Studies with Bicyclo[2.2.2]octenes. V.[1] The Total Synthesis of (±)-Patchouli Alcohol

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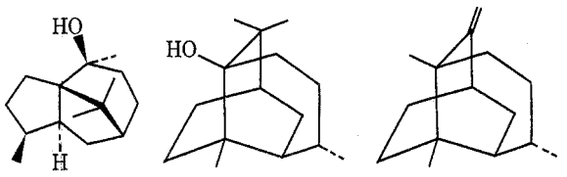
A stereospecific total synthesis of (±)-patchouli alcohol (**2**) *via* the key intermediate alcohol **14a** is described. A modified Reformatsky procedure was used to convert ketone **4** in high yield into a mixture of the conjugated esters **9a** and **10a** without concurrent formation of nonconjugated esters. Dissolving metal reduction of the conjugated esters gave alcohols **14a** and **15a** (4:1), whose relative configurations were readily assigned by pmr spectroscopy. The sequence was completed *via* the intermediates **14c**, **16**, **18a**, **18c**, and **18e**.

Patchouli alcohol and seychellene are two tricyclic sesquiterpenes which have been isolated from patchouli oil, an important raw material for the composition of perfumes.

Patchouli alcohol has been the subject of a large volume of both degradative and synthetic work, the most recent of which, up to the commencement of our work, was that of Büchi and coworkers.[3-6] The original structure **1** which Büchi attempted to synthesize was, however, incorrect, and it was only by a fortuitous rearrangement in the final steps of the synthesis that he arrived at patchouli alcohol, which was later shown to have a different structure (**2**) by X-ray investigations.[7] It was this ambiguity which led us to design a more direct synthesis of the revised structure based on bicyclo[2.2.2]octene intermediates.



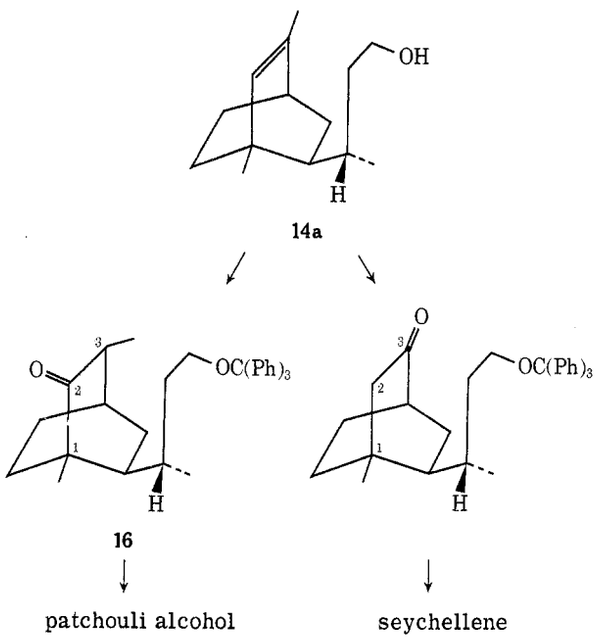
1 **2** **3**

(−)-patchouli alcohol (−)-seychellene

The hydrocarbon seychellene (**3**) was isolated recently by Ourisson and Wolff[8] from patchouli oil obtained from the Seychelles Islands. The similarity in structure between seychellene and patchouli alcohol suggested a synthetic route to seychellene utilizing intermediates which had previously been prepared for the synthesis of patchouli alcohol.

The crucial intermediate in both syntheses was the olefin **14a**. The plan involved the modification of the olefinic bridge of this compound to yield a bicyclo[2.2.2]octanone **16** with the ketone function at C_2 for patchouli alcohol, and a bicyclo[2.2.2]octanone with the ketone at C_3 for seychellene.

This paper describes the synthesis of (±)-patchouli alcohol, while the accompanying paper[9] outlines details of the synthesis of (±)-seychellene.



14a

16

patchouli alcohol seychellene

Results and Discussion

Entry into the bicyclo[2.2.2]octane ring system was gained *via* the Diels–Alder reaction of 1,3-dimethyl-1,3-cyclohexadiene with methyl vinyl ketone to give ketone **4** as the major product,[10] whose structure and stereochemistry have been rigorously established. The conversion of **4** to the planned intermediate **14a** appeared to be a simple task in theory, since a wide variety of methods are available for extending carbon chains by a two-carbon fragment.[11] The immediate objective was thus a simple and effective method of preparing the conjugated esters **9a** and/or **10a** from the ketone **4**.

The Wadsworth–Emmons method[12] proved disappointing, since only low yields of conjugated esters were obtained, together with a high proportion of starting material. Similarly, other workers[13] have found that many ketones, including a substituted pregnan-20-one, were inert to the Wadsworth–Emmons reagent; this was attributed to the stringent steric requirements of the reagent.

On the other hand, it was gratifying to find that the β-hydroxy ester **6** could be obtained consistently in

(1) Part IV: R. P. Gregson, R. N. Mirrington, and K. J. Schmalzl, *Aust. J. Chem.*, **25**, 531 (1972).

(2) (a) Abstracted in part from the Ph.D. thesis of K. J. Schmalzl, University of Western Australia, May 1971. (b) The award of a Commonwealth Postgraduate Scholarship to K. J. S. is gratefully acknowledged.

(3) G. Büchi and R. E. Erickson, *J. Amer. Chem. Soc.*, **78**, 1262 (1956).

(4) G. Büchi, R. E. Erickson, and N. Wakabayashi, *ibid.*, **83**, 927 (1961).

(5) G. Büchi and W. D. MacLeod, Jr., *ibid.*, **84**, 3205 (1962).

(6) G. Büchi, W. D. MacLeod, Jr., and J. Padilla O., *ibid.*, **86**, 4438 (1964).

(7) M. Dobler, J. D. Dunitz, B. Gubler, H. P. Weber, G. Büchi, and J. Padilla O., *Proc. Chem. Soc.*, 383 (1963).

(8) G. Wolff and G. Ourisson, *Tetrahedron*, **25**, 4903 (1969).

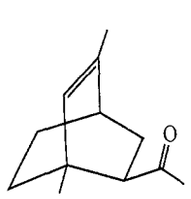
(9) R. N. Mirrington and K. J. Schmalzl, *J. Org. Chem.*, **37**, 2877 (1972).

(10) R. N. Mirrington and K. J. Schmalzl, *ibid.*, **34**, 2358 (1969).

(11) See H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, Chapter 8, for many leading references.

(12) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).

(13) A. K. Bose and R. T. Dahill, Jr., *J. Org. Chem.*, **30**, 505 (1965).



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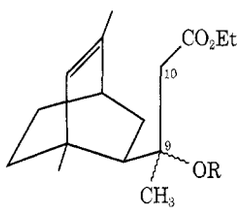
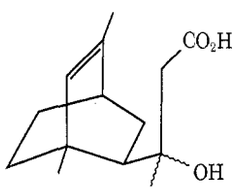


5, R = ZnBr
6, R = H
7, R = $COCH_3$



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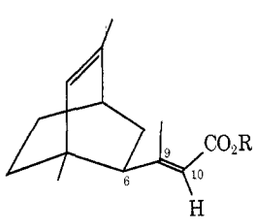
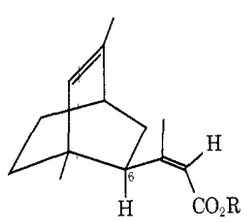
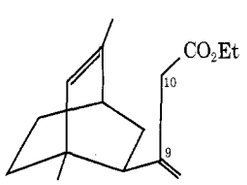
yields of up to 90% *via* the Reformatsky reaction on the ketone **4**. The difficulty with this approach soon became apparent, however, when attempted dehydration of the β-hydroxy ester by a number of the usual methods under acidic conditions resulted in rearrangement of the bicyclo[2.2.2]octene skeleton to an aromatic compound. Some aspects of this rearrangement and of its mechanism have been reported in an earlier paper.[1]



9a, R = Et
b, R = H



10a, R = Et
b, R = H



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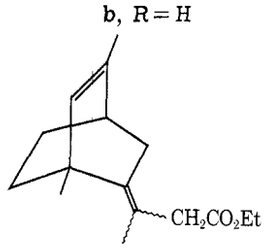

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Dehydration of **6** without rearrangement was accomplished using phosphorus oxychloride in pyridine. The conjugated esters **9a** and **10a** were obtained, contaminated with the nonconjugated ester **11**. The other β,γ-unsaturated ester **12** was not detected, and this was not unexpected as there would be serious $A^{(1,3)}$ strain[14,15] between the C_1 methyl group and the substituents on the exocyclic double bond. The preparation of conjugated esters by dehydration of β-hydroxy esters[16] has this obvious weakness in the general case, since significant quantities of the nonconjugated esters are usually formed.

The product of the Reformatsky reaction was itself of some interest, because it might have been expected that a mixture of the 9*R* and 9*S* epimers of **6** would have been obtained. It appeared, however, that only one, or certainly predominantly one epimer was formed, but no positive identification has been possible. This question was not pursued further at the time as it obviously had little or no bearing on the structure of the conjugated esters **9a** and **10a** obtained from **6**, either by dehydration or by acetylation and elimination (see below).

In view of the problems associated with the dehydration of the hydroxy ester **6**, an alternative procedure was designed involving acetylation of the tertiary alcohol and subsequent elimination of acetic acid from the acetate **7** by base, to yield the conjugated esters **9a** and **10a** exclusively.[17] The acetate **7** was obtained in good yield from the hydroxy ester **6** using acetyl chloride and *N*,*N*-dimethylaniline.[18] An alternate and more convenient procedure was to treat the Reformatsky complex **5** directly with acetyl chloride and *N*,*N*-dimethylaniline.

The acetate **7** was readily converted to a mixture of the conjugated *Z* and *E* esters **10a** and **9a** by elimination of acetic acid with sodium ethoxide. A variety of other bases were tried, including sodium hydride, potassium *tert*-butoxide, and even basic alumina. Sodium ethoxide was found to be the most convenient and would be especially useful when the conjugated esters were prone to isomerization under strongly basic conditions.

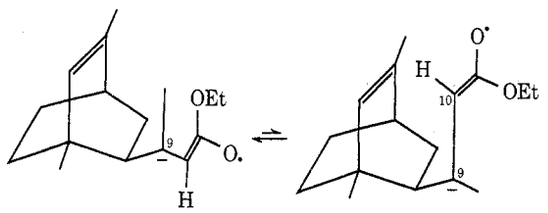
Even in cases where the β,γ-unsaturated esters were more stable than the α,β-unsaturated esters, the latter could be formed almost exclusively by this method.[17] This observation, together with the simplicity of the procedure and low cost of the reagents, make this a very useful high-yielding method for large-scale preparation of α,β-unsaturated esters *via* the Reformatsky reaction,[19] particularly in view of the great variety of ketones reactive under Reformatsky conditions.[16]

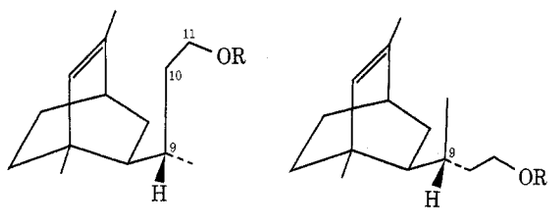
The conjugated esters **9a** and **10a** were easily distinguished by their pmr spectra. The characteristic signals were due to H_6 and the C_9 vinyl methyl group. In the *Z* ester **10a** there was strong deshielding of H_6 by the coplanar carboxyl group. This signal, a doublet of doublets, was obscured by the quartet of the ester resonance in **10a**, but was clearly visible in the spectrum of the corresponding *Z* acid **10b** at 4.05 ppm. The signal for H_6 in the pmr spectrum of the *E* acid **9b** was situated much further upfield at 2.27 ppm as expected, since the carboxyl group was now remote from H_6. The strong deshielding of H_6 in the *Z* ester and acid also indicated that the preferred conformation was as shown, since rotation about the C_6–C_9 bond to alternative conformations would not be expected to give rise to such a strong deshielding effect on H_6. In addition, other conformations would be unlikely because of prohibitive steric interactions between either the ester group or the C_9 methyl group and other functions in the molecule.

(14) F. Johnson and S. K. Malhotra, *J. Amer. Chem. Soc.*, **87**, 5492 (1965).
(15) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).
(16) R. L. Shriner, *Org. React.*, **1**, 1 (1942).
(17) K. H. Fung, K. J. Schmalzl, and R. N. Mirrington, *Tetrahedron Lett.*, 5017 (1969).
(18) J. D. Cocker and T. G. Halsall, *J. Chem. Soc.*, 4262 (1956).
(19) Since the completion of this section and the subsequent appearance of our communication,[17] a similar procedure has been reported by Engel, *et al.*,[20] using steroidal substrates. This procedure is analogous to that of Linstead, *et al.*,[21] who used *aqueous* bases to obtain conjugated *acids* from β-acyloxy esters.
(20) C. R. Engel, V. S. Salvi, and L. Ruest, *Can. J. Chem.*, **48**, 3425 (1970).
(21) R. P. Linstead, L. N. Owen, and R. F. Webb, *J. Chem. Soc.*, 1211 (1953).

Further evidence for the preferred conformation of both the *Z* and *E* esters was obtained from the chemical shifts of the C_9 vinyl methyl doublets. In the *Z* ester **10a** there was strong shielding of this methyl to δ 1.57 by the olefinic bridge. In the *E* ester **9a** this shielding effect was counteracted by the strong deshielding effect of the coplanar carboxyl group so that the net effect was to shift the signal to δ 1.92. An alternative preferred conformation for the *E* ester, obtained by rotating the side chain around the C_6–C_9 bond through 180°, was unlikely, since no strong shielding of the C_{10} olefinic proton was observed. In fact, the C_{10} olefinic proton signals of the *Z* and *E* esters both occurred near 5.5 ppm. This value is very similar to that of the olefinic proton signals in the pmr spectra of the conjugated esters ethyl β,β-diethylacrylate and ethyl cyclohexylideneacetate, obtained from diethyl ketone and cyclohexanone, respectively.[17]

Reduction of the conjugated esters **9a** and **10a** with lithium in ammonia and ethanol yielded the alcohols **14a** and **15a** in a ratio of 4:1, respectively. This ratio could be accounted for by consideration of the two most likely conformations **13a** and **13b** of the intermediate radical anion (only one canonical form represented). The conformer **13b** would be somewhat less preferred than **13a** because the steric interaction of the π cloud of the olefinic bridge with the protons of the freely rotating C_9 methyl group in **13a** should be less severe than with the rigidly fixed H_{10} in **13b**. If protonation of the radical anion at C_9 were mainly occurring from the less hindered side (remote from the C_1 methyl group), **13a** would give **14a** while **13b** would give **15a**. The most important single factor determining the success of the synthesis of patchouli alcohol as well as of seychellene[9] was the ability to distinguish these two epimers **14a** and **15a**, and the finding that the major one had the desired stereochemistry.





a, R = H
b, R = Ac
c, R = C(Ph)$_3$

The reduction was usually carried out on a mixture of *Z* and *E* esters. To eliminate the very remote possibility that the *Z* ester was yielding **15a** almost exclusively, while the *E* ester was yielding **14a**, the reduction was also carried out on pure *E* ester **9a**. The ratio of products **14a** and **15a** obtained was unchanged.

Isolation of a minor product from any reaction mixture, except in the most trivial cases, must be regarded with great caution and always raises the question of rearrangement. The pmr spectrum of the alcohol of minor abundance, however, showed all the characteristic signals of the bicyclo[2.2.2]octene skeleton and, furthermore, apart from the position of the C_9 methyl doublet, these signals were virtually superimposable on those of the major epimer **14a**. The methyl doublet of the minor epimer was more shielded than that of the major epimer (0.55 ppm compared to 0.78 ppm) and we have observed as expected[22] that in all cases where the side chain was endo to the olefinic bridge, the pmr signals were strongly shielded relative to signals in the corresponding exo isomers. It was inconceivable, therefore, that the minor epimer with the highly shielded C_9 methyl group could have an exo side chain. In addition, hydrochlorination of the acetate **15b** caused a downfield shift of the C_9 methyl doublet in the pmr spectrum, confirming that the shielding effect was due to the olefinic bridge. The major epimer **14a** was also shown to have its side chain endo when the system was cyclized in the final steps of the synthesis.

In short, no epimerization about C_6 or rearrangement had occurred during the reduction, and the two anticipated products **14a** and **15a** were obtained.

It was the simple observation of the difference in chemical shift of the C_9 methyl doublets which formed the basis of the assignment of stereochemistry to the major and minor epimers. If both alcohols **14a** and **15a** were to adopt that conformation which minimized the 1,3-diaxial-like interactions with the methyl group at C_1, the C_9 methyl would be close to the olefinic bridge in **15a**, whereas in **14a** it would be much more remote. It was then apparent that the major epimer with the less shielded C_9 methyl signal in its pmr spectrum was **14a**, which had the stereochemistry required for the synthesis of (±)-patchouli alcohol and (±)-seychellene.

This large difference in the chemical shift of the C_9 methyl doublets was quite consistent, regardless of the function at the end of the side chain (Table I), although with triphenylmethyl (trityl) ethers the difference was significantly smaller. The effect was similar when either the olefinic bridge or the carbonyl group at C_2 was the shielding function.

TABLE I
CHEMICAL SHIFTS[a] OF C_9 METHYL GROUPS

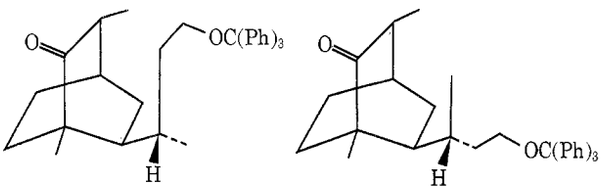
Compd	C_9 methyl doublet[b]	Compd	C_9 methyl doublet[b]	Difference[c]
14a	0.78	**15a**	0.55	0.23
14b[d]	0.81	**15b**[d]	0.57	0.24
14c	0.62	**15c**	0.48	0.14
16	0.67	**17**	0.50	0.17

[a] Measured for CCl_4 solutions on a Varian A-60 spectrometer. Chemical shifts in parts per million downfield from TMS as internal standard. [b] J = 6.5 Hz. [c] Parts per million. [d] The preparation and spectral properties of this compound appear in the accompanying paper.[9]

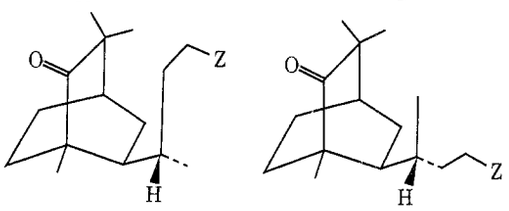
The trityl ether **14c** was treated with diborane in tetrahydrofuran[23] and the organoborane was oxidized

(22) I. Botica and R. N. Mirrington, *Aust. J. Chem.*, **24**, 1467 (1971), and references cited therein; A. A. Othman, M. A. Qasseem, and N. A. J. Rogers, *Tetrahedron*, **23**, 87 (1967).
(23) G. Zweifel and H. C. Brown, *Org. React.*, **13**, 1 (1963).

directly with chromium trioxide–pyridine to yield the ketone **16**. This direct procedure not only saved time and material but was also found to be necessary in the present case. Much difficulty was experienced in the oxidation of the organoborane to the intermediate alcohol with aqueous alkaline hydrogen peroxide because of the extreme insolubility of the trityl ether in the reaction medium. Organoboranes have been oxidized directly before using chromic acid,[24] but this method is obviously not applicable to the oxidation of acid-sensitive systems. It was found that chromium trioxide–pyridine could be used without any complications; this method could be of general applicability especially with water-insoluble compounds.



16 **17**



18 **19**

a, Z = OH
b, Z = OC(Ph)$_3$
c, Z = OTs
d, Z = OCONHPh
e, Z = I
f, Z = Br
g, Z = H

The relative stereochemistry of the C_3 methyl group in the ketone **16** was assigned as depicted, since one would anticipate exclusive attack of diborane from the less hindered side[23] of the olefin **14c**, and the above oxidation conditions should not cause epimerization. In any case this stereochemistry was not vital, since alkylation in the next step destroyed the asymmetric center at C_3.

Potassium triphenylmethide was found to be a vastly superior base to sodium hydride or potassium *tert*-butoxide for the alkylation of the ketone **16**. The ketone was converted quantitatively by titration to its enolate anion, which reacted rapidly with methyl iodide at 20°. The usual objection to the use of potassium triphenylmethide as the base in alkylation reactions is the difficulty in separation of the alkylated ketones from the triphenylmethane produced in the titration.[25] This was not a problem in the present case, because the ketone **18b** was not isolated, but converted to the alcohol **18a** by hydrogenolysis of the trityl ether function. Chromatography at this stage of the synthesis readily separated the triphenylmethane formed in the titration and in the hydrogenolysis from the alcohol **18a**. The tosylate **18c**, prepared in the usual way, was converted to the iodide **18e** by treatment with sodium iodide in acetone.

Magnesium metal was used with great success by Leroux[26] in the cyclization of γ-halo ketones to the corresponding cyclobutanols. However, the iodide **18e** was found to be completely inert to magnesium. Prolonged heating with magnesium in tetrahydrofuran, even on addition of equimolar amounts of mercuric chloride,[26] resulted in *recovery of the iodide unchanged*. Similarly, the bromide **18f** was found by Danishefsky[27] to be inert to magnesium.

The iodide **18e** was successfully cyclized using sodium in tetrahydrofuran at 100° in a sealed tube. The two products isolated were (±)-patchouli alcohol (**2**) and the acyclic ketone **18g**. These results are in agreement with those of Danishefsky and Dumas, who cyclized the bromide **18f** to (±)-patchouli alcohol using similar conditions.[27]

The reasons for the inertness of **18e** and **18f** to the action of magnesium are not clear at present. Further studies of the scope and mechanism of this interesting intramolecular cyclization[28] using various reagents and substrates are currently in progress in this laboratory.

Experimental Section

Analyses were carried out by the CSIRO Microanalytical Service, Melbourne. Melting points and boiling points are uncorrected; the latter refer to the bath temperature. Infrared spectra were measured on a Perkin-Elmer 337 grating infracord spectrophotometer using carbon tetrachloride solutions. Pmr spectra were measured with a Varian A-60 spectrometer using carbon tetrachloride solutions unless otherwise specified, with TMS as internal standard. A Varian Aerograph Series 1400 gas chromatograph was used for vpc analysis with nitrogen carrier gas at a flow rate of 15 ml/min. Columns were 5 ft × 0.125 in. of 5% UCON and 5% DEGS on nonacid-washed Chromosorb W (80–100 mesh), and 3% SE-30 on Varaport 30 (100–120 mesh). Preparative vpc was carried out using a Wilkens Aerograph Autoprep, Model A-700 with helium as the carrier gas. The aluminum column was 12 ft × 0.375 in. of 10% Carbowax 20M on non-acid-washed Chromosorb W (44–60 mesh).

Reformatsky Reaction with Ketone 4.—Zinc powder (15 g), which had been activated by washing successively with 5% hydrobromic acid, water, ethanol, and acetone and dried at 100°, was added to a solution of 17 g of the ketone **4** and 24 g of bromoacetic ester in 350 ml of dry benzene. The mixture was stirred and heated, and 0.3 g of iodine was added to initiate the reaction. Stirring and heating were continued so that the mixture refluxed gently for 2 hr after the commencement of the reaction. After cooling, the solution was decanted and the excess sludge of zinc powder was washed with benzene. The zinc complex was destroyed by shaking the combined benzene solutions with 20% aqueous sulfuric acid at 0°, and the benzene layer was subsequently washed with 5% aqueous sulfuric acid, aqueous sodium carbonate, and water, then dried over anhydrous sodium sulfate. Evaporation of the solvent yielded 23.5 g (92%) of the crude hydroxy ester **6**: ir 3520 (OH), 1720 cm^{-1} (ester); pmr δ 5.44 (br s, 1, H_2), 4.12 (q, J = 7 Hz, 2, ester), 3.44 (br s, 1, OH), 2.23 (br s, 2, C_{10} methylene), 1.73 (d, J = 1.6 Hz, 3, C_3 vinyl methyl), 1.27 (t, J = 7 Hz, 3, ester), 1.27 (s, 3, C_1 methyl), 0.95 (s, 3, C_9 methyl). The analytical sample was prepared by microdistillation, bp 102° (0.1 mm). *Anal.* Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.49; H, 9.64.

Hydrolysis of Hydroxy Ester 6.—A solution of 2 g of the hydroxy ester in 50 ml of 50% aqueous ethanol containing 5 g of sodium hydroxide was refluxed for 45 min. The solution was cooled, acidified with dilute hydrochloric acid at 0°, and extracted with ether. The ethereal solution was extracted with aqueous sodium carbonate and, after acidification at 0° with dilute hydrochloric acid, the precipitated organic acid was extracted with ether. The extract was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to yield 1.5 g (84%) of the crude crystalline hydroxy acid **8**, which crystallized from hexane as colorless prisms: mp

(24) H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2951 (1961).
(25) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, pp 188–189.
(26) Y. Leroux, *Bull. Soc. Chim. Fr.*, 359 (1968).
(27) S. Danishefsky and D. Dumas, *Chem. Commun.*, 1287 (1968).
(28) H. O. House, J. Riehl, and C. G. Pitt, *J. Org. Chem.*, **30**, 650 (1965).

134–135°; ir 3525 (OH), 1695 cm^{-1} (acid); pmr ($CDCl_3$) δ 6.70 (very br, 2, OH), 5.47 (br s, 1, H_2), 2.46, 2.30 (AB q, J_{AB} = 16 Hz, 2, C_{10} methylene), 2.30 (br s, 1, H_4), 1.75 (d, J = 1.5 Hz, 3, C_3 vinyl methyl), 1.30 (s, 3, C_1 methyl), 1.10 (s, 3, C_9 methyl). *Anal.* Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.55; H, 9.38.

Dehydration of Hydroxy Ester 6 with Phosphorus Oxychloride in Pyridine.—A solution of 0.9 g of the hydroxy ester in 5 ml of dry pyridine was treated with 1 g of redistilled phosphorus oxychloride, and the solution was stirred for 3 hr at 60°. The reaction mixture was then poured into water and extracted with hexane. The extract was washed with dilute hydrochloric acid and water, then dried over anhydrous sodium sulfate. Evaporation of the solvent yielded 0.63 g of a mixture of the esters **9a**, **10a**, and **11**, in a ratio of *ca.* 3:1:1, respectively, by pmr. The ir and pmr spectra of **9a** and **10a** are described below. No attempt was made to isolate the nonconjugated ester **11**, which gave rise to characteristic pmr signals at δ 4.79 (s, C=CH_2), 2.78 (s, C_{10} methylene), and 1.00 (s, C_1 methyl).

Acetylation of Hydroxy Ester 6.—A mixture of 5 ml of acetyl chloride, 20 ml of *N*,*N*-dimethylaniline (purified to remove traces of *N*-methylaniline), 20 ml of chloroform, and 0.99 g of the hydroxy ester were refluxed for 20 hr. The resultant blue solution was diluted with water, acidified at 0° with dilute hydrochloric acid, and extracted with ether. The ether extract was washed with dilute HCl and water and dried over anhydrous sodium sulfate, and the solvent was evaporated to yield 1.1 g of the crude acetate, which was purified by rapid chromatography over 30 g of neutral activity I alumina.[29] The yield of purified acetate **7** was 0.90 g (78%): ir 1730 cm^{-1} (ester and acetate); pmr δ 5.43 (br s, 1, H_2), 4.06 (q, J = 7 Hz, 2, ester), 2.69 (s, 2, C_{10} methylene), 2.28 (br s, 1, H_4), 1.91 (s, 3, acetate methyl), 1.75 (d, J = 1.6 Hz, 3, C_3 vinyl methyl), 1.23 (t, J = 7 Hz, 3, ester), 1.23 (s, 3, tertiary methyl), 1.19 (s, 3, tertiary methyl). The analytical sample was obtained by microdistillation, bp 130° (0.4 mm). *Anal.* Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 69.95; H, 9.23.

Modified Acetylation Procedure.—A mixture of 50 g of ketone **4**, 58 g of bromoacetic ester, and 45 g of activated zinc powder in 800 ml of dry benzene was treated as previously described and the resultant benzene solution of the zinc complex was decanted. The excess sludge of zinc powder was washed with small portions of dry benzene, and the combined solutions were treated at 0° with 450 ml of purified *N*,*N*-dimethylaniline and 150 ml of acetyl chloride. An immediate blue-black tarry deposit separated and, after stirring for several minutes at 20°, the mixture was heated on a steam bath under gentle reflux overnight. The reaction mixture was then poured into excess dilute HCl at 0°, and the tarry residue was stirred and washed with hexane. The washings were combined with the hexane extract of the acidified reaction mixture and the hexane solution was then washed with dilute HCl, aqueous sodium carbonate, and water and dried over anhydrous sodium sulfate and the solvent was evaporated to yield 82 g (95%) of the crude acetate **7**.

Unsaturated Esters 9a and 10a.—The acetate **7** (0.17 g) was treated at 20° with sodium ethoxide solution (0.12 g of sodium in 2 ml of ethanol) for 30 min, the reaction mixture was then poured into water, and the unsaturated esters were extracted with hexane. The extract was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to yield 0.12 g (89%) of the mixture of esters **9a** and **10a** (2.5:1).

In large-scale preparations the crude acetate prepared by the modified acetylation procedure was used without further purification. Treatment of 84 g of acetate with sodium ethoxide solution (14 g of sodium in 400 ml of ethanol) for 80 min at 20° with stirring gave 60 g of the crude unsaturated esters, isolated as above. The esters were separated by chromatography over neutral activity I alumina. The *Z* ester **10a** was eluted first with hexane: ir 1710 (ester), 1630 cm^{-1} (conjugated double bond); pmr δ 5.50 (br s, 2, olefinic protons), 4.06 (q, J = 7 Hz, 2, ester) (superimposed on the doublet of doublets for H_6), 2.32 (br s, 1, H_4), 1.79 (d, J = 1.6 Hz, 3, C_3 vinyl methyl), 1.57 (d, J = 1.2 Hz, 3, C_9 vinyl methyl), 1.24 (t, J = 7 Hz, 3, ester), 0.97 (s, 3, C_1 methyl). The analytical sample was obtained by preparative vpc at 190°, followed by microdistillation, bp 95° (0.4 mm). *Anal.* Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.52; H, 9.89.

(29) The grade of alumina was important as the acetate was unstable on basic alumina, from which the only products eluted were unsaturated esters.

The *E* ester **9a** was eluted with hexane and hexane–benzene (9:1): ir 1710 (ester), 1630 cm^{-1} (conjugated double bond); pmr δ 5.50 (br s, 2, olefinic protons), 4.05 (q, J = 7 Hz, 2, ester), 2.3[30] (br s, 1, H_4), 1.92 (d, J = 1.3 Hz, 3, C_9 vinyl methyl), 1.81 (d, J = 1.8 Hz, 3, C_3 vinyl methyl), 1.23 (t, J = 7 Hz, 3, ester), 0.98 (s, 3, C_1 methyl). The analytical sample was obtained by preparative vpc at 190°, followed by microdistillation, bp 115° (1 mm). *Anal.* Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.21; H, 9.90.

Hydrolysis of Esters 9a and 10a. A. The *E* Ester 9a.—A solution of 0.63 g of the ester in 25 ml of 50% aqueous ethanol containing 2.5 g of sodium hydroxide was refluxed for 8 hr. The crude acid **9b** (0.53 g, 94%) was isolated in the manner described for **8**. The acid crystallized from hexane as colorless prisms: mp 138–139°; ir 1685 (acid), 1625 cm^{-1} (conjugated double bond); pmr δ 12.11 (br s, 1, OH), 5.60 (br s, 1, H_{10}), 5.50 (br s, 1, H_2), 2.34[30] (br s, 1, H_4), 1.93 (br s, 3, C_9 vinyl methyl), 1.82 (d, J = 1.8 Hz, 3, C_3 vinyl methyl), 1.00 (s, 3, C_1 methyl). *Anal.* Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 75.93; H, 9.31.

B. The *Z* Ester 10a.—A solution of 0.45 g of the ester in 25 ml of 50% aqueous ethanol containing 2 g of sodium hydroxide was refluxed for 10 hr. The crude *Z* acid **10b** (0.37 g, 92%) was isolated in the manner described for **8**. The acid crystallized from hexane as colorless, flat needles which sublimed readily on heating: mp 162–163°; ir 1685 (acid), 1625 cm^{-1} (conjugated double bond); pmr δ 11.62 (br s, 1, OH), 5.61 (q, J = 1.3 Hz, 1, H_{10}), 5.48 (br s, 1, H_2), 4.05 (dd, $J_{6,5n} + J_{6,5x}$ = 16 Hz, 1, H_6), 2.33 (br s, 1, H_4), 1.80 (d, J = 1.5 Hz, 3, C_3 vinyl methyl), 1.64 (d, J = 1.3 Hz, 3, C_9 vinyl methyl), 1.00 (s, 3, C_1 methyl). *Anal.* Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.45; H, 9.02.

Lithium–Ammonia Reduction of Esters 9a and 10a.—Following the general procedure of Stork and Darling,[31] 17 g of the mixture of esters **9a** and **10a** (2.5:1) in 200 ml of dry ethanol and 150 ml of ether was added to 1000 ml of liquid ammonia. Lithium metal (11 g) was added in portions with stirring over 1 hr. The blue color persisted throughout the solution for some time after the addition of the last few portions of lithium metal. The ammonia was evaporated by stirring and the cautious addition of water. The aqueous alkaline reaction mixture was extracted with ether. The extract was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to yield 13.5 g (94%) of the crude mixture of alcohols **14a** and **15a**. A portion (7.5 g) was chromatographed on 300 g of neutral activity I alumina, and elution with benzene–ether (9:1) yielded 4.8 g (60%) of the major epimer **14a**: ir 3630, 3430 cm^{-1} (OH); pmr δ 5.47 (br s, 1, H_2), 3.51 (m, 2, C_{11} methylene), 2.35 (br s, 1, OH), 2.27 (br s, 1, H_4), 1.73 (d, J = 1.7 Hz, 3, C_3 methyl), 1.08 (s, 3, C_1 methyl), 0.78 (d, J = 6.5 Hz, 3, C_9 methyl). The analytical sample was prepared by microdistillation, bp 97° (0.1 mm). *Anal.* Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.75; H, 11.67.

The minor epimer **15a** (1.2 g, 15%) was eluted with benzene–ether (9:1) and benzene–ether (4:1): ir 3630, 3430 cm^{-1} (OH); pmr δ 5.46 (br s, 1, H_2), 4.11 (br s, 1, OH), 3.55 (t, J = 7 Hz, 2, C_{11} methylene), 2.27 (br s, 1, H_4), 1.73 (d, J = 1.7 Hz, 3, C_3 vinyl methyl), 1.07 (s, 3, C_1 methyl), 0.55 (d, J = 6.5 Hz, 3, C_9 methyl). The analytical sample was obtained by preparative vpc at 190°, followed by microdistillation, bp 100° (0.1 mm). *Anal.* Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.95; H, 11.56.

Preparation of the Trityl Ether 14c.—A solution of 3.3 g of the alcohol **14a** in 50 ml of benzene and 3 ml of pyridine was heated with 6.0 g of trityl chloride under gentle reflux for 5 hr. The solution was cooled to 0° and the crystalline pyridine hydrochloride was filtered by suction. The filtrate was evaporated almost to dryness and the residue was dissolved in hexane and applied to a column of 300 g of neutral activity I alumina. Elution with hexane and hexane–benzene (4:1) yielded 6.0 g (85%) of the trityl ether **14c**, which crystallized from ethanol as colorless prisms: mp 105–106°; pmr δ 5.47 (br s, 1, H_2), 3.02 (m, 2, C_{11} methylene), 2.24 (br s, 1, H_4), 1.74 (d, J = 1.7 Hz, 3, C_3 vinyl methyl), 1.15 (s, 3, C_1 methyl), 0.62 (d, J = 6.5 Hz, 3, C_9 methyl). *Anal.* Calcd for $C_{33}H_{38}O$: C, 87.95; H, 8.50. Found: C, 88.12; H, 8.48.

(30) The signal for H_6 at about δ 2.2 was superimposed on this broad singlet.

(31) G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, **86**, 1761 (1964).

A mixture of alcohols **14a** and **15a** (4:1) was also tritylated as above, and, in the pmr spectrum of the mixture of trityl ethers **14c** and **15c** obtained, the characteristic signals of the minor epimer **15c** were seen to be δ 1.04 (s, C_1 methyl), 0.48 (d, J = 6.5 Hz, C_9 methyl).

Hydroboration–Oxidation of Trityl Ether 14c.—Diborane was passed through a stirred solution of 27 g of the trityl ether in 140 ml of dry tetrahydrofuran under nitrogen at 20°,[23] until pmr analysis of an aliquot of the reaction mixture showed the complete disappearance of the olefinic signal due to the starting material. Water was then added dropwise to destroy excess hydride. The mixture was then poured into water and the organoborane was extracted with benzene. The solvents were evaporated and the residue was dissolved in 250 ml of pyridine. The pyridine solution was added to chromium trioxide–pyridine complex[32] (40 g of chromium trioxide in 400 ml of pyridine) and the mixture was left overnight at 20°. The reaction mixture was then poured into 1500 ml of ether and the red precipitate was filtered by suction and washed several times with ether. The combined filtrate and washings were then shaken with excess 10% hydrochloric acid at 0° to remove the pyridine. The ether solution was washed exhaustively with dilute HCl at 0° and then with dilute aqueous sodium carbonate and water, and dried over anhydrous sodium sulfate. Evaporation of solvent yielded the crude ketone **16**, which was purified by recrystallization from ethanol. The yield after one recrystallization was 14 g (50%). The ketone crystallized from ethyl acetate as colorless prisms: mp 154–155°; ir 1710 cm^{-1} (ketone); pmr δ 3.02 (m, 2, C_{11} methylene), 2.15 (br q, J = 7.5 Hz, 1, H_3), 1.10 (d, J = 7.5 Hz, 3, C_3 methyl), 1.01 (s, 3, C_1 methyl), 0.67 (d, J = 6.5 Hz, 3, C_9 methyl). *Anal.* Calcd for $C_{33}H_{38}O_2$: C, 84.93; H, 8.21. Found: C, 84.72; H, 8.14.

A mixture of the trityl ethers **14c** and **15c** (4:1) was converted *via* hydroboration–oxidation (as above) to a mixture of the ketones **16** and **17**. Pmr analysis of the mixture showed the characteristic signals of the minor epimer **17** to be δ 0.90 (s, C_1 methyl), 0.50 (d, J = 6.5 Hz, C_9 methyl).

Preparation of Keto Alcohol 18a.—The ketone **16** (6 g) was dissolved in 100 ml of 1,2-dimethoxyethane (glyme) in a flask sealed with a rubber septum cap. By means of a syringe, potassium triphenylmethide solution, prepared by stirring potassium with triphenylmethane in glyme in a septum-sealed flask,[33] was added to the ketone until the red color of the triphenylmethide ion just persisted. Methyl iodide (20 ml) was then injected; the solution warmed noticeably; and potassium iodide precipitated immediately. The mixture was left overnight at 20°, poured into water, and extracted with ether. The ether extract was washed with water and dried over anhydrous sodium sulfate and the solvent was evaporated to yield the trityl ether **18b**, which was of course contaminated with triphenylmethane. The crude product was not purified but was dissolved in 400 ml of ethanol; 1 g of 5% palladium on charcoal was added; and the mixture was shaken under 2.5 atm of hydrogen at 20° for 17 hr. After filtration of the catalyst and evaporation of the ethanol, the product was separated from the triphenylmethane by chromatography over 300 g of neutral activity I alumina. Elution with hexane and hexane–ether (9:1) yielded triphenylmethane together with minor amounts of other aromatic products,[33] while 2.4 g (78%) of the alcohol **18a** was eluted with hexane–ether (1:2) and ether. Vpc analysis showed a single peak on 3% SE-30 at 170°: ir[34] 3625, 3480 (OH), 1715 cm^{-1} (ketone); pmr[34] δ 3.52 (m, 2, C_{11} methylene), 3.12 (br s, 1, OH), 1.11 (s, 6, 2 tertiary methyls), 0.93 (s, 3, tertiary methyl), 0.90 (d, J = 6.5 Hz, 3, C_9 methyl). The analytical sample was prepared by microdistillation, bp 112° (0.02 mm). *Anal.* Calcd for $C_{13}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.52; H, 10.78.

The phenylurethane **18d** of this alcohol was prepared in the usual manner[35] and crystallized from hexane–benzene as colorless prisms: mp 142–143° (lit.[27] mp 165°);[36] ir 3430 (NH), 1735 (urethane carbonyl), 1710 cm^{-1} (ketone); pmr ($CDCl_3$) δ 4.13 (br t, J = 6.5 Hz, 2, C_{11} methylene), 1.14 (s, 6, two tertiary methyls), 0.96 (s, 3, tertiary methyl), 0.92 (d, J = 6.5 Hz, 3, C_9 methyl). *Anal.* Calcd for $C_{22}H_{31}O_3N$: C, 73.91; H, 8.74. Found: C, 74.24; H, 8.89.

Preparation of Tosylate 18c.—The alcohol **18a** (0.25 g) was treated with 0.60 g of *p*-toluenesulfonyl chloride in 18 ml of pyridine at −15° for 12 hr. Ten drops of water were then added and the reaction mixture was left for an additional 45 min at −15°. After addition to excess dilute HCl at 0°, the reaction mixture was extracted with hexane. The extract was washed with dilute aqueous sodium carbonate and water and then dried over anhydrous sodium sulfate. Evaporation of solvent yielded 0.38 g (92%) of the crude tosylate **18c** which crystallized from benzene–hexane as colorless prisms: mp 99–100°; ir 1710 cm^{-1} (ketone); pmr δ 3.95 (m, 2, C_{11} methylene), 2.47 (s, 3, aromatic methyl), 1.08 (s, 3, tertiary methyl), 1.00 (s, 3, tertiary methyl), 0.83 (s, 3, tertiary methyl), 0.83 (d, J = 6.5 Hz, 3, C_9 methyl). *Anal.* Calcd for $C_{22}H_{32}O_4S$: C, 67.32; H, 8.22; S, 8.15. Found: C, 67.62; H, 8.38; S, 7.90.

Preparation of Iodide 18e.—Following an established procedure,[37] 0.50 g of the tosylate **18c** was stirred with 1.5 g of sodium iodide in 20 ml of acetone at 20° for 20 hr, after which time a considerable quantity of sodium tosylate had precipitated. The reaction mixture was poured into water and the iodide was extracted with hexane. The extract was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to yield the crude iodide **18e**, which was purified by chromatography over 40 g of neutral activity I alumina. Elution with hexane–ether (9:1) yielded 0.40 g (90%) of the iodide **18e** as a colorless liquid. Vpc analysis showed a single peak on 3% SE-30 at 170°: ir 1710 cm^{-1} (ketone); pmr δ 3.65–2.8 (very complex m, 2, C_{11} methylene), 1.10 (s, 3, tertiary methyl), 1.06 (s, 3, tertiary methyl), 0.93 (s, 3, tertiary methyl), 0.86 (d, J = 6.5 Hz, 3, C_9 methyl). When an attempt was made to obtain an analytical sample of **18e**, either by preparative vpc or by microdistillation, it decomposed slightly to give a pale yellow oil, which analyzed about 2% high for carbon and 0.8% low for iodine.

Attempted Cyclization of 18e with Magnesium and Mercuric Chloride.—The iodide **18e** (50 mg) in 1.5 ml of tetrahydrofuran which had been freshly distilled from sodium–naphthalene was treated with 15 mg of magnesium powder and 45 mg of mercuric chloride. The mixture was heated in a sealed flask at 80–90° for 2 hr and then poured into water. Extraction with hexane resulted in recovery of the iodide unchanged (pmr and vpc).

Cyclization of Iodide 18e with Sodium.—A solution of 0.20 g of the iodide in 5 ml of tetrahydrofuran, which had been freshly distilled from sodium–naphthalene, was transferred to a thick-walled glass tube. Fine sodium sand (0.15 g), prepared by shaking molten sodium in paraffin oil, was added and the tube was sealed and heated at 90–100° for 4 hr. The surface of the metal became coated with a powdery deposit which soon crumbled and revealed the shiny metallic surface of the residual sodium. The tube was left overnight at 20°, the seal was broken, and the red solution was poured into water. After acidification with dilute HCl, the product was extracted with hexane. The extract was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to leave 0.12 g of a colorless oil. The ir spectrum of this crude product showed some free hydroxyl absorption (3610 cm^{-1}) and carbonyl absorption (1705 cm^{-1}). Analysis of the mixture by vpc showed it to contain two major products, A and B, which accounted for 62% of the total area under all the peaks (40 and 22%, respectively). When the reaction was carried out in more dilute solution (10–20 mg of iodide in 5 ml of tetrahydrofuran), a cleaner reaction product was obtained. Vpc analysis in this case showed A to constitute 45% of the total area and B 31%. The retention times of A and B on 5% DEGS at 120° were 6 and 2.5 min, respectively. A and B were isolated by preparative vpc on 10% Carbowax 20M at 200°.

The constituent A was a colorless semisolid which was readily purified by sublimation to give (±)-patchouli alcohol (**2**): mp 46–47° (lit.[27] mp 39–40°); ir 3610 (free OH), 1380, 1370, and 1363 cm^{-1} (methyls);[38] pmr δ 1.06 (s, 6, two tertiary methyls),

(32) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, **75**, 422 (1953).

(33) H. O. House and V. Kramar, *J. Org. Chem.*, **27**, 4146 (1962).

(34) The ir and pmr spectra were identical with copies of spectra of the alcohol kindly forwarded by Dr. Danishefsky.

(35) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., London, 1962, p 264.

(36) In a recent letter Dr. Danishefsky has conceded the possibility of having confused the melting points of the epimers **18d** and **19d**. He reported[27] the melting point for **19d** as 145°.

(37) R. S. Tipson, M. A. Clapp, and L. H. Cretcher, *J. Org. Chem.*, **12**, 133 (1947).

(38) A noteworthy feature of the ir spectrum of patchouli alcohol was these three strong, well-resolved absorptions. Presumably the "doublet" at 1380 and 1370 cm^{-1} was due to symmetric and asymmetric *gem*-dimethyl stretching vibrations.

0.82 (s, 3, tertiary methyl), 0.80 (d, J = 6.5 Hz, 3, secondary methyl). The vpc retention time[39] (5% UCON, 5% DEGS) and ir and pmr spectra were superimposable on those of naturally occurring (−)-patchouli alcohol.[40] The mass spectrum was also identical with that of the natural product.

Constituent B was the oily acyclic ketone **18g**: ir 1705 cm^{-1} (ketone); pmr δ 1.09 (s, 3, tertiary methyl), 1.07 (s, 3, tertiary methyl), 0.88 (s, 3, tertiary methyl), 0.86 (d, J = 6.5 Hz, 3, C_9 methyl); mass spectrum m/e 222 (M^+).

(39) The synthetic material was mixed with naturally occurring (−)-patchouli alcohol and peak enhancement was observed on the two columns at various temperatures.

(40) Naturally occurring (−)-patchouli alcohol, mp 56°, was isolated from patchouli oil which was generously donated by Plaimar Ltd., Perth. The higher boiling fractions of the oil were chromatographed over neutral alumina to give patchouli alcohol of high purity.

Registry No.—(±)-**2**, 5986-55-0; **4**, 34996-60-6; **6**, 34996-61-7; **7**, 34996-62-8; **8**, 34996-63-9; **9a**, 34996-28-3; **9b**, 34996-64-0; **10a**, 34996-65-1; **10b**, 34996-66-2; (±)-**14a**, 29450-72-4; (±)-**14c**, 29448-20-2; (±)-**15a**, 29448-21-3; (±)-**16**, 34996-70-8; (±)-**18a**, 21682-97-3; (±)-**18c**, 34996-72-0; (±)-**18d**, 21683-01-2; (±)-**18e**, 34996-74-2; (±)-**18g**, 21682-98-4.

Studies with Bicyclo[2.2.2]octenes. VI.[1] The Total Synthesis of (±)-Seychellene[2]

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A stereospecific total synthesis of (±)-seychellene is described from the alcohol **2**, which was previously prepared for the synthesis of patchouli alcohol. The key stage in the sequence was the relatively efficient conversion of the olefinic bridge in **2** to the exocyclic methylene function in **21** *via* a modified hydrochlorination–dehydrochlorination procedure. The sequence was completed *via* the intermediates **22**, **25**, **26a**, and **26c**. Attempts to acylate the olefinic ester **7** gave none of the desired ketone **11**, but afforded instead the rearranged acetate **8** and/or the ketone **9**, depending on the reaction temperature.

The sesquiterpenoid (−)-seychellene was isolated from patchouli oil obtained from the Seychelles Islands, and was assigned the structure and absolute stereochemistry depicted in **1**.[4] The similarity in structure between seychellene and patchouli alcohol suggested a synthetic route to seychellene utilizing alcohol **2**, a key intermediate for the synthesis of patchouli alcohol.[1]

Two approaches to an intramolecular alkylation which could be used to construct the tricyclic seychellene skeleton are outlined in Scheme I. Path A suffers from the disadvantage that either the nitrile, aldehyde, or methyl ketone function of the cyclized product **4** must be converted to a methyl group in seychellene. On the other hand, norseychellanone (**5**), the path B intramolecular alkylation product, ought to be readily converted to seychellene by the reported procedure[5] of reaction with methyllithium, followed by dehydration of the resultant tertiary alcohol with thionyl chloride–pyridine.

Preliminary investigations were carried out on both pathways to assess their relative merits. The unsaturated aldehyde **3b** would have been the most useful of the type A alkylations from the point of view of generation of the C_2 methyl by a Wolff–Kishner reduction.[6] The preparation of this unsaturated aldehyde from the ketone **6**,[1] however, would be far from trivial.[7] The preparation of the unsaturated nitrile **3a** *via* the corresponding cyanohydrin was abandoned when difficulty was experienced in preparing the latter in good yield from the ketone **6** using acetone cyanohydrin.[8]

It is known[9] that acylation of 1-methylcyclohexene with polyphosphoric acid in acetic acid under specified conditions yields 2-acetyl-1-methylcyclohexene, and therefore it was envisaged that a compound of the type **3c** might be prepared by acylation of the corresponding olefin with the same reagent. Initially we studied the acylation of the readily available[10] model ester **7**.

At 55–60°, the major product of the reaction of **7** with polyphosphoric acid in acetic acid was the rearranged secondary acetate **8**. There was little or no tertiary acetate **10**, which was perhaps the expected major product, and furthermore, none of the desired ketone **11** was detected. At 75–80°, a mixture of compounds was isolated of which greater than 90% (pmr and vpc) were **8** and **9** in a ratio of 1:1.7. At 85–90°, the sole product was the ketone **9**. The movement of the double bond from the endocyclic to the exocyclic position prior to acylation has also been observed by other workers in the acylation of 1-ethylcyclohexene catalyzed by stannic chloride.[11] It was the remarkable isolation of **9** in good yield which aroused interest in the present case, since ozonolysis of **9** to the corresponding ketone **12** provided the analogy for a useful method of preparing a type B intramolecular alkylation precursor such as **25**. It was found, however, that, when the primary acetate **13** was treated with polyphosphoric acid in acetic acid under identical conditions to those used for the methyl ester **7**, none of the expected conjugated ketone analogous to **9** was obtained. The mixture of

(1) Part V: R. N. Mirrington and K. J. Schmalzl, *J. Org. Chem.*, **37**, 2871 (1972), accompanying paper.

(2) Some of the work described herein has appeared in a preliminary communication: K. J. Schmalzl and R. N. Mirrington, *Tetrahedron Lett.*, 3219 (1970).

(3) (a) Abstracted in part from the Ph.D. thesis of K. J. Schmalzl, University of Western Australia, May 1971. (b) The award of a Commonwealth Postgraduate Scholarship to K. J. S. is gratefully acknowledged.

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(5) J. E. McMurry, *J. Amer. Chem. Soc.*, **90**, 6821 (1968).

(6) F. E. King, D. H. Godson, and T. J. King, *J. Chem. Soc.*, 1117 (1955).

(7) M. de Botton, *Bull. Soc. Chim. Fr.*, 2466 (1966).

(8) (a) R. Gardi, P. P. Castelli, R. Gandolfi, and A. Ercoli, *Gazz. Chim. Ital.*, **91**, 1250 (1961); (b) A. Ercoli and P. de Ruggieri, *J. Amer. Chem. Soc.*, **75**, 650 (1953).

(9) S. B. Kulkarni and Sukh Dev, *Tetrahedron*, **24**, 561 (1968).

(10) R. N. Mirrington and K. J. Schmalzl, *J. Org. Chem.*, **34**, 2358 (1969).

(11) J. K. Groves and N. Jones, *Tetrahedron Lett.*, 1161 (1970).