5).—To a suspension of α,γ-patchoulene (8.44 g., 0.041 mole) in 20 ml. of acetone and 5 ml. of water was added, in portions, 10.0 g. (0.063 mole) of powdered potassium permanganate with vigorous stirring. The oxidation was allowed to continue for 15 hours and the reaction mixture was diluted with water, cooled and saturated with sulfur dioxide gas until practically colorless. The mixture was then extracted with ether and the ether extracts washed with dilute sodium bicarbonate solution. All basic extracts were acidified with hydrochloric acid, extracted with ether and the ether solution washed with water, dried over anhydrous magnesium sulfate and concentrated to 2.24 g. of acidic product. It was then heated under reflux with 4 ml. of water while 10 ml. of concentrated nitric acid was added carefully. Heating was continued for 1 hour and the mixture cooled and poured into water. Organic material was extracted into ether and the ether solution washed with small portions of water until the washes were almost neutral. The solution was dried over anhydrous magnesium sulfate, the ether removed and replaced with about 5 ml. of formic acid. After standing at 5° for several days, the solution deposited colorless crystals which were separated and recrystallized from formic acid and/or ligroin to constant m.p. 225–227°; infrared spectrum (KBr): 3333–2500, 1695, 1672, 1449, 1408, 1379, 1307, 1282, 1266, 1250, 1235, 1188, 1087, 1064, 1053, 940, 728 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.92; H, 8.33.

Norpatchoulidicarboxylic Acid Anhydride.—A solution of 3 g. of norpatchoulidicarboxylic acid in 50 ml. of acetic anhydride was refluxed for 1 hour. The acetic acid and the acetic anhydride were removed by distillation under reduced pressure and the light brown crystalline residue sublimed and recrystallized from hexane giving colorless needles, m.p. 110.5–112.0°, $[\alpha]^{31}D$ + 38° (*c* 0.51, $CHCl_3$).

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.21; H, 8.04.

Dimethyl Norpatchoulidicarboxylate (6).—To a solution of crude norpatchoulidicarboxylic acid (2.0 g., 0.0083 mole) in 50 ml. of ether was added slowly an ether solution of diazomethane (prepared from 3.3 g., 0.037 mole, of N-nitrosomethylurea by adding the compound in portions to a cooled, saturated potassium hydroxide solution covered with ether) and the mixture allowed to stand overnight. The solution was dried over anhydrous magnesium sulfate and the ether removed to yield 1.82 g. of crude diester which was dissolved in benzene and passed through a column of 40 g. of alumina (I). Benzene eluted 1.01 g. (43%) of diester as a colorless oil; infrared spectrum (CCl_4): 2857, 1709, 1453, 1429, 1366, 1266–1235, 1220, 1163, 1066, 1020, 995 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 67.45; H, 8.90.

Hydrolysis of Norpatchoulidicarboxylic Acid Anhydride.—To 5 ml. of a saturated solution of sodium carbonate in water was added 50 mg. (0.23 mmole) of norpatchoulidicarboxylic acid anhydride and the mixture subsequently refluxed for 1 hour. The solution was extracted with ether, the aqueous phase acidified with hydrochloric acid, extracted with ether, the ether layer washed with water, dried over magnesium sulfate, and concentrated to yield 33 mg. (61%) of crude norpatchoulidicarboxylic acid. The product was recrystallized from 85% formic acid and had m.p. 226–227°, mixed m.p. 225-226° with authentic norpatchoulidicarboxylic acid.

Barbier–Wieland Degradation of 6.—A solution of phenylmagnesium bromide in ether was prepared in the usual manner and titrated to determine its concentration. To 5 ml. (5.13 mmoles of phenylmagnesium bromide) of this solution in 10 ml. of dry ether was slowly added with stirring 500 mg. (1.87 mmoles) of the diester in 10 ml. of dry ether. The mixture was heated under reflux for 2 hours, cooled and treated with a solution of 5 g. of ammonium chloride in 15 ml. of water. The ether layer was separated and the water extracted once with ether. The combined ether extracts were washed with water and dried over anhydrous magnesium sulfate. After the ether had been evaporated the resulting crude diphenylcarbinol ester was taken up in 1 ml. of acetic anhydride and 2 ml. of acetic acid and heated under reflux for 2 hours. The solution was taken to dryness and the residue dissolved in *n*-hexane and passed through a column containing 30 g. of alumina (I). Hexane eluted biphenyl and 50% benzene–hexane eluted 180 mg. (26%) of diphenylethylene ester. Rechromatography in 50% benzene–hexane over alumina followed by recrystallization from petroleum ether afforded the pure compound, m.p. 154–155°, λ_{max}^{EtOH} 227 (11,200).

Anal. Calcd. for $C_{26}H_{30}O_2$: C, 83.38; H, 8.07. Found: C, 83.17; H, 7.91.

Ozonization of 11.—A solution of the diphenylethylene ester (84 mg., 0.22 mmole) in 5 ml. of acetic acid was allowed to react with ozone (*ca.* 3 mg./min., output of Welsbach Ozonizer, model T19, with oxygen input) at 27° for 7 hours. The solution was concentrated *in vacuo*, suspended in 25 ml. of water and heated under reflux for 30 minutes. Organic material was extracted from the cooled mixture with ether, the ether extracts washed with water, dilute sodium bicarbonate solution and dried over anhydrous magnesium sulfate. Removal of the ether afforded 40 mg. of pale yellow oil which was dissolved in 5% benzene–petroleum ether and passed through a column of 3 g. of alumina (I). The product (15 mg.) was eluted with 50% benzene–petroleum ether and distilled for analysis; infrared spectrum in CS_2: 2940, 1739, 1282, 1110, 1064 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 68.41; H, 9.30.

β-Patchoulene (17). A.—A solution of patchouli alcohol (5.0 g., 0.023 mole) and concentrated sulfuric acid (1.0 g.) in 50 ml. of anhydrous ethyl ether was heated under reflux for 30 minutes. After 15 minutes the reaction mixture had separated into two phases. At the end of the reaction, the mixture was poured into water and the ether

layer separated and washed with water, dilute sodium bicarbonate solution, water, and dried over anhydrous magnesium sulfate. The ether was removed and the resulting oil distilled through a semi-micro column. Most of the material (3.2 g., 70%) distilled at 66–68° (0.6 mm.) and was dissolved in *n*-hexane and passed through a column containing 225 g. of alumina (I). The hydrocarbon was eluted with *n*-hexane (25-ml. fractions) and each fraction distilled under reduced pressure for the determination of its index of refraction and specific rotation.

Fraction	Weight, g.	$n^{25}D$	$[\alpha]^{30}D$ (*c*, chloroform)
1–9	0.00	....	.....
10	.21	1.4964	.....
11	.89	1.4978	−42.3° (10.14)
12	1.05	1.4978	−42.6 (10.51)
13	0.55	1.4977	−43.7 (10.54)
14	.17	1.4989	.....
15	.03	....	.....

β-Patchoulene (fraction 12) gave an intense orange-brown color with tetranitromethane and was distilled for analysis; infrared spectrum (pure liquid): 2857, 1493, 1471, 1380, 1360, 1190, 1111, 1064, 970, 952, 926 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.31; H, 12.12.

B.—A mixture of patchouli alcohol (5.0 g., 0.023 mole) and a crystal of iodine was heated under reflux at 15–17 mm. for 1 hour. The product was distilled through a semi-micro column at 0.2 mm. and chromatographed over alumina to yield 2.6 g. (57%) of β-patchoulene identical with that obtained above (infrared spectrum).

C.—Dehydration of patchouli alcohol according to the procedure of O'Connor and Nace[42] proceeded smoothly and in good yield to give β-patchoulene (infrared spectrum).

D.—α,γ-Patchoulene was treated with sulfuric acid in ether as described for the dehydration of patchouli alcohol. The ether solution was separated, washed with dilute sodium bicarbonate solution, water, and dried over anhydrous magnesium sulfate. Removal of the ether yielded a colorless oil which was distilled under reduced pressure and found to be identical with β-patchoulene (infrared spectrum).

β-Patchouli Diol.—A solution of β-patchoulene (0.83 g., 0.0041 mole) in 5 ml. of reagent pyridine was added slowly and with cooling to a solution of osmium tetroxide (1.0 g., 0.0038 mole) in 10 ml. of reagent pyridine and the mixture allowed to stand for 21 days at 27°. Most of the pyridine was removed *in vacuo* and the brown residue was taken up in a mixture of benzene (20 ml.) and ethanol (20 ml.), to which was added mannitol (14 g.) and a solution of potassium hydroxide (14 g.) in a mixture of water (35 ml.) and ethanol (70 ml.). The mixture was heated under reflux for 6 hours, allowed to cool to 27°, concentrated *in vacuo* to half its volume and extracted with 3 volumes of ether. All ether extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the ether yielded 1.02 g. of a viscous oil which was dissolved in petroleum ether and passed through a column of alumina (IV) (30 g.). Petroleum ether eluted 0.46 g. (48%) of crystalline product which was recrystallized from petroleum ether to constant m.p. 122.8–123.5°; infrared spectrum (CCl_4, CS_2): 3571, 3472, 2899, 1475, 1453, 1389, 1370, 1333, 1290, 1133, 1087, 1038, 1000, 975, 898, 828 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.37; H, 10.77.

In a second preparation of β-patchouli diol on a larger scale a yield of 65% of recrystallized material was obtained.

Patchoulidione (18).—A mixture of β-patchouli diol (200 mg., 0.84 mmole) in 10 ml. of reagent acetic acid and lead tetraacetate (440 mg., 1.0 mmole) in 10 ml. of reagent acetic acid was allowed to react for 14 hours at 27°. The reaction mixture was poured into water and the organic material extracted with ether. Ether extracts were washed with water, cold dilute sodium bicarbonate solution, water, and dried over anhydrous magnesium sulfate. Removal of the ether yielded a crystalline product which was recrystallized from cold petroleum ether to constant m.p. 95–96°; infrared spectrum (CCl_4, CS_2): 2874, 1695, 1481, 1453, 1427, 1393, 1370, 1333, 1163, 1149, 1087, 1053, 1036, 1000, 990 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.12; H, 9.96.

Unsaturated Ketone 21.—Cyclization of patchoulidione 18 was accomplished with several different catalysts.

A.—To a solution of *ca.* 30 mg. of patchoulidione in a few drops of methanol at 0° was added slowly 5 ml. of a 5% solution of sodium methoxide in methanol and the mixture allowed to come to 27° overnight. After removal of the methanol *in vacuo*, the product was taken up in water and extracted into ether. Removal of the ether after drying over anhydrous magnesium sulfate yielded a crystalline product which, after sublimation, had m.p. 76–78°, λ_{max}^{EtOH} 260 (11,000); infrared spectrum in CS_2: 2858, 1656, 1613, 1389, 1235, 1099, 926, 893, 870 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.44; H, 10.27.

B.—A solution of *ca.* 30 mg. of patchoulidione in petroleum ether was passed through a column containing basic (*p*H 8–9) alumina (3 g.). After 15 hours on the column, the product was eluted with 10% acetone–petroleum ether and after treatment with 2,4-dinitrophenylhydrazine reagent yielded a red derivative which was recrystallized from ethanol to constant m.p. 165–166°, λ_{max}^{EtOH} 392 (27,000).

Anal. Calcd. for $C_{21}H_{26}N_4O_4$: C, 63.30; H, 6.58. Found: C, 63.27; H, 6.79.

In a second preparation the crude product was sublimed and the crystalline sublimate recrystallized from petroleum ether to constant m.p. 79.5–80°. A 2,4-dinitrophenylhydrazone identical to that described above was prepared from this crystalline product.

C.—A solution of patchoulidione (100 mg.) in 5 ml. of anhydrous ethyl ether was allowed to react with 1 ml. of boron trifluoride etherate at 27° for 2 days. The reaction mixture was poured into water and the aqueous layer extracted with additional ether. Ether extracts were washed once with water and then dried over anhydrous magnesium sulfate. The ether was removed and a petroleum ether solution of the residue passed through a column of neutral alumina (I) (3 g.). Elution of the column with 5% ethyl acetate–petroleum ether afforded a practically quantitative yield of 21, m.p. 78–79°, indistinguishable from any of the above preparations.

Oxidation of β-Patchoulene (17). A. Ozone.—A solution of β-patchoulene (2.0 g., 0.0098 mole) in 50 ml. of reagent ethyl acetate was allowed to react with ozone (output of Welsbach ozonizer, model T19, with oxygen input) at −70° until the solution showed the characteristic blue color of a saturated ozone solution. The mixture was then poured onto ice and allowed to stand for 20 hours. Ethyl acetate was removed *in vacuo* and the aqueous residue heated under reflux for 2 hours. The organic material was extracted with ether and the ether extracts were washed with cold 1% sodium hydroxide solution, water, and dried over anhydrous magnesium sulfate. Removal of the ether afforded 1.8 g. of a brown oil which could not be further purified. Basic extracts were acidified with hydrochloric acid and the acids extracted with ether. The ether extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the ether gave 0.65 g. of partially crystalline material which was purified by repetition of the salt–acid extraction, decolorization of the product in acetone–water with activated charcoal, and crystallization from acetone–water followed by isopropyl ether–petroleum ether to give pure homocamphoric acid (19), m.p. 239–240°, $[\alpha]^{26}D$ + 66° (*c* 1.80, methanol); lit.[6]: m.p. 234°, $[\alpha]D$ +66° 14′ (methanol).

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.48; H, 8.21.

B. **Chromic Acid.**[6]—To a stirred solution of β-patchoulene (11.5 g., 0.056 mole) in 120 ml. of acetic acid was added a solution of chromium trioxide (34.5 g., 0.35 mole) in 115 ml. of 65% acetic acid over a period of 2 hours at 27°. After being heated on the steam-cone for 30 minutes, the mixture was cooled and excess acetic acid distilled under reduced pressure. The residue was shaken with 150 ml. of 40% sulfuric acid and extracted several times with ether. Ether extracts were washed with sodium carbonate solution,

(42) G. L. O'Connor and H. R. Nace, *J. Am. Chem. Soc.*, **77**, 1578 (1955).

water, and dried over anhydrous magnesium sulfate. Removal of the ether yielded 5.82 g. of a neutral oil. The basic solutions were washed once with ether, acidified with hydrochloric acid, and the acids extracted with ether. The ether extracts were washed with water and dried over anhydrous magnesium sulfate and yielded 4.85 g. of acidic material. All attempts to isolate the keto acid described by Treibs,[6] Zimmerman,[10] and Koller[11] failed. The acids were separated by dissolving the mixture in hot acetone, adding water and boiling until most of the acetone had been removed. On cooling the solution crystals of homocamphoric acid separated, m.p. 241–242°, pure or mixed with a sample obtained by ozonolysis.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.62; H, 8.54.

The more water-soluble camphoric acid was extracted with ether and recrystallized from benzene–ligroin to constant m.p. 186–187°; lit.[6] m.p. 187°.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.30; H, 8.14.

A portion of the camphoric acid was heated under reflux in acetic anhydride for 20 hours and the resulting anhydride recrystallized from ligroin to constant m.p. 227–227.5°; lit.[6] m.p. 221°.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.83; H, 7.69.

Dehydrogenation of Patchouli Alcohol (1).—Dehydrogenations were carried out by the method of Anderson.[12] The dehydrogenation tube was loosely charged with 2.0 g. of palladium-on-charcoal catalyst supported on 2.0 g. of acid-washed asbestos. Benzyl benzoate heated to reflux temperature brought the catalyst column to 320–325°, and the flow of nitrogen through the tube was slowly increased to 100 ml./minute. Patchouli alcohol (5.0 g., 0.023 mole), kept liquid by means of an infrared lamp, was admitted through the dropping funnel at a rate of 1 drop (*ca.* 25 mg.) per 4 minutes (total time 16 hours). The material in the traps was collected in petroleum ether and the resulting solution washed with 3 portions of 85% phosphoric acid. After being washed with petroleum ether, the acid was diluted with 4 volumes of water and the azulene extracted into petroleum ether. The petroleum ether was removed through a Vigreux column to yield 700 mg. of deep blue oil. The oil was redissolved in petroleum ether and passed through a column of alumina (I) (20 g.). After being washed thoroughly with petroleum ether, the column was eluted with 10% benzene–petroleum ether which afforded S-guaiazulene. The picrate was prepared by adding the stoichiometric amount of picric acid and dissolving the mixture in the minimum volume of warm ethanol. Cooling and recrystallization gave S-guaiazulene picrate, m.p. 120–121°, pure or mixed with a sample prepared from guaiol. The non-azulenic products were filtered through 50 g. of alumina (I) in petroleum ether which was subsequently removed and the products fractionally distilled at 11 mm. Nearly all the material distilled at 114° and proved to be (infrared spectrum) predominantly β-patchoulene possibly containing a small amount of the α,γ-isomers.

Patchoulene Oxides (24, 25).—Patchoulene (10 g., 49 mmoles), obtained by the dehydration of patchouli alcohol with phosphorus oxychloride in pyridine, and chloroform (50 ml.) was placed in a three-neck flask equipped with a thermometer, drying tube and a dropping funnel. The flask was cooled in an ice-bath and the solution stirred magnetically. Peracetic acid, (13 g., technical grade supplied by Becco Chemical Co.) in 100 ml. of chloroform was buffered with 1 g. of anhydrous sodium acetate and allowed to drop into the patchoulene solution during 20 minutes. The temperature was kept between 1 and 4° and the reaction was followed by titration of unused peracetic acid and when no more peracetic acid was being consumed the reaction was stopped (5 hours). The solution was extracted with 10% potassium hydroxide solution, washed with water, dried over magnesium sulfate, and the chloroform removed on a steam-bath to yield 14 g. of patchoulene oxide mixture containing some crystals. This mixture was diluted with petroleum ether, allowed to stand for 1 hour and the crystals formed were collected on a filter. Removal of the petroleum ether from the filtrate gave crude patchoulene oxide mixture which was used without further purification.

***trans*-α-Patchouli Diol (26).**—The crystalline material formed in the epoxidation of α,γ-patchoulene was recrystallized from benzene to give pure *trans*-α-patchouli diol, long needles, m.p. 198–199°, $[\alpha]^{30.2}D$ −126° (*c* 1.28, EtOH); infrared spectrum (KBr, Baird model B infrared spectrophotometer): 735, 820, 885, 925, 985, 1000, 1020, 1040, 1050, 1090, 1120, 1160, 1210, 1280, 1310, 1340, 1360, 1380, 1450, 1470, 2900, 3380 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 74.58; H, 11.00. Found: C, 75.57; H, 10.97.

Patchoulione (31). A.—Crude undistilled patchoulene oxide (14 g.) was mixed with 100 ml. of benzene, cooled to 10° in an ice-bath, and 1 ml. of boron trifluoride etherate (freshly distilled) added. The reaction mixture, which turned a brilliant dark red immediately, was allowed to stand at room temperature for 13 minutes and was then washed with sodium carbonate solution, then water, dried over magnesium sulfate and concentrated. Distillation of the residue through a 14″ spinning band column gave 5.1 g. of faintly yellow patchoulione which solidified in a refrigerator. Recrystallization from petroleum ether at −70° afforded pure patchoulione, m.p. 48.5–50.0°, $[\alpha]^{25}D$ −64° (*c* 1.93, CCl_4).

B.—A solution of β,γ-patchoulene (2.12 g., 0.01 mole) in 100 ml. of ethyl acetate at −70° was allowed to react with ozone (output of a Welsbach ozonizer, model T19, oxygen input, delivering approximately 12 mg. ozone/minute) until the characteristic blue color of a saturated ozone solution developed in the reaction mixture (1–2 hours) and the spent gas stream liberated iodine from a saturated potassium iodide solution. The reaction mixture was concentrated *in vacuo* to half its volume and hydrogenated at 27° and atmospheric pressure over 200 mg. of platinum oxide. After hydrogen uptake ceased (approximately 35% of the calculated amount for the reduction of a monozonide was taken up), the catalyst was removed by filtration and the ethyl acetate evaporated. The resulting residue (2.09 g.) was dissolved in *n*-pentane and passed through a column containing 100 g. of alumina (I). Patchoulione (0.52 g., 23%) was eluted with 10% ethyl acetate–pentane. Purification was accomplished by recrystallization from methanol or petroleum ether at −70°.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.34, 81.44; H, 10.85, 10.91.

Reaction of the ketone with 2,4-dinitrophenylhydrazine reagent proceeded slowly to yield an orange derivative, m.p. 187.5–188.5°.

Anal. Calcd. for $C_{21}H_{28}N_4O_4$: C, 62.98; H, 7.05. Found: C, 62.92; H, 7.14.

α-Oximinopatchoulione (32).—To a solution of patchoulione (200 mg., 0.91 mmole) in 1.0 ml. of absolute ethanol was added 1.0 ml. of a solution of sodium ethoxide in absolute ethanol (38 mg./ml.). The mixture was cooled in ice and freshly distilled isoamyl nitrite (0.2 ml., 1.7 mmoles) was added. After 15 hours at 27° carbon dioxide was bubbled through the solution and the sodium carbonate filtered off and washed with ethanol. The residue was dissolved in water, extracted with ether and the ether extracts combined with the ethanol solution, and dried over anhydrous magnesium sulfate. After the ether had been evaporated the residue was dissolved in petroleum ether and passed through a column containing 10 g. of silica gel. Petroleum ether containing increasing concentrations of ethyl acetate eluted a small amount of viscous oil and 50% ethyl acetate–petroleum ether eluted 112 mg. (49%) of a compound which crystallized on trituration with *n*-hexane. Recrystallization from *n*-hexane afforded α-oximinopatchoulione, m.p. 181–182°.

Anal. Calcd. for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30. Found: C, 71.66; H, 9.26.

***trans*-α-Patchouli Diol Monoacetate (27).**—*trans*-α-Patchouli diol (1 g., 4.2 mmoles) was added to a mixture of 5 g. of acetic anhydride and 5 ml. of anhydrous pyridine. The solution was refluxed for 15 minutes, cooled to room temperature and poured slowly into a solution of sodium carbonate containing crushed ice. After the evolution of carbon dioxide subsided the mixture was extracted with ether and the ether layer washed successively with cold hydrochloric acid, sodium carbonate solution, and water until neutral. The ether solution was dried over magnesium sulfate and

after evaporation yielded a white solid, which after recrystallization from petroleum ether, gave 0.85 g. (72%) of plates, m.p. 147–150°, $[\alpha]^{30.8}D$ −109° (*c* 1.51, $CHCl_3$); infrared spectrum (10% in CS_2, Perkin–Elmer model 137 Infracord): 740, 800, 830, 865, 895, 917, 943, 983, 1010, 1030, 1053, 1066, 1100, 1135, 1156, 1180, 1250, 1320, 1368, 1380, 1430, 1745, 2985, 3570, 3675 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.68; H, 10.33.

Patchoulenol (33).—*trans*-α-Patchouli diol monoacetate (0.69 g.) was placed in a small distilling flask and heated in a Wood's metal bath to 300° for 30 minutes. The pyrolysis mixture was cooled, diluted with ether, washed with sodium carbonate solution and with water, dried over magnesium sulfate and concentrated to a light brown oil. This crude product was chromatographed over Alcoa alumina (II). Elution with petroleum ether yielded a brown oil and later on a colorless fraction which crystallized. Recrystallization from petroleum ether at −70° gave patchoulenol (200 mg., 37% yield) as white crystals, m.p. 56.0–57.5°, $[\alpha]^{30.5}D$ −91° (*c* 1.78, $CHCl_3$). The compound is extremely soluble in all types of organic solvents and recrystallization is accompanied by heavy loss of material; infrared spectrum (10% in CCl_4): 701, 730, 850, 873, 886, 955, 980, 1030, 1045, 1100, 1153, 1187, 1213, 1278, 1324, 1365, 1377, 1387, 1461, 1475, 2900, 2950, 3550, 3660 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.59; H, 11.13.

Patchouli Alcohol (1).—Patchoulenol (54 mg., 0.25 mmole) was hydrogenated in 25 ml. of 95% alcohol over platinum catalyst prepared from 25 mg. of platinum oxide. The theoretical amount of hydrogen was taken up within 40 minutes. To remove platinum the alcohol solution was filtered and concentrated to an oil (51 mg., 94%) which crystallized when seeded with authentic patchouli alcohol. The compound had m.p. 54.5–56.0°, mixed m.p. 54.0–56.5° with authentic patchouli alcohol and the infrared spectra were identical in every respect.

5-Oxopatchouli Alcohol (28).—*trans*-α-Patchouli diol (9.0 g., 42.4 mmoles) was added to a solution of potassium dichromate (4.5 g., 15 mmoles, 107% of theory) in *ca.* 200 ml. of acetic acid and the solution was allowed to stand for 10 hours. Acetic acid was distilled from the reaction mixture under reduced pressure until a viscous sirup remained which was diluted with water and extracted with ether. The ether solution was washed with water, sodium hydroxide solution, water, dried over magnesium sulfate and the solvent removed to yield 7.9 g. of a white solid. Recrystallization from hexane gave 6.2 g. of 5-oxopatchouli alcohol, m.p. 107.5–108.0°, $[\alpha]^{30.8}D$ −59° (*c* 1.16, $CHCl_3$). An additional crop (1.5 g.) was obtained from the mother liquor to raise the yield to 7.7 g. (86%); infrared spectrum (10% in $CHCl_3$): 830, 850, 890, 915, 936, 987, 1019, 1027, 1060, 1102, 1210–1240, 1282, 1332, 1350, 1375, 1384, 1395, 1420, 1460, 1485, 1710, 2960, 3540, 3640 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.32; H, 10.41.

5-Oxoepipatchouli Alcohol (30). A.—Chromium trioxide (900 mg.) was dissolved in 9 ml. of ice-cold pyridine. *cis*-α-Patchouli diol (570 mg.) was added to the mixture which was allowed to stand overnight. The reaction mixture was poured into water, extracted with a mixture of benzene and ether and filtered to remove insoluble substances. The organic layer was separated and extracted successively with hydrochloric acid, dilute potassium hydroxide, and water, dried over magnesium sulfate and concentrated. Chromatography of the crude product over 6 g. of Alcoa alumina (activity I) yielded 5-oxoepipatchouli alcohol (40 mg., 7%), m.p. 163–164°, $[\alpha]^{30.8}D$ −67° (*c* 1.03. $CHCl_3$); infrared spectrum (10% in $CHCl_3$): 848, 908, 938, 991, 1010, 1032, 1068, 1105, 1142, 1154, 1205–1240, 1338, 1375, 1390, 1414, 1454, 1477, 1700, 2940, 3550 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.12; H, 10.41.

B.—For the preparation of norpatchoulidicarboxylic acid a mixture of α- and γ-patchoulene was oxidized with potassium permanganate and the products were separated into acidic and neutral components. The neutral portion deposited crystals on long standing which were filtered and recrystallized from cyclohexane to give 5-oxoepipatchouli alcohol as pale yellow needles. The identity was proved by infrared spectrum and mixed melting point comparison.

Epipatchouli Alcohol (29). A.—In a 250-ml. erlenmeyer flask was placed 3 g. of α,γ-patchoulene (14.9 mmoles; prepared by pyrolysis of patchouli acetate) and 50 ml. of chloroform and the mixture cooled to −5° in an ice–salt-bath. To this solution 55 ml. of a 0.9 *M* perbenzoic acid solution (15.9 mmoles) in benzene was added at once and the reaction mixture allowed to stand in a refrigerator. Titration after 18.5 hours showed that the oxidation was 92.5% complete. The solution was subsequently extracted with 5% potassium hydroxide, washed with water, dried over sodium sulfate and the solvent removed on a rotary evaporator to yield 3.45 g. of crude α,γ-patchoulene oxide which was distilled through a small Claisen column and two fractions collected: fraction 1, b.p. 66–74° (1.1 mm.), 0.616 g.; fraction 2, b.p. 84–86° (2.0 mm.), 1.287 g.

The two fractions had identical infrared spectra (no solvent, Infracord): 800, 825, 834, 848, 892, 1068, 1235, 1370, 1377, 1470, 1698(w), 1721(w), 2950 cm.$^{-1}$. An infrared spectrum of the pot residue showed strong carbonyl absorption. Fractions 1 and 2 were combined and used for further transformations. Excess lithium aluminum hydride was suspended in 50 ml. of tetrahydrofuran (freshly distilled from lithium aluminum hydride), 1.9 g. of α,γ-patchoulene oxide added, and the solution refluxed for 4 days. The reaction mixture was cooled and excess lithium aluminum hydride decomposed by dropwise addition of dilute aqueous potassium hydroxide solution until a white precipitate separated from the solution. The solution was decanted, the precipitate rinsed with ether three times, and the combined solutions dried over magnesium sulfate. After the solvent had been removed, the crude product (2.1 g.) was chromatographed over 60 g. of Woelm alumina (neutral, activity II). Epipatchouli alcohol (511 mg., 27%) was eluted with 50% benzene–petroleum ether mixture. The compound was recrystallized from hexane and had m.p. 119.0–120.5°, $[\alpha]^{31.5}D$ −33° (*c* 0.53, $CHCl_3$), yield 323 mg. (17%), mol. wt. 222 (mass spectrum); infrared spectrum (10% in CCl_4): 913, 1073, 1110, 1379, 1389, 1460, 2900(sh), 2950, 3040, 3650 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{25}O$: C, 81.02; H, 11.79. Found. C, 80.82; H, 11.75.

B.—5-Oxoepipatchouli alcohol (30)(1.5 g., 6.35 mmoles) was suspended in a mixture of 120 ml. of trimethylene glycol, 5 ml. of hydrazine hydrate (85%, tech. grade) and 3 g. of potassium hydroxide and heated in an oil-bath. The bath temperature was raised to 175° during 1 hour by which time the reaction mixture had become homogeneous. At 185°, the solution began to reflux gently and the bath was kept at that temperature for 3 hours. The reflux condenser was replaced with a distilling head, the bath temperature was raised to 250° over a period of 2 hours and about 5 ml. of distillate which collected was discarded. After 1 hour at 250°, the mixture was cooled, 200 ml. of water added and extracted four times with 150-ml. portions of ether. The combined ether layer was washed with dilute hydrochloric acid, and with water, dried over magnesium sulfate and concentrated. Chromatography of the crude product (595 mg.) over 20 g. of Woelm alumina (activity II, neutral) yielded 479 mg. (37%) of α-patchoulene eluted with hexane and identified by infrared spectrum. Epipatchouli alcohol (23 mg., 1.6%) was eluted with hexane containing 5% ethyl acetate, recrystallized from hexane three times to m.p. 120.0–121.5°, mixed m.p. with epipatchouli alcohol from A was 118.0–120.5° and the infrared spectra were identical.

Norpatchoulidicarboxylic Acid Monomethyl Ester (7) and Dimethyl Norpatchoulidicarboxylate (6). A.—Norpatchoulidicarboxylic acid (10.2 g., 43 mmoles) was dissolved in 65 ml. of anhydrous methanol containing 3.3 g. of concentrated sulfuric acid and the solution was allowed to stand at room temperature for 7 hours. The mixture was then poured into 400 ml. of ice-water and made basic by addition of a sodium hydroxide solution. The cloudy solution was extracted with ether, the ether layer washed with water, dried over magnesium sulfate, and concentrated to yield 4.0 g. (36%) of norpatchoulidicarboxylic acid dimethyl ester. The basic, aqueous solution from the extraction was acidified with hydrochloric acid, extracted with ether, washed with water, dried over magnesium sulfate, and concentrated to 7.5 g. of a viscous yellow oil which was chroma-

tographed over 220 g. of silica gel (Davison). Elution with 1% ethyl acetate in chloroform afforded 6.4 g. of crude norpatchoulidicarboxylic acid monomethyl ester as a clear, viscous oil. The crude half ester (4.4 g.) was dissolved in 25 ml. of ether and excess benzylamine was added. After the mixture had been allowed to stand for 15 minutes, the crystals of the benzylammonium salt were collected on a filter and rinsed with ether. The salt was recrystallized from ethyl acetate giving fine needles, m.p. 130–140° dec. Repeated recrystallization did not change the melting point; infrared spectrum (KBr): 689, 745, 770, 1175, 1195, 1225, 1270, 1320, 1350, 1360–1370, 1380, 1440, 1455, 1470, 1510, 1635, 1725, broad O–H or N–H from 2400 to 3100, 3450 cm.$^{-1}$.

Anal. Calcd. for $C_{21}H_{31}NO_4$: C, 69.77; H, 8.65; N, 3.88. Found: C, 70.28; H, 9.22; N, 3.69.

This salt was stirred into water and after acidification with hydrochloric acid, crystals of norpatchoulidicarboxylic acid monomethyl ester deposited slowly. They were collected on a filter, washed with water, and dried in high vacuum over phosphorus pentoxide. The dry half-ester was dissolved in ether and a small amount of insoluble material removed by filtration. After the ether had been evaporated, the half-ester was recrystallized from hexane to give pure norpatchoulidicarboxylic acid monomethyl ester (850 mg.), m.p. 70–72°, $[\alpha]^{31.3}D$ −37° (*c* 1.62, $CHCl_3$). A second crop of 300 mg. was recovered from the mother liquor; infrared spectrum (10% in CCl_4): 725, 875, 940, 1025, 1055, 1145, 1177, 1195, 1230, 1275, 1295(sh), 1375, 1395, 1410, 1440, 1465, 1690, 1735, broad O–H region characteristic of carboxylic acids.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 65.94; H, 8.64.

B.—To an ice-cold solution of sodium methoxide, prepared by the addition of *ca.* 300 mg. of sodium to 5 ml. of anhydrous methanol, norpatchoulidicarboxylic acid anhydride (700 mg.) was added and the solution stored at 0° for 24 hours and then at 23° for 6 hours. The volume of the reaction mixture was reduced to approximately one-quarter on a rotary evaporator, diluted with 50 ml. of ether, extracted with 20% hydrochloric acid solution, washed with water, dried over magnesium sulfate, and concentrated to yield 763 mg. (91%) of crude norpatchoulidicarboxylic acid monomethyl ester as an oil. The half-ester was purified *via* its benzylammonium salt, as described above, to yield the pure half-ester, m.p. 70–72°.

Norpatchoulidicarboxylic Acid Isomonomethyl Ester (8).—Dimethyl norpatchoulidicarboxylate (330 mg., 1.23 mmoles) was dissolved in 2.5 ml. of 0.5 *N* methanolic potassium hydroxide solution (1.25 mmoles of potassium hydroxide) and the solution refluxed for 9 hours. The reaction mixture was subsequently poured into water and extracted with ether. The aqueous phase was acidified with hydrochloric acid, extracted with ether and the ether layer washed with water, dried over magnesium sulfate, and concentrated to 275 mg. (88%) of crude norpatchoulidicarboxylic acid isomonomethyl ester which crystallized after 3 days Two recrystallizations from hexane gave colorless, thick plates of the pure half-ester, m.p. 86–87°, $[\alpha]^{26.5}D$ −32° (*c* 3.67, $CHCl_3$); infrared spectrum (10% in CCl_4): 720, 955, 1025, 1070, 1180, 1195, 1250, 1265(sh), 1340, 1375, 1395, 1425, 1437, 1465, 1475, 1700, 1725 cm.$^{-1}$, broad O–H region characteristic of carboxylic acids.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 66.32; H, 8.83.

3-Carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]oct-8-ene (43).—Norpatchoulidicarboxylic acid monomethyl ester (156 mg.) was dissolved in 20 ml. of benzene containing 450 mg. of lead tetraacetate (95% active lead) and the mixture refluxed for 16 hours while protected by a drying tube. The solution was cooled, extracted successively with dilute potassium iodide solution, sodium thiosulfate solution, sodium bicarbonate solution, and with water. The organic layer was dried over magnesium sulfate and concentrated to 176 mg. of an oil which was chromatographed over 3 g. of Merck alumina (acid washed, activity II) using a mixture of 5% benzene in hexane as eluent to yield 111 mg. of an oil which exhibited a strong tetranitromethane test and ϵ 4,770 at 210 mμ. Gas chromatography showed the presence of three major components. 3-Carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]oct-8-ene (53 mg.) was isolated by chromatography of the olefin mixture (380 mg.) over 15 g. of Woelm alumina (neutral, activity III) using hexane as eluent. Distillation through a micro-Hickman column gave a material having $[\alpha]^{35}D$ −320° (*c* 10.5 in $CHCl_3$); nuclear magnetic resonance spectrum (60 mc.): 4.97, 6.41, 6.95, 8.52, 8.86, 8.91, 8.96, 9.00 τ; infrared spectrum (10% in CCl_4): 913, 942, 1015, 1060, 1075, 1125, 1163, 1200, 1228, 1265, 1305, 1317, 1356, 1370, 1380, 1388, 1440, 1465, 1630, 1735, 2880, 2960 cm.$^{-1}$; (no solvent, Infracord): 825, 845(sh) in addition to the bands above.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.88; H, 9.55.

The other two substances were separated by gas chromatography. One compound was identified as 3-carbomethoxy-2,2,6-trimethylbicyclo[3.3.0]oct-5(6)-ene (**41**) by its infrared and nuclear magnetic resonance spectra and analysis by gas chromatography which showed the presence of only one compound. The last compound had an infrared spectrum (10% in CCl_4): 915, 978, 1045, 1065, 1163, 1185, 1200, 1216, 1255, 1275, 1312, 1353, 1367, 1390, 1443, 1465, 1683, 1740, 2880, 2960 cm.$^{-1}$; nuclear magnetic resonance spectrum (60 mc.): 4.97, 6.35, 8.78, 8.93, 9.04, 9.16 τ.

3-Carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]octane (40).—3-Carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]-oct-8-ene (60 mg., 0.29 mmole) was reduced in absolute alcohol over a platinum catalyst prepared from 15 mg. of platinum oxide. Uptake of hydrogen was complete after 4.9 ml. (77%) had been absorbed. The catalyst was removed by filtration and the ethanol evaporated to yield 36 mg. of 3-carbomethoxy-2,2,6-*endo*-trimethylbicyclo-[3.3.0]octane, $[\alpha]^{28.5}D$ −50° (*c* 0.94, $CHCl_3$), mol. wt. 210 (mass spectrum); infrared spectrum (10% in CCl_4): 931, 963, 1005, 1030, 1065, 1160, 1182, 1197, 1215(sh), 1240, 1253, 1275, 1303, 1373, 1394, 1431, 1465, 1475(sh), 1733, 2880, 2950 cm.$^{-1}$.

Norcedrenedicarboxylic Acid (4,4,6-*exo*-Trimethylbicyclo-[3.3.0]octane-1,3-dicarboxylic Acid) (35).—Norcedrenedicarboxylic acid was prepared from cedrene by a sequence analogous to that used for the preparation of norpatchoulidicarboxylic acid from α,γ-patchoulene. In a typical run, 140 g. of cedrene (Givaudan Delawanna) gave 32 g. of pure norcedrenedicarboxylic acid, m.p. 213–214° (lit.[32] m.p. 209°, $[\alpha]^{14}D$ −39° (*c* 0.708, $CHCl_3$)).

Norcedrenedicarboxylic Acid Anhydride.—The anhydride was prepared by the procedure used for the preparation of norpatchoulidicarboxylic acid anhydride. From 4.0 g. of norcedrenedicarboxylic acid, there was obtained 3.2 g. (87%) of norcedrenedicarboxylic acid anhydride, m.p. 129.5–130.3° (lit.[43] m.p. 128–128.5°, $[\alpha]D$ +50° (*c* 1.19. $CHCl_3$)).

Norcedrenedicarboxylic Acid Monomethyl Ester (37).—To a solution of 3.3 g. (1.8 ml.) of concentrated sulfuric acid in 16.5 g. (20.5 ml.) of methanol was added 3.3 g. of norcedrenedicarboxylic acid and the mixture refluxed for 1 hour. The solution was poured into 300 ml. of water, extracted with ether, and the ether layer washed with sodium carbonate solution. The sodium carbonate extract was acidified with hydrochloric acid and the organic acids were extracted into ether. Working up in the usual manner gave 3.3 g. of an oil, which crystallized on standing. Recrystallization from petroleum ether yielded 1.6 g. (46%) of norcedrenedicarboxylic acid monomethyl ester which had m.p, 95–97° (lit.[32] m.p. 97°), $[\alpha]^{25}D$ −40° (*c* 1.62, $CHCl_3$); infrared spectrum (10% in CCl_4): 700, 1030, 1070 1100, 1145, 1175, 1235, 1270, 1300, 1375, 1390, 1415, 1440, 1467, 1690, 1735 cm.$^{-1}$, broad O–H region characteristic of carboxylic acids.

Dimethyl Norcedrenedicarboxylate (36).—To an ethereal solution of norcedrenedicarboxylic acid (5.0 g., 0.021 mole) was added 85 ml. of 0.175 *N* diazomethane solution (0.0149 mole) (prepared from du Pont EXR-101) with swirling. The reaction mixture was extracted immediately with base, washed with water, dried over magnesium sulfate and concentrated to yield 2.14 g. of dimethyl norcedrenedicarboxylate. The liquid ester was purified by distillation under high vacuum through a small distilling flask; infrared spectrum (10% in CCl_4): 705, 824, 863, 930, 965,

(43) L. Ruzicka, Pl. A. Plattner and G. W. Kusserow, *Helv. Chim. Acta*, **25**, 85 (1942).

995, 1030, 1070, 1095, 1130, 1175, 1200, 1220, 1240, 1290, 1360, 1380, 1420, 1450, 1720, 2850, 2920 cm.$^{-1}$.

Norcedrenedicarboxylic Acid Isomonomethyl Ester (38). A.—Dimethyl norcedrenedicarboxylate (110 mg.) was dissolved in 20 ml. of methanolic potassium hydroxide containing 1 ml. of water and subsequently refluxed for 4 hours. The volume of the mixture was reduced to one-quarter on a rotary evaporator and worked up in the usual manner to give a crystalline compound which after two recrystallizations from hexane had m.p. 130.5–132.0° (lit.[33] m.p. 130–131°), $[\alpha]^{25}D$ −39° (*c* 1.29, $CHCl_3$); infrared spectrum (10% in CCl_4): 708, 850, 920, 966, 995, 1032, 1077, 1105, 1137, 1163, 1186, 1210, 1245, 1304, 1352, 1376, 1395, 1425(sh), 1439, 1467, 1700, 1725 cm.$^{-1}$, broad O–H region characteristic of carboxylic acids. Hydrolysis of norcedrenedicarboxylic acid isomonomethyl ester (100 mg.) by refluxing in 5 *N* methanolic potassium hydroxide solution for 20 hours yielded 92 mg. of crude norcedrenedicarboxylic acid. Recrystallization from formic acid gave pure norcedrenedicarboxylic acid, m.p. 214–215°, pure and mixed with authentic material.

B.—To a solution of 10 ml. of methanol in which *ca.* 50 mg. of sodium had been dissolved was added norcedrenedicarboxylic acid anhydride (117 mg., 0.52 mmole). After 14 minutes at room temperature, the mixture was poured into water and extracted with ether. Work up in the usual manner yielded 130 mg. (97%) of an oil which crystallized when seeded with norcedrenedicarboxylic acid isomonomethyl ester. Recrystallization from hexane gave a pure sample.

3-Carbomethoxy-2,2,6-*exo*-trimethylbicyclo[3.3.0]oct-4-ene (39).—A mixture of norcedrenedicarboxylic acid monomethyl ester (1.52 g., 6.0 mmoles) and lead tetraacetate (4.5 g., 10.2 mmoles, 95% active lead) in 300 ml. of benzene was refluxed under nitrogen for 14 hours. The mixture was poured into an aqueous solution of ferrous sulfate, extracted with ether, the ether layer washed with water, with a solution of sodium carbonate, again with water, dried over magnesium sulfate and concentrated to yield 1.22 g. of neutral material. The product was fractionated and the portion (750 mg.) that distilled at bath temperature 110° (0.4 mm.) was separated into two components by gas chromatography using a packing of 15% Dow Corning compound no. 11 on firebrick. 3-Carbomethoxy-2,2,6-*exo*-trimethylbicyclo[3.3.0]oct-4-ene (105 mg.) was eluted first and was purified further by filtration in hexane solution through a small column of Woelm alumina (neutral, activity III) followed by distillation through a micro-Hickman column under high vacuum; $[\alpha]^{30}D$ −283° (*c* 2.05, $CHCl_3$), $n^{26}D$ 1.4696; nuclear magnetic resonance spectrum (60 mc.): 4.54, 6.16, 6.70, 8.72, 8.85, 8.95 τ; infrared spectrum (10% in CCl_4): 650, 846, 915, 950, 980, 1023, 1036, 1156, 1197, 1245, 1275, 1335, 1367, 1387, 1438, 1455, 1663, 1732, 2880, 2960, 3060(sh) cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.20; H, 9.75.

3-Carbomethoxy-2,2,6-trimethylbicyclo[3.3.0]oct-5(6)-ene (41).—The other compound obtained by gas chromatographic separation of the above product was purified by the same procedure to give a liquid ester $[\alpha]^{25}D$ +36° (*c* 2.13, $CHCl_3$), $n^{25}D$ 1.4792; nuclear magnetic resonance spectrum (60 mc.): 6.40, 7.66, 8.37, 9.07, 9.17 τ; infrared spectrum (10% in CCl_4): 835, 882, 913, 940, 1041, 1063, 1202, 1228, 1260, 1297, 1324, 1355, 1372, 1382, 1390, 1441, 1450, 1735, 2860, 2960 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.46; H, 9.92.

3-Carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]octane (40).—3-Carbomethoxy-2,2,6-trimethylbicyclo[3.3.0]oct-5-(6)-ene (64 mg., 0.31 mmole) was reduced in absolute alcohol over a platinum catalyst prepared from 30 mg. of platinum oxide. After 10.2 ml. had been absorbed the catalyst was removed by filtration and the alcohol solution concentrated. The residue was dissolved in hexane containing 5% benzene and filtered through a column of 3 g. of Merck alumina (acid-washed, activity III). Distillation through a micro-Hickman column gave 3-carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]-octane (61 mg., 95%), $[\alpha]^{28.5}$ −47° (*c* 0.95, $CHCl_3$) as a colorless oil. Both the mass spectrum and the infrared spectrum (32 peaks) of this compound were identical in every respect with those of the product obtained by catalytic reduction of 3-carbomethoxy-2,2,6-*endo*-trimethylbicyclo[3.3.0]oct-8-ene derived from patchouli alcohol; mol. wt. 210 (mass spectrum).

3-Carbomethoxy-2,2,6-*exo*-trimethylbicyclo[3.3.0]octane (42).—3-Carbomethoxy-2,2,6-*exo*-trimethylbicyclo[3.3.0]-oct-4-ene (102 mg., 0.49 mmole) was reduced in absolute alcohol over a platinum catalyst prepared from 16 mg. of platinum oxide. The reaction was worked up as described above to yield 92 mg. (89%) of 3-carbomethoxy-2,2,6-*exo*-trimethylbicyclo[3.3.0]octane, $[\alpha]^{30.4}$ −75° (*c* 0.94, $CHCl_3$), mol. wt. 210 (mass spectrum); infrared spectrum (10% in CCl_4): 705, 915, 932, 973, 1035, 1140, 1158, 1185, 1202, 1225, 1241, 1258, 1297, 1374, 1394, 1417, 1464, 1735, 2880, 2960 cm.$^{-1}$.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA, MINNEAPOLIS 14, MINN., AND THE DEPARTMENT OF CHEMISTRY, IOWA STATE UNIVERSITY, AMES, IOWA]

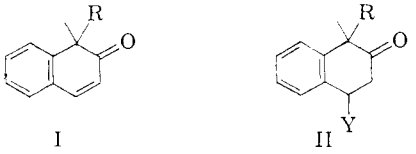
Alkali-induced Reactions of 1-Methyl-1-dichloromethyl-2(1H)-naphthalenone and Related Compounds

BY R. M. DODSON,[1a] JOHN R. LEWIS,[1b] WILLIAM P. WEBB,[1a] ERNEST WENKERT[1b] AND R. D. YOUSSEFYEH[1b]

RECEIVED JULY 20, 1960

Base treatment of 1-methyl-1-dichloromethyl-2(1H)-naphthalenone yields 1-methyl-2-naphthol, 1-methyl-3-naphthoic acid and a cinnamic acid. Similar treatment of 1-methyl-1-dichloromethyl-2-tetralone produces 1-methyl-3,4-dihydro-3-naphthoic acid and 1-methyl-3-naphthoic acid. Rational mechanisms for these and similar rearrangements involving cyclobutanone intermediates are presented. The trapping of a bridged cyclobutanone is described.

It has been noted in two previous studies that 1-methyl-1-dichloromethyl-2(1H)-naphthalenone (Ia), the Reimer–Tiemann product of 1-methyl-2-naphthol, and its dihydro derivative IIa undergo a chemical change in alkaline media.[2a,b] The present report represents an extension of these observations.



I II

a, R = $CHCl_2$, Y = H
b, R = CH_2Cl, Y = H
c, R = $CHCl_2$, Y = OH
d, R = $CHCl_2$, Y = OEt
e, R = CHClOH
f, R = CHO

(1) (a) University of Minnesota; (b) Iowa State University.

(2) (a) R. M. Dodson and W. P. Webb, *J. Am. Chem. Soc.*, **73**, 2767 (1951); (b) E. Wenkert and T. E. Stevens, *ibid.*, **78**, 5627 (1956).