Tetrahedron Vol. 43, No. 5, pp. 825 to 834, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00

STEREOCONTROLLED TOTAL SYNTHESIS OF (±)-NORPATCHOULENOL AND TWO METABOLITES OF PATCHOULI ALCOHOL, (±)-HYDROXY PATCHOULI ALCOHOL AND THE CORRESPONDING (±)-CARBOXYLIC ACID

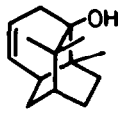
HARUKI NIWA, TAKASHI HASEGAWA, NORIKAZU BAN,
and KIYOYUKI YAMADA*

Department of Chemistry, Faculty of Science, Nagoya University,
Chikusa, Nagoya 464 Japan

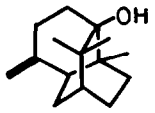
(*Received in Japan* 22 *December* 1986)

Abstract - The first total synthesis of the two biooxidation products of patchouli alcohol (**2**), (±)-hydroxy patchouli alcohol (**3**) and the corresponding (±)-carboxylic acid **4**, has been achieved in highly stereocontrolled manners. Synthesis of (±)-norpatchoulenol (**1**), the real odoriferous substance of patchouli oil, has been accomplished by the biogenetic route via (±)-**3** and (±)-**4**.

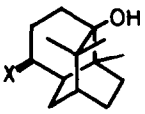
The structurally novel norsesquiterpenoid norpatchoulenol (**1**) is a minor component of commercial patchouli oil and has been shown to be the real odoriferous substance of this important essential oil.[1] The structure and absolute stereochemistry of norpatchoulenol have been established by chemical and spectroscopic studies coupled with the X-ray crystallographic analysis as depicted in the formula **1**.[2] Structurally and biogenetically, norpatchoulenol (**1**) is obviously closely related to the sesquiterpenoids patchouli alcohol (**2**),[3] the major component of patchouli oil, and seychellene (**5**)[4] and cycloseychellene (**6**),[5] the other minor components of this essential oil. In 1975, Ourisson and Teisseire carried out the administration experiment of patchouli alcohol (**2**) to rabbits and isolated two biooxidation products, hydroxy patchouli alcohol (**3**) and the corresponding carboxylic acid **4**.[6] Based on this administration experiment they proposed the biogenesis of norpatchoulenol (**1**) from patchouli alcohol (**2**) as shown in Scheme I.[6] Recently microbial conversion of patchouli alcohol (**2**) into hydroxy patchouli alcohol (**3**) has been reported.[7]



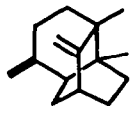
1



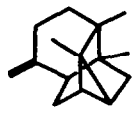
2



3 X = CH_2OH
4 X = COOH



5

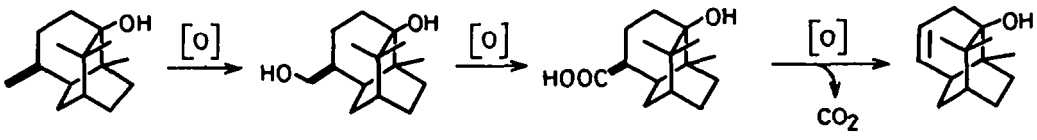


6

These six natural products possess the intriguing carbon framework, a tricyclo[5.3.1.$0^{3,8}$]undecane skeleton. While a number of total syntheses of **1**,[8] **2**,[9,10] **5**,[9,11] and **6**[11c,12] have been reported, there seems to be no report of the synthetic studies on hydroxy patchouli alcohol (**3**) and the corresponding carboxylic acid **4**, the metabolites of patchouli alcohol (**2**). During the past several years, we have been engaged in the synthetic studies on the sesquiterpenoids of patchouli oil, culminating in the synthesis of patchouli alcohol (**2**),[9] seychellene (**5**),[9] and cycloseychellene (**6**).[12] As part of our continuing studies in this field, we wish to describe herein the full details of the first,

highly stereocontrolled total synthesis of hydroxy patchouli alcohol (**3**) and the corresponding carboxylic acid **4** in racemic forms,[13] and the details of the synthesis of racemic norpatchoulenol (**1**) from **3** and **4** in the biogenetic manner.[13]

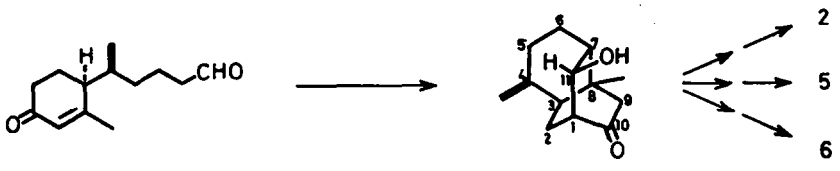
Scheme I. Biogenesis of norpatchoulenol (**1**) from patchouli alcohol (**2**).



2 3 4 1

The crucial intermediate in our previous synthesis of (+)-patchouli alcohol (**2**), seychellene (**5**) and cycloseychellene (**6**) was a tricyclo[5.3.1.$0^{3,8}$]undecane derivative **8**, which was obtained by a novel double cyclization reaction of a conjugated cyclohexenone aldehyde **7** in a single step (Scheme II).[9,12]

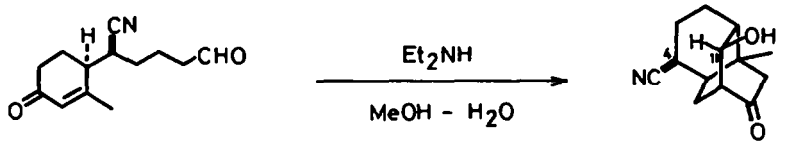
Scheme II.



7 8

For the synthesis of hydroxy patchouli alcohol (**3**) and the carboxylic acid **4**, we required a compound which possesses the functionalized methyl group or the synthetic equivalent with the correct stereochemistry at the C-4 position in the tricyclo[5.3.1.$0^{3,8}$]undecane skeleton in **8**. However, direct and selective functionalization of the secondary methyl group appended to the C-4 position in the tricyclo[5.3.1.$0^{3,8}$]undecane skeleton such as **8** was anticipated to be difficult. As the key intermediate for the present synthesis, we have chosen a tricyclic keto nitrile **10**, which possesses a nitrile group with the desired stereochemistry at the C-4 position in the tricyclo[5.3.1.$0^{3,8}$]undecane skeleton and may be obtained by the double cyclization reaction of a conjugated cyclohexenone aldehyde **9** in a single step as in the case of the cyclization of **7** into **8** (Scheme III). Thus, the first task of the present synthesis has been focused on the construction of **9** having the desired stereochemistry at two asymmetric centers.

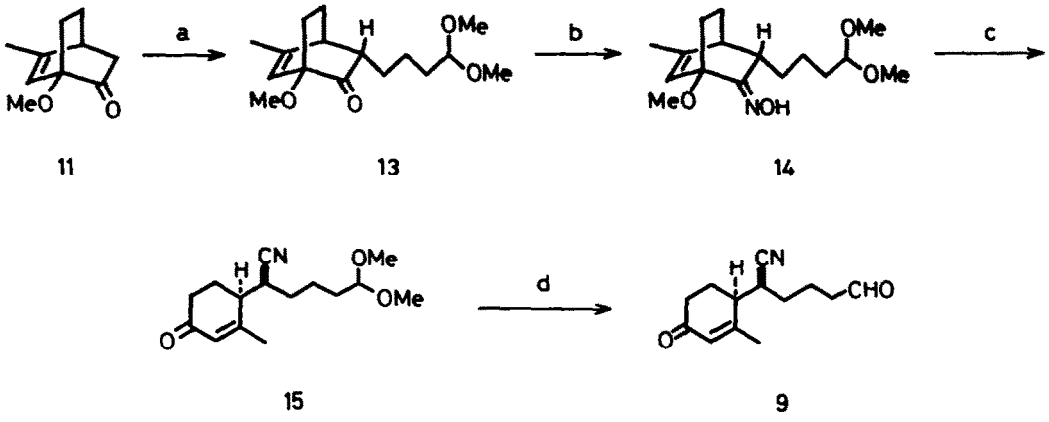
Scheme III.



9 10

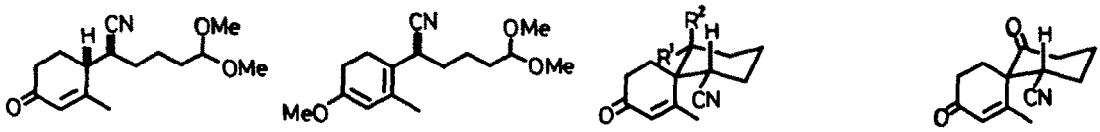
The preparation of **9** started from readily accessible 1-methoxy-5-methylbicyclo[2.2.2]octan-5-en-2-one (**11**)[14] (Scheme IV). The lithium enolate derived from **11** with LDA was treated with 4,4-dimethoxybutyl iodide (**12**)[15] to give the alkylated ketone **13** as a single isomer in 78% yield. This

Scheme IV.



(a) i LDA; ii $(MeO)_2CHCH_2CH_2CH_2I$ (**12**). (b) NH_2OH. (c) TsCl-LiCl, Py. (d) AcOH-H_2O.

high stereoselectivity in the alkylation may be due to kinetic preference for approach of the alkylating reagent from the presumed less hindered face of the bicyclic enone **11** (i.e. syn to the double bond in **11**). During our investigations, the similar stereoselective alkylation of **11** was reported by other workers.[16] The alkylated ketone **13** was converted into the oxime **14** in 99% yield. A crucial step in the preparation of **9** was the Beckmann fragmentation reaction of the oxime **14** into the conjugated cyclohexenone acetal **15**.[17] The Beckmann fragmentation reaction of **14** was effected with TsCl in pyridine in the presence of a large amount of LiCl to give the desired product **15** (57%) together with the diastereomer **16** (7%) and the diene **17** (35%). When this reaction was performed under the same conditions as described above in the absence of LiCl, the preferential formation of **17** at the expense of **15** was observed. Deacetalization of **15** (AcOH-H_2O) provided the desired conjugated cyclohexenone aldehyde **9**. Double cyclization of **9** proceeded smoothly on treatment with Et_2NH in MeOH-H_2O to give the key intermediate, the tricyclic keto nitrile **10** (41% yield from **15**) together with two spiro compounds, **18** (17%) and **19** (17%) (Scheme III). The stereochemistry of the OH group in **10** was determined as shown in the formula **10** by the ^1H NMR spectrum, in which a signal due to H-11 appeared at δ 3.97 as a doublet of doublets with coupling constants of 4.3 and 1.8 Hz. The structures of **18** and **19** were unambiguously established by the X-ray crystallographic analysis of **18** (Figure 1) and PCC[18] oxidation of **18** and **19**, both of which formed the same spiro ketone **20**.



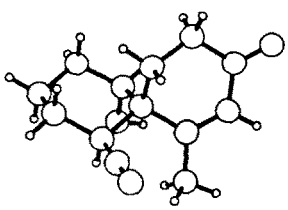
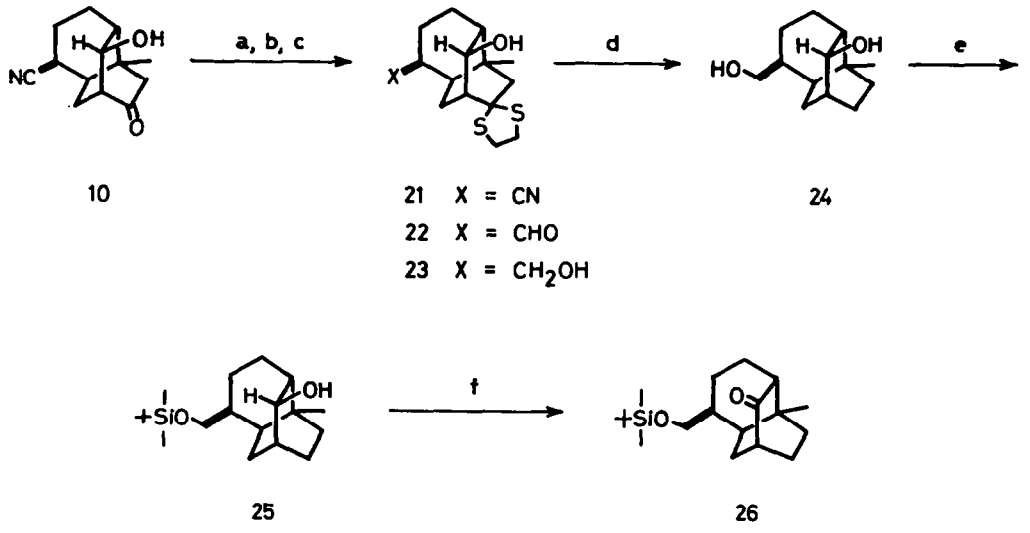


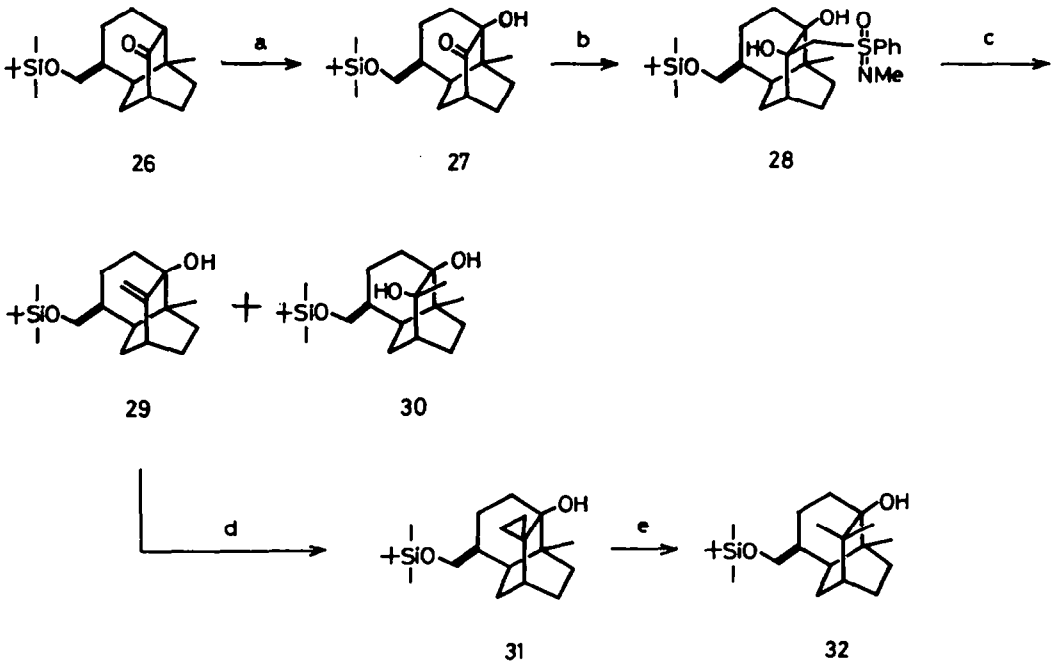
Figure 1. Computer-generated perspective drawing of **18**.

Scheme V.



(a) $(CH_2SH)_2$, $BF_3{\cdot}OEt_2$. (b) DIBAL. (c) $NaBH_4$.
(d) Raney Ni (W-2). (e) TBDMSCl, DMAP-Et_3N. (f) PCC.

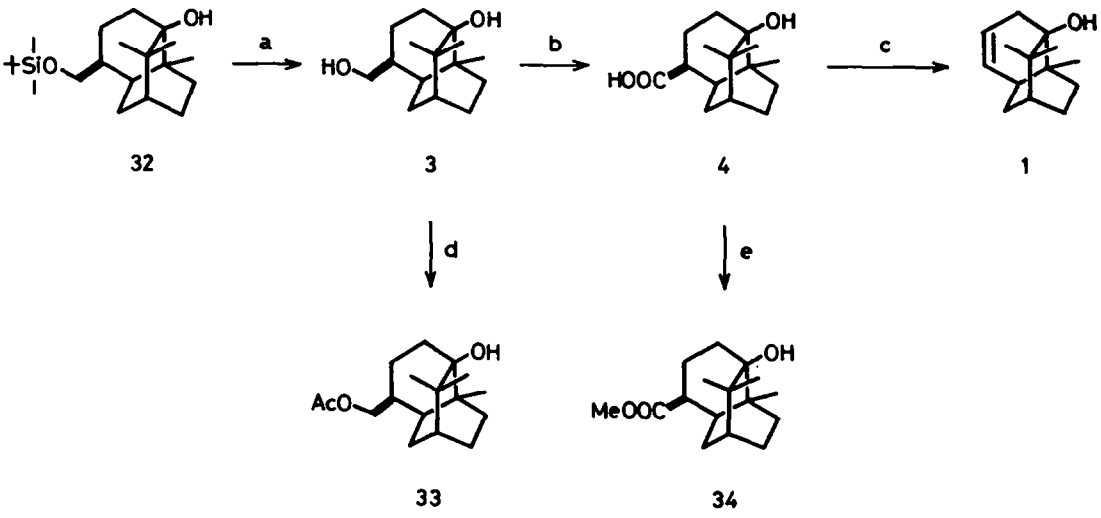
Scheme VI.



(a) i LDA; ii $MoO_5{\cdot}Py{\cdot}HMPA$. (b) $PhSO(=NMe)CH_2Li$. (c) Al-Hg.
(d) CH_2N_2-CuOTf. (e) H_2/PtO_2.

Thus, the key intermediate, the tricyclic keto nitrile **10** was in hand. The keto nitrile **10** was converted into the diol **24** in 75% overall yield by four steps: (1) thioacetalization; (2) DIBAL reduction; (3) $NaBH_4$ reduction; (4) desulfurization (Scheme V). The primary hydroxyl group in **24** was selectively protected as the t-butyldimethylsilyl ether[19] to give **25** (99%), which was oxidized with PCC[18] into the ketone **26** (87%). Bridgehead hydroxylation[9] of the lithium enolate derived from **26** (LDA, -78 °C) was effected with MoO_5·Py·HMPA[20] to give the α-hydroxy ketone **27** in 73% yield (Scheme VI). The α-hydroxy ketone **27** was converted into the olefin **29** in 67% overall yield by the Johnson's procedure:[21] (1) addition of $PhSO(=NMe)CH_2Li$ (THF, -78 °C); (2) reductive elimination (Al-Hg, 100:100:1 AcOH-THF-H_2O). Interestingly, the reductive elimination of the β-hydroxysulfoximine derivative **28** (a 1:1 mixture of the diastereomers concerning the sulfur atom) with Al-Hg into **29** was markedly affected by the content of water in the reaction medium. For example, when the reduction was performed in the medium containing H_2O in relatively high concentration (15:15:1 AcOH-THF-H_2O), the undesired compound **30** (the stereochemistry of the newly formed tertiary methyl group was not elucidated) was formed in 34% yield, while the desired olefin **29** was obtained in 31% yield. By contrast, reduction of **28** in the medium with relatively low water concentration (100:100:1 AcOH-THF-H_2O) was found to give the desired **29** in 70% yield. Cyclopropanation[22] of **29** was effected by reaction with CH_2N_2 in the presence of CuOTf to yield the cyclopropane derivative **31** in 79% yield. Catalytic hydrogenation of **31** over PtO_2 in AcOH-AcONa provided the protected hydroxy patchouli alcohol **32** in 83% yield. Desilylation of **32** with Bu_4NF yielded (±)-hydroxy patchouli alcohol (**3**) [mp 132.5-133 °C, 97%], the ^1H NMR spectrum of which was identical with that of natural **3** (Scheme VII). For the further structural confirmation, synthetic (±)-**3** was converted to the corresponding acetate **33** (85%), the spectral (IR, ^1H NMR, and mass) properties of which were identical in all respects with those of the authentic sample derived from natural **3**. Furthermore, PDC[23] oxidation of (±)-**3** provided the corresponding (±)-carboxylic acid **4** in 97% yield. The ^1H NMR spectrum of the derived methyl ester **34** was identical to that of the authentic sample obtained from natural **4**. Finally, decarboxylative oxidation of (±)-**4** under the conditions reported by Kochi[24] gave (±)-norpatchoulenol (**1**) (mp 155-160 °C in a sealed tube, 31% yield).[6] The ^1H NMR, IR, and mass spectral properties of synthetic (±)-**1** were completely identical in all respects with those of natural **1**.

Scheme VII.



(a) Bu_4NF. (b) PDC. (c) $Pb(OAc)_4$-$Cu(OAc)_2$.
(d) Ac_2O-Py. (e) CH_2N_2.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were taken on either a JASCO Model IRS or a JASCO Model IR-810 spectrophotometer in $CHCl_3$ solution unless otherwise stated. ^1H NMR spectra were recorded on a JEOL FX-90QE (90 MHz) spectrometer in $CDCl_3$ solution unless otherwise noticed: chemical shifts (δ) are reported in ppm downfield from internal TMS and coupling constants in Hz. Low resolution mass spectra (MS) were recorded on a Hitachi RMU-6C instrument. High resolution mass spectra (HRMS) were measured on a JEOL JMS-DX300 instrument. Fuji-Davison silica gel BW-80 was used for column chromatography. Merck precoated silica gel $60F_{254}$ plates, 0.25 mm thickness, were used for analytical thin layer chromatography (TLC) and Merck silica gel PF_{254} for preparative TLC. Unless otherwise indicated, the organic solutions obtained by extractive workup were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure by a rotary evaporator.

4,4-Dimethoxybutyl iodide **12**. To a stirred solution of ethyl 4-bromobutyrate (3.7 ml, 26 mmol) in hexane (50 ml) and toluene (17 ml) under nitrogen at -100 °C was added dropwise a 1.76 M solution of diisobutylaluminum hydride in toluene (16.1 ml, 28.3 mmol) over the period of 45 min. After 15 min, MeOH (13 ml) was cautiously added dropwise to the reaction mixture and the resulting mixture was warmed to room temperature. To the mixture were added saturated aqueous potassium sodium tartrate solution (20 ml) and Celite (8 g). The mixture was vigorously stirred for a while and filtered through a pad of Celite. The filter cake was washed with ether (300 ml). The filtrate and washings were combined, washed with brine, dried, and concentrated to give the crude oil of 4-bromobutanal[15c] (5 g), which was used for the next reaction without further purification. A mixture of the crude oil of 4-bromobutanal (5 g) and NH_4Cl (54 mg) in anhydrous MeOH (150 ml) was heated at reflux for 10 min. After cooling, the mixture was diluted with saturated aqueous $NaHCO_3$ solution (10 ml) and concentrated in vacuo. The resulting residue was extracted with ether (4 x 100 ml). The combined organic layers were washed with brine, dried, and concentrated to give the crude oil of 4,4-dimethoxybutyl bromide[15b] (4.9 g), which was used for the next reaction without further purification. A mixture of the crude oil of 4,4-dimethoxybutyl bromide (4.9 g), NaI (29.8 g, 200 mmol), and anhydrous $CaCO_3$ (9.9 g, 100 mmol) in anhydrous acetone (135 ml) was vigorously stirred at room temperature for 1 h and concentrated in vacuo. The resulting residue was diluted with ether (50 ml) and passed through a column of Florisil. The column was washed with ether (150 ml). The filtrate and washings were combined and concentrated to give the oily residue. Purification by column chromatography on silica gel (1:1 hexane-ether) provided **12**[15a] (4.09 g, 65% overall yield from ethyl 4-bromobutyrate) as a colorless oil: IR 1125 cm^{-1}; ^1H NMR δ 1.63-2.00 (4H, m), 3.19 (2H, t, J = 7.0), 3.31 (6H, s), 4.35 (1H, t, J = 5.5); MS m/z 244 (M^+), 243, 213, 185.

Alkylated ketone **13**. To a stirred solution of diisopropylamine (0.33 ml, 2.4 mmol) in anhydrous THF at -78 °C under nitrogen was added dropwise a 1.63 M solution of n-butyllithium in hexane (1.3 ml, 2.1 mmol). After 20 min, a solution of **11**[14] (111 mg, 0.668 mmol) in anhydrous THF (1.0 ml) was added slowly to the solution of LDA at -78 °C. After being stirred for 40 min, the solution was warmed to -20 °C. To the solution were added 1.8 ml of dry hexamethylphosphramide and then a solution of **12** (550 mg, 2.25 mmol) in anhydrous THF (1 ml). The reaction mixture was stirred at -20 °C for 1.5 h. The reaction was quenched at -20 °C with saturated aqueous NH_4Cl solution (0.5 ml). The mixture was warmed to room temperature, diluted with water (1 ml), and extracted with hexane (4 x 15 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (1:2 hexane-ether) to give **13** (149 mg, 78%) as a colorless oil: IR 1727, 1441, 1322, 1128 cm^{-1}; ^1H NMR δ 1.87 (3H, d, J = 2.0), 2.65 (1H, m), 3.29 (6H, s), 3.29 (1H, m), 3.47 (3H, s), 4.33 (1H, br t, J = 5.4), 5.76 (1H, m); MS m/z 282 (M^+), 254, 251, 239, 222, 219, 124, 75 [HRMS. Found: 282.1834 (M^+). $C_{16}H_{26}O_4$ requires: 282.1831].

Oxime **14**. To a solution of **13** (325 mg, 1.15 mmol) in MeOH (11 ml) and H_2O (1.1 ml) was added hydroxylamine hydrochloride (244 mg, 3.51 mmol) and sodium acetate (474 mg, 5.78 mmol). The mixture was heated at reflux for 9 h. After cooling, the reaction mixture was concentrated in vacuo. The residue was diluted with saturated aqueous $NaHCO_3$ solution (5 ml) and extracted with ether (4 x 15 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (100:100:1 hexane-EtOAc-Et_3N) to provide **14** (339 mg, 99%) as a colorless oil: IR 3610, 3260, 1127, 1104, 1070, 1047 cm^{-1}; ^1H NMR δ 1.86 (3H, d, J = 2.0), 2.54 (1H, m), 2.70 (1H, br dt, J = 10.4, 2.9), 3.30 (6H, s), 3.46 (3H, s), 4.35 (1H, br t, J = 5.8), 5.93 (1H, m); MS m/z 297 (M^+), 280, 248, 217, 202, 186, 114, 85, 75 [HRMS. Found: 297.1933 (M^+). $C_{16}H_{27}NO_4$ requires: 297.1938].

Conjugated cyclohexenone acetal **15**. A mixture of **14** (61.0 mg, 0.205 mmol) and LiCl (87 mg, 2.1 mmol) in anhydrous pyridine (1.5 ml) was stirred for 10 min at room temperature under nitrogen. To the mixture was added p-toluenesulfonyl chloride (157 mg, 0.823 mmol). The reaction mixture was stirred for 4 h at room temperature and diluted with EtOAc (10 ml). The resulting mixture was washed successively with water (3 ml), saturated aqueous $CuSO_4$ solution (3 x 5 ml), and brine. The organic layer was dried and concentrated to give the oily residue. Purification by preparative TLC on silica gel (100:100:1 hexane-EtOAc-Et_3N) afforded **15** (31.0 mg, 57%) as colorless crystals, **16** (4.0 mg, 7%) as a colorless oil, and **17** (20.0 mg, 35%) as a colorless oil, respectively. **15**: mp 55-56 °C (cyclohexane); IR 2250, 1667, 1625, 1384, 1128, 1074, 1050 cm^{-1}; ^1H NMR δ 1.2-1.9 (6H, m), 2.02 (3H, br s), 2.1-2.9 (6H, m), 3.33 (6H, s), 4.34 (1H, br t, J = 4.7), 5.96 (1H, br q, J = 1.1); MS m/z 265 (M^+), 264, 234, 218, 202, 175, 109, 75. (Found: C, 67.75; H, 9.04; N, 5.24. $C_{15}H_{23}NO_3$ requires: C, 67.89; H, 8.74; N, 5.28%). **16**: IR 2260, 1670, 1625, 1387, 1128, 1072, 1051 cm^{-1}; ^1H NMR δ 1.4-1.9 (6H, m), 2.00 (3H, br s), 2.1-2.8 (5H, m), 2.97 (1H, m), 3.34 (6H, s), 4.37 (1H, m), 6.03 (1H, m); MS m/z 265 (M^+), 264, 250, 234, 218, 202, 175, 109, 75 [HRMS. Found: 264.1579 (M^+-1). $C_{15}H_{22}NO_3$ requires: 264.1599]. **17**: IR 2250, 1662, 1641, 1607, 1384, 1127, 1075, 1050 cm^{-1}; ^1H NMR δ 1.4-2.0 (6H, m), 1.74 (3H, br s), 2.0-2.8 (4H, m), 3.32 (6H, s), 3.59 (3H, s), 3.59 (1H, m), 4.35

(1H, m), 4.78 (1H, br s); MS m/z 279 (M^+), 264, 248, 232, 216, 162, 124, 75 [HRMS. Found: 279.1847 (M^+). $C_{16}H_{25}NO_3$ requires: 279.1835].

Conjugated cyclohexenone aldehyde **9**. A solution of **15** (112 mg, 0.422 mmol) in AcOH (1.7 ml) and H_2O (0.8 ml) was stirred at 60 °C for 1.5 h. After cooling, the reaction mixture was diluted with toluene (5 ml) and concentrated in vacuo. The oily residue was diluted with saturated aqueous $NaHCO_3$ solution (5 ml) and extracted with EtOAc (4 x 15 ml). The combined organic layers were washed with brine, dried, and concentrated to give **9** (109 mg), which was directly used for the next reaction without further purification. **9**: IR 2720, 2260, 1729, 1668, 1625, 1387 cm^{-1}; ^1H NMR δ 2.04 (3H, br s), 5.95 (1H, m), 9.72 (1H, br, s); MS m/z 219 (M^+), 191, 176, 148, 109, 83.

Tricyclic keto nitrile **10**. A solution of crude **9** (109 mg, ca. 0.42 mmol) and Et_2NH (1.2 ml) in MeOH (11.4 ml) and H_2O (0.6 ml) was stirred at 70 °C for 1.5 h under nitrogen. After cooling, the reaction mixture was concentrated in vacuo. The oily residue was diluted with H_2O (2 ml) and extracted with EtOAc (4 x 7 ml). The combined organic layers were washed with brine, dried, and concentrated. The crude products were separated by preparative TLC on silica gel (2:1 benzene-acetone) to give **10** (38.0 mg, 41% from **15**), **18** (16.0 mg, 17% from **15**), and **19** (16.0 mg, 17% from **15**) as colorless crystals, respectively. **10**: mp 205-206 °C ($CHCl_3$); IR 3620, 3430, 2250, 1725, 1072 cm^{-1}; ^1H NMR δ 1.03 (3H, s), 2.14 (2H, m), 2.54 (1H, m), 2.95 (1H, m), 3.97 (1H, dd, J = 4.3, 1.8); MS m/z 219 (M^+), 201, 173, 160, 106. (Found: C, 71.14; H, 8.04; N, 6.40. $C_{13}H_{17}NO_2$ requires: C, 71.20; H, 7.82; N, 6.39%). **18**: mp 188-190 °C (EtOH); IR (KBr) 3300, 2260, 1660, 1609, 1116 cm^{-1}; ^1H NMR δ 2.24 (3H, d, J = 1.4), 3.52 (1H, m), 4.18 (1H, m), 5.97 (1H, br q, J = 1.4); MS m/z 219 (M^+), 191, 176, 148, 109 [HRMS. Found: 219.1236 (M^+). $C_{13}H_{17}NO_2$ requires: 219.1258]. **19**: mp 141-143 °C (benzene); IR (KBr) 3300, 2260, 1648, 1619, 1090 cm^{-1}; ^1H NMR δ 2.02 (3H, d, J = 1.4), 3.72 (1H, m), 6.09 (1H, br q, J = 1.4); MS m/z 219 (M^+), 191, 176, 148, 109 [HRMS. Found: 219.1239 (M^+). $C_{13}H_{17}NO_2$ requires: 219.1258].

X-Ray analysis of **18**. Crystals of **18** were obtained by slow crystallization from EtOH. D_{measd} was measured by floatation. Crystal data of **18** were as follows: $C_{13}H_{17}NO_2$, M_r = 219.13; monoclinic, space group $P2_1/n$, a = 12.194(2) Å, b = 7.941(1) Å, c = 11.848(1) Å, β = 100.25(1)°; V = 1129.0(3) Å^3; D_{calcd} = 1.291 g/cm^3, D_{measd} = 1.296 g/cm^3; z = 4. Total 2099 reflections with 2θ < 126° were collected on a RIGAKU AFC-5R automated four-circle diffractometer using graphite monochromated Cu Kα radiation (1.54178 Å). Structure was solved by Monte-Carlo direct method with the aid of MULTAN 78 program system using 1817 non zero unique reflections and refined by full-matrix least square program. The final R value was 0.052 (R_w = 0.056). A computer-generated perspective drawing of **18** is given in Fig. 1.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW.

Oxidation of **18** and **19** into spiro ketone **20**. To a stirred solution of **18** (42.0 mg, 0.192 mmol) in CH_2Cl_2 (2.0 ml) was added PCC (130 mg, 0.603 mmol) at room temperature. After 2 h, additional PCC (130 mg, 0.603 mmol) was added and stirring was continued for 1 h at room temperature. The reaction mixture was diluted with ether (5 ml) and passed through a short column packed with Florisil. The column was washed with EtOAc (30 ml). The filtrate and washings were combined and concentrated. The oily residue was purified by preparative TLC on silica gel (3:1 benzene-acetone) to give **20** (24.5 mg, 59%) as colorless crystals: mp 164-166 °C (benzene); IR 2260, 1714, 1676, 1628, 1119 cm^{-1}; ^1H NMR δ 1.97 (3H, d, J = 1.5), 3.39 (1H, dd, J = 9.2, 6.8), 6.16 (1H, br q, J = 1.5); MS m/e 217 (M^+), 189, 174, 161, 83. (Found: C, 71.88; H, 7.03; N, 6.51. $C_{13}H_{15}NO_2$ requires: C, 71.87; H, 6.96; N, 6.45%).

Oxidation of **19** (47.0 mg, 0.214 mmol) with PCC (280 mg, 1.30 mmol) and purification of the crude products by the procedure described above afforded also **20** (24.8 mg, 53%).

Thioacetal **21**. A solution of **10** (200 mg, 0.912 mmol), and BF_3 etherate (0.05 ml, 0.41 mmol) in ethanedithiol (4 ml) was stirred at room temperature for 1.5 h. The reaction mixture was diluted with 10 N NaOH solution (5 ml), and extracted with EtOAc (4 x 50 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by preparative TLC on silica gel (3:1 benzene-acetone) to give **21** (263 mg, 98%) as colorless crystals: mp 180-180.5 °C (hexane-$CHCl_3$); IR 3430, 2250, 1138, 1062 cm^{-1}; ^1H NMR δ 0.87 (3H, s), 2.26 (2H, br s), 2.50 (1H, ddd, J = 14.4, 11.1, 3.2), 2.88 (1H, m), 3.1-3.5 (4H, m), 3.84 (1H, ddd, J = 7.2, 3.6, 3.6); MS m/z 295 (M^+), 267, 249, 235, 217, 202, 174, 91, 61 [HRMS. Found: 295.1044 (M^+). $C_{15}H_{21}NOS_2$ requires: 295.1064].

Aldehyde **22**. To a stirred solution of **21** (41 mg, 0.14 mmol) in toluene (1.3 ml) and CH_2Cl_2 (0.6 ml) at -78 °C under nitrogen was added dropwise a 1.76 M solution of diisobutylaluminum hydride in toluene (0.32 ml, 0.56 mmol) slowly. After stirring for 2 h, the reaction was quenched with 2 N H_2SO_4 (1 ml) at -78 °C and the mixture was warmed to room temperature with vigorous stirring. After being stirred for 2 h at room temperature, the mixture was extracted with EtOAc (4 x 10 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by preparative TLC on silica gel (2:3 hexane-EtOAc) to give **22** (38 mg, 91%) as a colorless oil: IR 3430, 2720, 1724, 1141, 1065 cm^{-1}; ^1H NMR δ 0.92 (3H, s), 2.0-2.2 (2H, m), 2.30 (2H, br s), 2.60 (1H, m), 3.1-3.5 (4H, m), 3.76 (1H, m), 9.54 (1H, s); MS m/z 298 (M^+), 252, 238, 205, 186, 149, 85, 83 [HRMS. Found: 298.1088 (M^+). $C_{15}H_{22}O_2S_2$ requires: 298.1062].

Alcohol **23**. To a stirred solution of **22** (38 mg, 0.13 mmol) in MeOH (1.2 ml) was added $NaBH_4$ (6.3 mg, 0.17 mmol). After stirring at room temperature for 30 min, the reaction mixture was diluted with H_2O (0.25 ml) and concentrated in vacuo. To the residue was added H_2O (1 ml) and the

mixture was extracted with EtOAc (4 x 5 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by preparative TLC on silica gel (1:2 hexane-EtOAc) to give **23** (36 mg, 94%) as colorless crystals: mp 151.5-152 °C (hexane-$CHCl_3$); IR 3650, 3440, 1139, 1060, 1003 cm^{-1}; ^1H NMR δ 0.89 (3H, s), 2.24 (2H, br s), 3.1-3.5 (6H, m), 3.75 (1H, m); MS m/z 300 (M^+), 282, 269, 240, 222, 207, 186, 105, 91 [HRMS. Found: 300.1219 (M^+). $C_{15}H_{24}O_2S_2$ requires: 300.1218].

Diol **24**. A mixture of **23** (87 mg, 0.29 mmol) and freshly prepared Raney Ni (activity W-2, ca. 5 g) in EtOH (5 ml) was heated at reflux for 1 h. After cooling, the mixture was decanted and the supernatant was separated. The precipitates were suspended in MeOH (20 ml) and the mixture was refluxed for 15 min and the supernatant was separated after cooling. This procedure was repeated five times. The combined supernatants were filtered through a pad of Celite, which was washed with MeOH. The filtrate and washings were combined and concentrated. The oily residue was purified by preparative TLC on silica gel (2:1 benzene-acetone) to give **24** (55 mg, 90%) as colorless crystals: mp 132-133 °C (hexane-ether); IR 3630, 3450, 1049 cm^{-1}; ^1H NMR δ 0.87 (3H, s), 3.38 (2H, m), 3.61 (1H, m); MS m/z 210 (M^+), 192, 174, 161 [HRMS. Found: 210.1590 (M^+). $C_{13}H_{22}O_2$ requires: 210.1619].

Silyl ether **25**. To a stirred solution of **24** (82 mg, 0.39 mmol) in anhydrous CH_2Cl_2 (7 ml) under nitrogen were added Et_3N (0.27 ml, 2.0 mmol), 4-(dimethylamino)pyridine (14 mg, 0.12 mmol) and t-butyldimethylsilyl chloride (117 mg, 0.776 mmol). After stirring at room temperature for 6 h, the reaction mixture was diluted with H_2O (3 ml) and extracted with ether (4 x 15 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by preparative TLC on silica gel (6:1 benzene-acetone) to give **25** (131 mg, 99%) as a colorless oil: IR 3430, 1255, 1108, 1086, 1030, 998, 834 cm^{-1}; ^1H NMR δ 0.04 (6H, s), 0.86 (3H, s), 0.90 (9H, s), 3.34 (2H, m), 3.62 (1H, m); MS m/z 324 (M^+), 309, 267, 249, 191, 175, 105, 81, 75, 73 [HRMS. Found: 324.2479 (M^+). $C_{19}H_{36}O_2Si$ requires: 324.2481].

Ketone **26**. To a stirred solution of **25** (28 mg, 0.087 mmol) in anhydrous CH_2Cl_2 (1 ml) was added PCC (48 mg, 0.22 mmol). The reaction mixture was stirred at room temperature for 40 min, diluted with ether (1 ml), and passed through a column of Florisil. The column was washed with ether (20 ml). The filtrate and washings were combined and concentrated under reduced pressure. The oily residue was purified by preparative TLC on silica gel (1:1 hexane-ether) to give **26** (24.2 mg, 87%) as an amorphous solid: IR 1712, 1255, 1108, 1065, 1006, 837 cm^{-1}; ^1H NMR δ 0.03 (6H, s), 0.88 (9H, s), 1.00 (3H, s), 3.37 (2H, d, J = 7.5); MS m/z 322 (M^+), 307, 265, 235, 173, 145, 131, 75, 73 [HRMS. Found: 307.2099 (M^+-Me). $C_{18}H_{31}O_2Si$ requires: 307.2093].

Bridgehead hydroxylation of ketone **26** to α-hydroxy ketone **27**. To a stirred solution of diisopropylamine (0.095 ml, 0.68 mmol) in anhydrous THF (2 ml) at -78 °C under nitrogen was added dropwise a 1.63 M solution of n-butyllithium in hexane (0.40 ml, 0.65 mmol) slowly. After 15 min, a solution of **26** (45.8 mg, 0.142 mmol) in anhydrous THF (1 ml) was added to the solution of LDA at -78 °C. After being stirred for 50 min at -78 °C, the mixture was warmed to -50 °C and the MoO_5·Py·HMPA complex (280 mg, 0.645 mmol) was added to the mixture in one portion. Stirring was continued for 30 min at -50 °C and the reaction was quenched with saturated aqueous NH_4Cl solution (1 ml) at -50 °C. The resulting mixture was warmed to room temperature and extracted with ether (3 x 15 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by preparative TLC on silica gel (1:1 hexane-ether) to give **27** (35 mg, 73%) as colorless crystals: mp 76-79 °C (pentane); IR 3590, 1721, 1254, 1084, 837 cm^{-1}; ^1H NMR δ 0.04 (6H, s), 0.89 (9H, s), 1.03 (3H, s), 2.33 (1H, m), 3.40 (2H, d, J = 7.0); MS m/z 338 (M^+), 323, 281, 263, 251 [HRMS. Found: 281.1573 (M^+-t-Bu). $C_{15}H_{25}O_3Si$ requires: 281.1573].

β-Hydroxysulfoximine **28**. To a stirred solution of N,S-dimethyl-S-phenylsulfoximine (150 mg, 0.886 mmol) and triphenylmethane (4 mg) in anhydrous THF (3 ml) at 0 °C under nitrogen was added dropwise a 1.56 M solution of n-butyllithium in hexane until an orange color persisted. After the stirring for 10 min, a solution of **27** (59 mg, 0.17 mmol) in anhydrous THF (3.5 ml) was added dropwise to the orange solution and the reaction mixture was stirred at 0 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution (2 ml). The resulting mixture was extracted with ether (4 x 15 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (5:1→2:1 hexane-ether) to give **28** (85 mg, 96%) as a 1:1 mixture of two diastereomers concerning the sulfur atom as an oil. Further separation of **28** by either TLC or column chromatography provided each diastereomer, **28a** [R_f 0.3 (1:1 hexane-ether)] and **28b** [R_f 0.2 (1:1 ether-hexane)] in pure state, respectively. **28a**: a colorless oil; IR 3440, 1248, 1147, 1084, 1054, 836 cm^{-1}; ^1H NMR δ 0.03 (6H, s), 0.86 (3H, s), 0.88 (9H, s), 2.59 (3H, s), 3.24 (1H, d, J = 13.7), 3.37 (2H, m), 3.49(1H, d, J = 13.7), 7.4-7.7 (3H, m), 7.8-8.0 (2H, m); MS m/z 507 (M^+), 492, 450, 281, 263, 251, 189, 171, 169, 161, 156, 154, 125, 106, 77, 75 [HRMS. Found: 450.2105 (M^+-t-Bu). $C_{23}H_{36}NO_4SSi$ requires: 450.2133]. **28b**: a colorless oil; IR 3440, 1248, 1142, 1083, 1058, 1013, 836 cm^{-1}; ^1H NMR δ 0.00 (6H, s), 0.87 (12H, s), 2.70 (3H, s), 3.29 (2H, d, J = 7.5), 3.60 (2H, br s), 7.4-7.6 (3H, m), 7.7-8.0 (2H, m); MS m/z 507 (M^+), 492, 450, 411, 355, 281, 263, 251, 189, 171, 169, 161, 156, 154, 125, 106, 77, 75, 73 [HRMS. Found: 450.2110 (M^+-t-Bu). $C_{23}H_{36}NO_4SSi$ requires: 450.2133].

Olefin **29**. β-Hydroxysulfoximine **28** (17.7 mg, 0.0349 mmol) was dissolved in THF (0.15 ml) and AcOH containing 1% H_2O (0.15 ml). Aluminum foil (20.0 mg, 0.741 mg-atom), which had been stirred for 20 sec with 2% aqueous mercuric chloride and washed successively with water, ethanol and ether, was added to the reaction mixture. The reaction mixture was stirred for 30 min and diluted with ether (2 ml). The resulting mixture was filtered through a pad of Celite, which was washed with ether (30 ml). The filtrate and washings were combined and washed with saturated aqueous $NaHCO_3$ solution (3 ml). The aqueous layer was extracted with ether (3 x 10 ml). The combined organic layers were

washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (10:1 hexane-ether) to give **29** (8.2 mg, 70%) and **30** (3.1 mg, 25%) as colorless crystals, respectively. **29**: mp 65-66 °C (not recrystallized); IR 3620, 3450, 1650, 1466, 1254, 1073, 1009, 837 cm^{-1}; ^1H NMR δ 0.03 (6H, s), 0.89 (9H, s), 0.94 (3H, s), 2.32 (1H, m), 3.37 (2H, m), 4.96 (1H, d, J = 1.1), 5.05 (1H, d, J = 1.1); MS m/z 336 (M^+), 321, 279, 261 [HRMS. Found: 336.2493 (M^+). $C_{20}H_{36}O_2Si$ requires: 336.2483]. **30**: mp 142-143 °C (benzene); IR 3620, 3480, 1470, 1253, 1057, 837 cm^{-1}; ^1H NMR δ 0.04 (6H, s), 0.87 (3H, s), 0.89 (9H, s), 1.33 (3H, s), 3.36 (2H, m); MS m/z 354 (M^+), 339, 297, 279, 222, 203, 187 [HRMS. Found: 297.1895 (M^+-t-Bu). $C_{16}H_{29}O_3Si$ requires: 297.1886].

Cyclopropane derivative **31**. To a solution of **29** (30.1 mg, 0.0894 mmol) in anhydrous benzene (2.2 ml) under nitrogen was added the CuOTf benzene complex (85 mg, 0.17 mmol). The resulting mixture was stirred at room temperature for 5 min. A stream of nitrogen (30 ml/min) was bubbled through an ethereal solution of CH_2N_2 (prepared from 5.3 g of N-methyl-N-nitrosourea). The nitrogen stream containing CH_2N_2 was dried by passing through a KOH tube and bubbled into the vigorously stirred reaction mixture at 20 °C (water bath temperature) until TLC showed disappearance of **29** (ca. 30-60 min). The reaction mixture was diluted with ether (5 ml) and passed through a column of Florisil. The column was washed with ether (30 ml). The filtrate and washings were combined and washed with 2 N NH_4OH (3 ml). The aqueous layer was extracted with ether (4 x 10 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (10:1 hexane-ether) to give **31** (24.8 mg, 79%) as a colorless oil: IR 3630, 3430, 1470, 1253, 1083, 837 cm^{-1}; ^1H NMR δ 0.05 (6H, s), 0.1-0.8 (4H, m), 0.90 (9H, s), 0.95 (3H, s), 3.41 (2H, m); MS m/z 350 (M^+), 332, 322, 293, 275 [HRMS. Found: 350.2643 (M^+). $C_{21}H_{38}O_2Si$ requires: 350.2641].

Protected hydroxy patchouli alcohol **32**. A mixture of **31** (6.2 mg, 0.018 mmol), AcONa (12 mg, 0.15 mmol) and PtO_2 (36 mg, 0.16 mmol) in AcOH (0.4 ml) was vigorously stirred at room temperature under hydrogen. After 1.5 h, the mixture was filtered off. The filtrate was diluted with ether (15 ml) and the organic solution was washed with saturated aqueous $NaHCO_3$ solution (7 ml). The aqueous layer was extracted with ether (3 x 10 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (10:1 hexane-ether) to give **32** (5.2 mg, 83%) as a colorless oil: IR 3650, 3470, 1470, 1393, 1253, 1090, 837 cm^{-1}; ^1H NMR δ 0.04 (6H, s), 0.85 (3H, s), 0.90 (9H, s), 1.08 (6H, s), 3.38 (2H, m); MS m/z 352 (M^+), 295, 277, 220 [HRMS. Found: 352.2772 (M^+). $C_{21}H_{40}O_2Si$ requires: 352.2795].

(±)-Hydroxy patchouli alcohol (**3**). To a stirred solution of **32** (5.2 mg, 0.015 mmol) in anhydrous THF (0.2 ml) under nitrogen was added a 1 M solution of Bu_4NF in THF (0.74 ml, 0.74 mmol). The reaction mixture was stirred at room temperature for 3 h and concentrated in vacuo. The resulting residue was diluted with H_2O (1 ml) and extracted with ether (5 x 5 ml). The combined organic layers were washed with brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (1:1 hexane-ether) to give (±)-**3** (3.4 mg, 97%) as colorless crystals: mp 132.5-133 °C (hexane-benzene); IR 3650, 3460, 1468, 1041 cm^{-1}; ^1H NMR δ 0.87 (3H, s), 1.09 (6H, s), 3.44 (2H, m); MS m/z 238 (M^+), 220, 207, 195, 73 [HRMS. Found: 238.1910 (M^+). $C_{15}H_{26}O_2$ requires: 238.1930].

Acetate **33**. A mixture of (±)-**3** (1.2 mg, 5.0 μmol), pyridine (0.5 ml) and Ac_2O (0.1 ml) was stirred at room temperature for 2.5 h. Concentration of the mixture afforded an oily residue, purification of which by preparative TLC on silica gel (1:2 hexane-ether) gave **33** (1.2 mg, 85%) as an amorphous solid: IR 3660, 3450, 1730, 1238, 1043 cm^{-1}; ^1H NMR δ 0.85, (3H, s), 1.08 (6H, s), 2.05 (3H, s), 3.89 (2H, d, J = 7.2); MS m/z 280 (M^+), 220, 205 [HRMS. Found: 280.2020 (M^+). $C_{17}H_{28}O_3$ requires: 280.2036].

(±)-Carboxylic acid **4**. A mixture of (±)-**3** (7.0 mg, 0.029 mmol) and PDC (60 mg, 0.16 mmol) in anhydrous DMF (0.10 ml) was stirred at room temperature for 13 h. The reaction mixture was diluted with H_2O (1.2 ml) and extracted with EtOAc (4 x 10 ml). The combined organic layers were washed successively with saturated aqueous $NaHSO_3$ solution (2 ml) and brine, dried, and concentrated. The oily residue was purified by column chromatography on silica gel (2:1 hexane-ether) to give (±)-**4** (7.2 mg, 97%) as a colorless oil: IR 3640, 3300-2500, 1700, 1043 cm^{-1}; ^1H NMR δ 0.90 (3H, s), 1.08 (3H, s), 1.11 (3H, s), 2.82 (1H, ddd, J = 10.8, 7.2, 3.6), 4.60 (1H, br s, OH); MS m/z 252 (M^+), 234, 209, 191, 158 [HRMS. Found: 252.1721 (M^+). $C_{15}H_{24}O_3$ requires: 252.1723].

Methyl ester **34**. A solution of (±)-**4** (1.8 mg, 7.1 μmol) in EtOAc (2 ml) was treated with CH_2N_2. Concentration and purification by preparative TLC on silica gel (2:1 hexane-ether) afforded **34** (0.9 mg, 47%) as a colorless oil: IR 3680, 3500, 1725 cm^{-1}; ^1H NMR δ 0.89 (3H, s), 1.08 (3H, s), 1.11 (3H, s), 2.70 (1H, m), 3.65 (3H, s); MS m/z 266 (M^+), 235, 223, 207, 81 [HRMS. Found: 266.1903 (M^+). $C_{16}H_{26}O_3$ requires 266.1882].

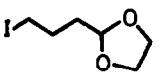
(±)-Norpatchoulenol (**1**). A mixture of (±)-**4** (17.5 mg, 0.0694 mmol), $Cu(OAc)_2 \cdot H_2O$ (2.4 mg, 0.012 mmol) and pyridine (0.07 ml, 0.9 mmol) in anhydrous benzene (0.5 ml) was stirred vigorously at room temperature for 30 min. To the resulting green solution was added quickly $Pb(OAc)_4$ (50 mg, 0.11 mmol) in one portion and the reaction vessel was tightly sealed and protected from light. The reaction mixture was heated at 90 °C with stirring for 2 h. After cooling, the sealed vessel was opened and the contents were filtered through a column of Florisil. The column was washed with ether (15 ml). The filtrate and washings were combined and concentrated in vacuo. The oily residue was purified by preparative TLC on silica gel (1:1 hexane-ether) to give (±)-**1** (4.4 mg, 31%) as colorless crystals. Further purification by sublimation (35 °C, 1 mmHg) provided pure (±)-**1**, mp 155-160 °C (sealed tube) [Lit.[8b] mp 135-141 °C (conditions for the mp measurement was not specified in ref. 8b)]. (±)-**1**: IR (CCl_4) 3625, 3500, 3020, 1650, 1464, 1390, 1370, 1049, 1001, 975, 700 cm^{-1}; ^1H NMR (CCl_4) δ 0.77 (3H, s), 1.06 (6H, s), 2.33 (1H, dd, J = 17.7, 4.1), 5.41 (1H, ddd, J = 10.1, 4.1,

2.9), 5.68 (1H, ddd, J = 10.1, 6.1, 3.6); MS m/z 206 (M^+), 191, 173, 163, 145, 122 [HRMS. Found: 206.1670 (M^+). $C_{14}H_{22}O$ requires: 206.1670].

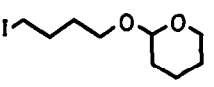
Acknowledgments - We express our cordial gratitudes to Professor G. Ourisson (Univ. Louis Pasteur, France) for providing us with the spectral copies of the authentic samples (**1**, **3**, **33**, and **34**). Financial support from the Ministry of Education, Science, and Culture (Grant-in-Aid for Special Project Research, Innovative Studies in Highly Selective Synthesis) is gratefully acknowledged.

References

1. P. Teisseire, P. Maupetit, and B. Corbier, Recherches (RBD), **1974**, No. 19, 8.
2. a) P. Teisseire, P. Maupetit, B. Corbier, and P. Rouillier, Recherches (RBD), **1974**, No. 19, 36. b) W. E. Oberhänsli and P. Schönholzer, Recherches (RBD), **1974**, No. 19, 62.
3. a) H. Gal, Ann Chem., **150**, 374 (1869); H. Gal, C. R. Acad. Sci. Paris, **68**, 406 (1869). b) J. de Montgolfier, C. R. Acad. Sci. Paris, **84**, 88 (1877). c) O. Wallach, Ann. Chem., **279**, 366 (1894). d) M. Dobler, J. D. Dunitz, B. Gubler, H. P. Weber, G. Büchi, and J. Padilla O, Proc. Chem. Soc., **1963**, 383.
4. a) N. Tsubaki, K. Nishimura, and Y. Hirose, Bull. Chem. Soc. Jpn., **40**, 597 (1967). b) G. Wolff and G. Ourisson, Tetrahedron Lett., **1968**, 3849; G. Wolff and G. Ourisson, Tetrahedron, **25**, 4903 (1969).
5. a) S. J. Terhune, J. W. Hogg, and B. M. Lawrence, Tetrahedron Lett., **1973**, 4705. b) M. R. Willcott, P. A. Morrison, J.-M. Assercq, S. C. Welch, and R. Inners, J. Org. Chem., **46**, 4819 (1981).
6. Luu Bang, G. Ourisson, and P. Teisseire, Tetrahedron Lett., **1975**, 2211.
7. Y. Suhara, S. Itoh, M. Ogawa, K. Yokose, T. Sawada, T. Sano, R. Ninomiya, and H. B. Maruyama, Appl. Environ. Microbiol., **42**, 187 (1981).
8. a) P. Teisseire, P. Pesnelle, B. Corbier, M. Plattier, and P. Maupetit, Recherches (RBD), **1974**, No. 19, 69. b) W. Oppolzer and R. L. Snowden, Tetrahedron Lett., **1978**, 3505. c) M. Bertrand, P. Teisseire, and G. Pelerin, Tetrahedron Lett., **21**, 2051 (1980); M. Bertrand, P. Teisseire, and G. Pelerin, Nouv. J. Chim., **7**, 61 (1983). d) Synthetic studies: J.-L. Gras, Tetrahedron Let., **1977**, 4117.
9. K. Yamada, Y. Kyotani, S. Manabe, and M. Suzuki, Tetrahedron, **35**, 293 (1979).
10. F. Näf, R. Decorzant, W. Giersch, and G. Ohloff, Helv. Chim. Acta, **64**, 1387 (1981), and the references cited therein.
11. a) H. Hagiwara, A. Okano, and H. Uda, J. Chem. Soc., Chem. Commun., **1985**, 1047. b) S. C. Welch, C.-Y. Chou, J. M. Gruber, and J.-M. Assercq, J. Org. Chem,. **50**, 2668 (1985). c) S. C. Welch, J. M. Gruber, and P. A. Morrison, J. Org. Chem., **50**, 2676 (1985), and references cited therein.
12. H. Niwa, N. Ban, and K. Yamada, Tetrahedron Lett., **24**, 937 (1983).
13. Preliminary communication: H. Niwa, T. Hasegawa, N. Ban, and K. Yamada, Tetrahedron Lett., **25**, 2797 (1984).
14. S. A. Monti, S.-C. Chen, Y.-L. Yang, S.-S. Yuan, and O. P. Bourgeois, J. Org. Chem., **43**, 4062 (1978).
15. a) H.-F. Chow and I. Fleming, J. Chem. Soc., Perkin Trans. 1, **1984**, 1815. b) J. S. Petersen, S. Toteberg-Kaulen, and H. Rapoport, J. Org. Chem., **49**, 2948 (1984). c) E. Vedejs, M. J. Arnost, and J. P. Hagen, J. Org. Chem., **44**, 3230 (1979).
16. S. A. Monti and T. R. Dean, J. Org. Chem., **47**, 2679 (1982). See also: R. L. Snowden and P. Sonnay, J. Org. Chem., **49**, 1464 (1984). Alkylation with **i** and **ii** was found to be unsatisfactory, resulting in the formation of the corresponding alkylation products in low yields.



i



ii

17. The similar Beckmann fragmentation reaction was reported: E. W. Colvin, S. Malchenko, R. A. Raphael, and J. S. Roberts, J. Chem. Soc., Perkin 1, **1973**, 1989.
18. E. J. Corey and J. W. Suggs, Tetrahedron Lett., **1975**, 2647.
19. S. K. Chaudhary and O. Hernandez, Tetrahedron Lett., **1979**, 99.
20. a) E. Vedejs, D. A. Engler, and J. E. Telschow, J. Org. Chem., **43**, 188 (1978). b) H. Mimoun, I. Seree de Roch, and L. Sajus, Bull. Soc. Chim. Fr., **1969**, 1481.
21. C. R. Johnson and R. A. Kirchhoff, J. Am. Chem. Soc., **101**, 3602 (1979).
22. R. G. Salomon and J. K. Kochi, J. Am. Chem. Soc., **95**, 3300 (1973).
23. E. J. Corey and G. Schmidt, Tetrahedron Lett., **1979**, 399.
24. J. D. Bacha and J. K. Kochi, Tetrahedron, **24**, 2215 (1968).