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STEREOCONTROLLED SYNTHESIS OF (-)-PREZIZANOL, (-)-PREZIZAENE, THEIR EPIMERS AND (-)-ALLOKHUSIOL†

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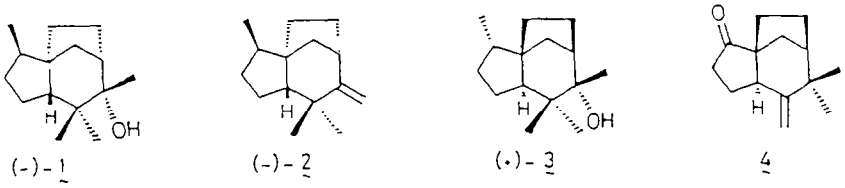
Abstract-- (-)-Prezizanol (-)-**1**, (-)-prezizaene (-)-**2**, isolated from Eremophila georgei Diels, and their epimers, **5** and **6**, were synthesized employing β-keto ester **7**, readily available from (R)-(+)-pulegone, as a starting material. cis-Epimers, **5** and **6** were obtained with over 95 % stereoselectivity via reductive methylation of enone **22**. The natural isomers, (-)-**1** and (-)-**2**, were synthesized via hydroxy-directed hydrogenation of the corresponding allylic alcohol **40** with a homogeneous catalyst.

INTRODUCTION

(-)-Prezizanol (-)-**1** and (-)-prezizaene (-)-**2** were isolated from the essential oil of Eremophila georgei Diels, a kind of sandalwood, by Ghisalberti and co-workers.[1] Their structures including absolute configuration were rigorously determined by chemical degradation[1] and X-ray crystallographic study.[2] Then, it was shown that sesquiterpenes containing the same [6,2,1,$0^{1,5}$]undecane skeleton



(-)-1 (-)-2 (-)-3 4

5 6

Fig 1

† Synthesis of Mono- and Sesquiterpenoids, Part 18: Part 17, see Kitahara, T.; Touhara, K.; Watanabe, H. and Mori, K. Tetrahedron in press.

†† Research fellow on leave from Takasago International Corporation in 1986-1989.

were present in vetiver oil.3,4) Bhattacharyya and co-workers isolated (+)-prezizaene (+)-**2**, first isolated by Andersen et al.,[3] and (+)-allokhusiol (+)-**3** from Indian vetiver oil.[5,6] In 1981, Nakanishi and co-workers reported the isolation of (-)-jinkohol from Agarwood (Jinkoh in Japanese, Aquilaria sp.) and elucidated its structure as depicted in **3**.[7] They, however, did not mention on the identity of (-)-jinkohol with (+)-allokhusiol (+)-**3**, and the sign of optical rotation was opposite between two natural products. It is remarkable that those tricyclic sesquiterpenes have been found only in vetiver oil, sandalwood and jinkoh (agarwood oil). They possess extremely strong woody note.

We have been interested in studying the structure-odor relationship among these tricyclic sesquiterpenes and reported chiral synthesis of (-)-khusimone **4** employing Lewis-acid catalyzed Diels-Alder reaction.[8] It is also interesting to clarify the contradiction between jinkohol and allokhusiol. As the first step of this research, we decided to develop a general method for the synthesis of prezizanol-type sesquiterpenes. A chiral synthesis of prezizanol (-)-**1** and prezizaene (-)-**2** was reported by Vettel and Coates.[9] The key step in their synthesis was a intramolecular ring expansion of (diazoethyl)hydrindanone, which gave a ca. 1 to 1 mixture of two products and thus tedious HPLC separation was necessary. The other was the synthesis of racemates (±)-**1** and (±)-**2** by Piers and co-workers requiring more than 25 steps.[10]

We wish to describe here an efficient and stereoselective synthesis of (-)-prezizanol (-)-**1**, (-)-prezizaene (-)-**2**, (-)-epiprezizanol (-)-**5**, (-)-epiprezizaene (-)-**6** and (-)-allokhusiol (-)-**3**.

SYNTHETIC PLAN

Our key intermediate was a bicyclic enone **C**. Selective reduction of **C** to a trans-fused ring system, gem-dimethylation and cyclization might be a rational approach to generate the tricyclic system. The enone **C** should be derivable from β-keto ester **7** through intermediates **A** and **B**. The β-keto ester was easily obtainable in optically pure form from (R)-(+)-pulegone by the reported procedure.[11]

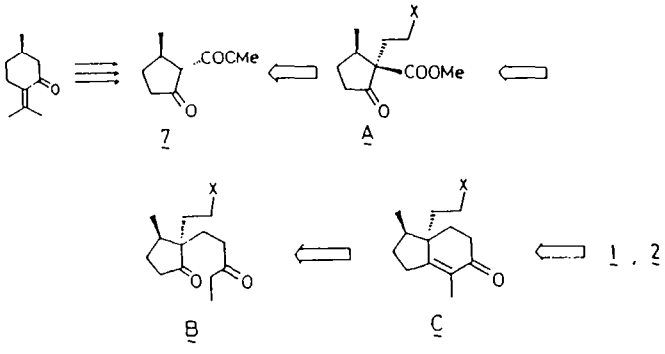
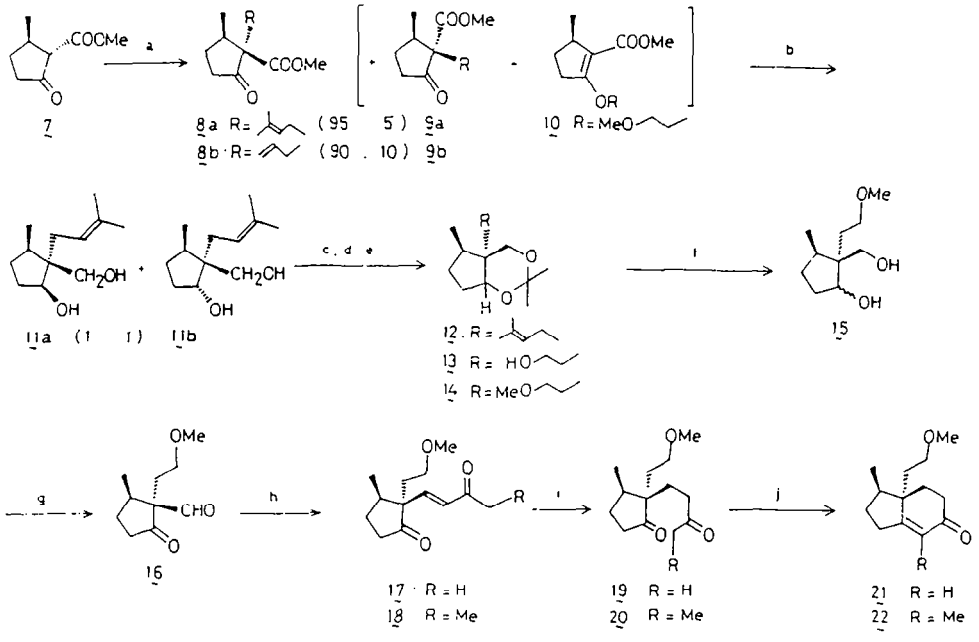


Fig II

PREPARATION OF THE KEY INTERMEDIATE ENONES, 21 AND 22

Alkylation of **7** with NaH and alkyl bromide such as $MeOCH_2CH_2Br$ both in THF and DMF gave an O-alkylated product almost exclusively. Reaction of **7** with allyl bromide was sluggish, requiring reflux for 24 h and diastereoselectivity was not high (90 : 10) as that with prenyl bromide. Alkylation of **7** with prenyl bromide in THF at room temp for 3 h gave **8a** and **9a** (95 : 5) in 90 % yield. The desired epimer **8a** was easily isolated by chromatography. Reduction of **8a** with $LiAlH_4$ gave a 1 to 1 mixture of oily diol **11a** and crystalline **11b** (98 %). The mixture was treated with 2,2-dimethoxypropane and p-TsOH to give a mixture of acetonide **12**. Ozonization of **12** and reductive work up with $NaBH_4$ gave a primary alcohol **13**, which was treated with MeI-NaH to give a methyl ether **14** (68 % from **11**). Hydrolysis of acetonide with 70 % AcOH gave a diol **15** (95 %). Swern oxidation[12] of **15** gave unstable β-keto aldehyde **16**. Refluxing **16** with oxoalkylidene triphenylphosphorane in benzene for 48 h gave α,β-unsaturated ketones **17** and **18** in 70 to 72 % yield from **15** respectively. Catalytic hydrogenation gave diketone **19** and **20** quantitatively. Cyclization with 2 % KOH in refluxing MeOH afforded the desired key intermediate, enones, **21** and **22** (70 %).[13]



a; NaH, RBr / THF b; LAH, Et_2O c; $CH_3C(OMe)_2CH_3$, p-TsOH d; O_3 / MeOH, $NaBH_4$
e; MeI, NaH / THF f; 70% CH_3COOH g; $(COCl)_2$, DMSO, Et_3N h; $Ph_3P=CHCOR$ / benzene, Δ i; H_2, Pd-C(10%) j; 2% KOH / MeOH, Δ

Fig III

BIRCH REDUCTION, REMARKABLE CIS-SELECTIVITY AND SYNTHESIS OF EPI-SERIES

Stork and co-workers reported that reductive alkylation of octalone **23** or tetrahydrindanone **25** yielded the trans-isomer **24** or **26** exclusively or mainly.[14] In the latter case, ratio of products **26** and **27** was 4 to 1. With this fact in mind, the enone **22** was submitted to the reductive methylation with Li-NH_3, MeI. Surprisingly, the major product was cis-isomer **28** (**28** / **29** = 95 / 5). Accordingly, metal-ammonia reduction of the enone with simple alkyl chain **30** was examined and the major product was again cis-isomer **31**. Stereochemistry of **28** and **31** was rigorously ascertained by comparing with the authentic samples prepared from enones **22** and **30** by catalytic hydrogenation. Corey and Engler reported a similar result that enone **32** gave cis-fused hydrindanone **33** both by catalytic hydrogenation and metal-ammonia reduction.[15]

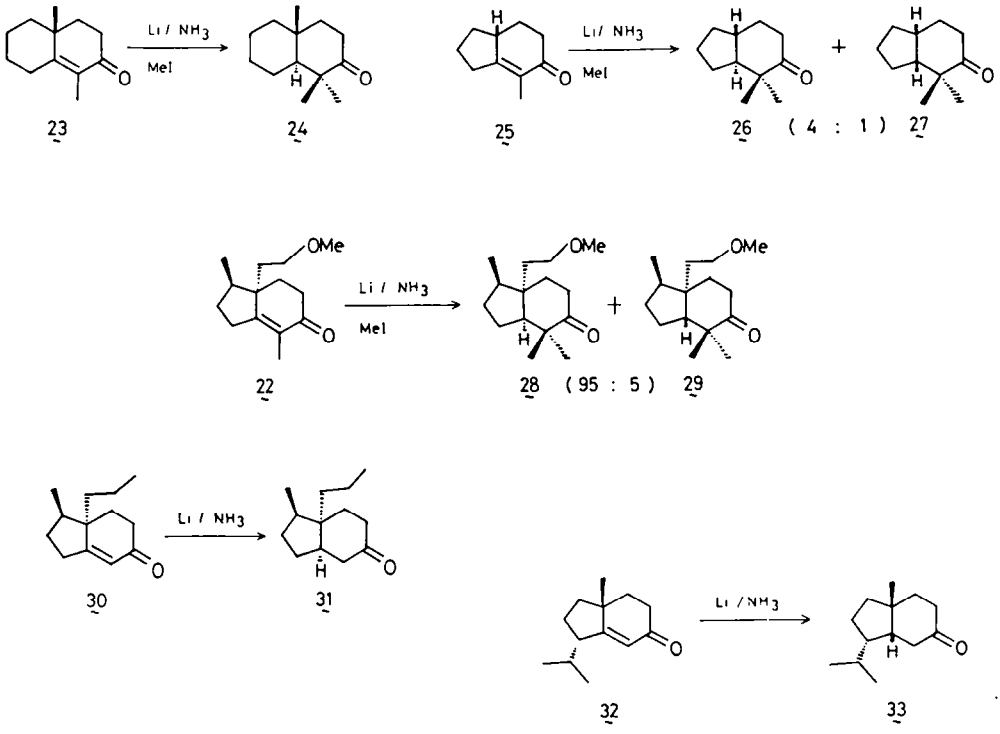
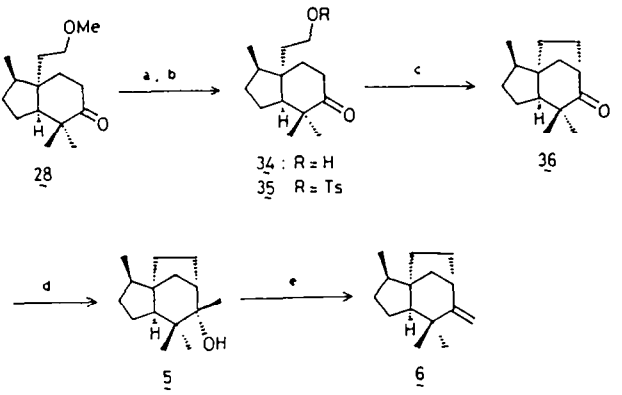


Fig IV

Treatment of **28** with BBr_3 in CH_2Cl_2 gave alcohol **34** with concomitant formation of unstable bromide causing to reduce the yield. On the other hand, the procedure reported by Niwa and co-workers[16] using BBr_3, NaI and crown ether afforded **34** in

85 % yield. Tosylation of **34** was followed by cyclization with t-BuOK in THF to give tricyclic ketone **36** (81 %). Addition of MeLi to **36** afforded (-)-epiprezizanol **5** stereoselectively (90 %). Dehydration of **5** with MsCl-Et_3N gave (-)-epiprezizaene **6** (74 %). Overall yields of **5** and **6** were 5.3 % and 3.9 % through 16 and 17 steps from (R)-(+)-pulegone.

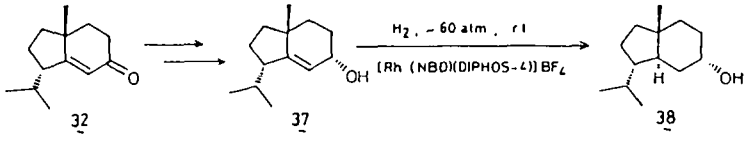


a; BBr_3, NaI, 15-Crown-5, CH_2Cl_2 b; p-TsCl, Py c; t-BuOK, THF d; MeLi /Et_2O
e; MsCl, Et_3N, CH_2Cl_2

Fig V

HYDROXY-DIRECTED HYDROGENATION TO GIVE TRANS-FUSED ISOMERS

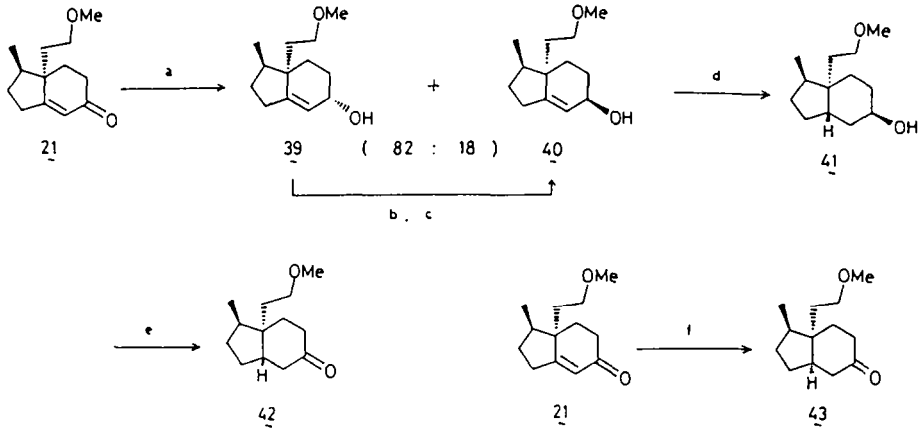
As reductive alkylation of **22** gave cis-epimer **28**, it was necessary to find an alternative route to the natural trans-isomer. Evans and Morrissey reported the stereoselective hydroxy-directed hydrogenation of **37** with a homogeneous catalyst, $[Rh(NBD)(DIPHOS-4)]BF_4$,[17] to give **38**. This procedure seemed to be applicable to our synthesis. Thus, the enone **21** was reduced with $NaBH_4$ to give a separable mixture of eq.-alcohol **39** and ax.-alcohol **40** in a ratio of 82 / 18 (-100 %). Inversion of eq.-OH in **39** was readily executed by Mitsunobu procedure[18] to give **40**. The combined yield of **40** was 73 % from the enone **21**.†



† Homologous enone **22** was not suitable substrate for this sequence, because Mitsunobu inversion of the intermediate with eq.-OH was extremely slow with only 10 % conversion by the presence of α-methyl group.

Although other reducing reagent such as LiB(sec-Bu)$_3$H, was examined, we could not achieve the selective reduction to give only **40** directly and the yield was poorer than that of $NaBH_4$ reduction.

Rhodium catalyst, [Rh(NBD)(DIPHOS-4)]ClO_4 was prepared by the known procedure.[19,20] Hydrogenation of **40** under the similar condition as reported[17] gave trans-fused alcohol **41** in 95 % yield with extremely high selectivity (98 / 2). After separation, pure **41** was oxidized with Jones' reagent to give trans-hydrindanone **42**, whose ^{1}H NMR spectrum was distinguishable from cis-isomer **43** prepared by catalytic hydrogenation of the enone **21**.



a; $NaBH_4$, MeOH b; Ph_3P, DEAD, PhCOOH, benzene c; K_2CO_3 / MeOH d; H_2, 55 atm, [Rh(NBD)(DIPHOS-4)]ClO_4 e; Jones f; H_2, Pd-C(10%)

Fig. VI

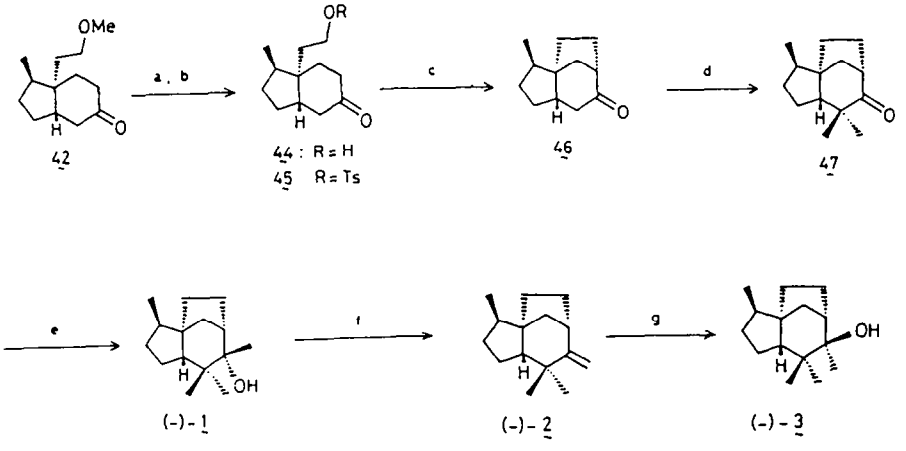
COMPLETION OF THE SYNTHESIS OF NATURAL ISOMERS

Conversion of the trans-precursor **42** to (-)-**1** and (-)-**2** was carried out in nearly the same manner as described for cis-isomers. Demethylation of **42**, tosylation and succesive cyclization gave tricyclic ketone **46** (70 %). The specific rotation of our **46** coincided with that reported by Coates.[9] gem-Dimethylation of **46** with excess MeI-KH in THF gave the trimethyl ketone **47**, which was treated with MeLi to give (-)-prezizanol (-)-**1** (72-81 % from **46**). The spectral data (IR, ^{1}H NMR) of the synthetic (-)-**1** were identical with those of an authentic sample. The specific rotation of (-)-**1**, $[\alpha]_D$ -49.9°(c=1.0, $CHCl_3$), was also in good agreement with that reported, $[\alpha]_D$-49.0°.[1,9]

Dehydration of (-)-**1** with MsCl-Et_3N afforded (-)-prezizaene (-)-**2** (73 %). The spectral data of (-)-**2** were again indistinguishable from those reported.[1] Synthesis of (-)-**1** and (-)-**2** was achieved in 5.1 % and 3.7 % overall yield through 19 and 20 steps from (R)-(+)-pulegone, respectively.

The structure elucidation of (-)-jinkohol (-)-3 was largely due to the fact that dehydration of jinkohol with $POCl_3$ in pyridine for 10 days gave (+)-prezizaene (+)-2. Our synthetic (-)-2, however, was not identical with so-called (+)-2 prepared from jinkohol in ^1H NMR and ^{13}C NMR spectra: especially the chemical shift of the secondary methyl group was distinguishable, (-)-2; ^1H NMR δ 0.87 ppm, d, J=7.2 Hz, ^{13}C NMR δ 20.0 ppm, (+)-2 from jinkohol; ^1H NMR δ 0.86 ppm, d, J=7.2Hz, ^{13}C NMR δ 14.3 ppm. In order to determine the stereochemistry of jinkohol, the antipode of the proposed structure for jinkohol (-)-3, was synthesized from the synthetic (-)-2. Oxymercuration of (-)-2 followed by demercuration with $NaBH_4$ afforded (-)-3, a diastereomer of (-)-1. The synthetic (-)-3 was again not identical with jinkohol, while spectral data of (-)-3 was indistinguishable from those of (+)-allokhusiol (+)-3 reported by Bhattacharyya.[5)]

In conclusion, synthesis of (-)-prezizanol (-)-1 and (-)-prezizaene (-)-2, the natural enantiomers of key substances in sandalwood, vetiver oil, their epimers, (-)-epiprezizanol (-)-5 and (-)-epiprezizaene (-)-6, and (-)-allokhusiol (-)-3, the antipode of the natural product from Indian vetiver oil, was achieved stereoselectively starting from (R)-(+)-pulegone. At the moment, relative stereochemistry of jinkohol is shown to be different from the structure as depicted in 3 and must be revised. Synthetic studies to solve this problem are in progress and will be reported in due course.



a; BBr_3, NaI, 15-Crown-5, CH_2Cl_2 b; p-TsCl, Py c; t-BuOK, THF d; MeI, KH, THF e; MeLi, Et_2O f; MsCl, Et_3N, CH_2Cl_2 g; $Hg(OAc)_2$, THF-H_2O, $NaBH_4$-NaOHaq.

Fig. VII

EXPERIMENTAL

All bps and mps were uncorrected. IR spectra were measured as films on a Jasco IRA-102 spectrometer unless otherwise stated. ^{1}H NMR spectra were recorded with TMS as an internal standard at 400 MHz on a Bruker AM-400 spectrometer unless otherwise stated. ^{13}C NMR were measured with TMS as an internal standard as $CDCl_3$ soln at 100 MHz on a Bruker AM-400 spectrometer. The multiplicities of ^{13}C NMR spectra were determined by a DEPT sequence. Optical rotations were measured on a Jasco DIP 140 Polarimeter. Mass spectra were measured on a JEOL DX-303 spectrometer at 70 eV or Hitachi M-80 at 20 eV. Merck Kieselgel 60 Art. 7734 and 7754 were used for SiO_2 column chromatography. GLC was used an HP-5890A instrument with PEG-20M 25 m x 0.2 mm capillary column (80-220°C, 4 °C/min, carrier gas He, 1 ml/min).

(2S,3R)-2-Methoxycarbonyl-3-methylcyclopentanone **7**. According to the method by Marx[5] and Wolinsky[6], **7** was prepared from (R)-(+)-pulegone, which was available from Takasago International Corporation. **7**; n_D^{21}1.4436, $[\alpha]_D^{21}$+105.3°(c=2.0, $CHCl_3$), IR ν_{max} 2950 (s), 1750 (s), 1720 (s), 1440 (m), 1130 (m), 1005 (m). ^{1}H NMR δ 1.20 (3H, d, J=6.5 Hz), 1.50 (1H, dddd, J=1.3, 2.8, 11.1, 12.4 Hz), 2.20 (1H, m), 2.37 (1H, dddd, J=2.9, 8.5, 11.2, 11.3 HZ), 2.43 (1H, dddd, J=0.9, 1.2, 8.0, 9.3 Hz), 2.60 (1H, m), 2.79 (1H, d, J=12.2 Hz), 3.77 (3H, s). ^{13}C NMR δ 19.3 (q), 29.3 (t), 36.4 (d), 38.7 (t), 52.4 (q), 62.9 (d), 169.6 (q), 211.8 (q). MS m/z 156 (M^+, 21), 141 (19), 123 (33), 109 (36), 101 (55), 96 (28), 69 (100), 55 (25). Found C, 61.20; H, 7.71, Calcd for $C_8H_{12}O_3$: C, 61.52; H,7.74 %.

(2R,3R)-2-Methoxycarbonyl-3-methyl-2-prenylcyclopentanone **8a**. To a suspension of 60 % NaH (6.0 g, 0.15 mol) in dry THF (300 ml), was added dropwise **7** (19.9 g, 0.13 mol) in dry THF (50 ml) at 10°C up to room temp and the mixture was stirred for 3 h. To this mixture, was added freshly distilled prenyl bromide (22.3 g, 0.15 mol) and the mixture was stirred for 3-5 h at room temp. The mixture was poured into 50 ml of water and extracted with ether (100 ml x 3). The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **8a** (25.8 g, 90 %). **8a** n_D^{20}1.4698; $[\alpha]_D^{20}$+123.9°(c=0.292, $CHCl_3$); IR ν_{max} 2950 (s), 1745 (s), 1725 (s), 1430 (m), 1220 (m); ^{1}H NMR δ 1.03 (3H, d, J=6.9 Hz), 1.63 (3H, brs), 1.68 (3H, brs), 1.78 (1H, dddd, J=6.6, 10.6, 10.9, 11.8 Hz), 2.05 (1H, m), 2.13 (1H, dddd, J=1.8, 2.5, 9.0, 11.5 Hz), 2.30 (1H, m), 2.52 (1H, dddd, J=0.7, 2.5, 8.0, 18.4 Hz), 2.55 (2H, d, J=8.0 Hz), 3.70 (3H, s), 4.90 (1H, m). ^{13}C NMR δ 17.6 (q), 17.9 (q), 25.9 (q), 28.2 (t), 29.6 (t), 38.3 (d), 39.1 (t), 51.7 (q), 63.4 (s), 118.4 (d), 135.9 (s), 171.2 (s), 216.5 (s) MS m/z 224 (M^+, 28), 206 (17), 165 (39), 149 (100), 141 (71), 125 (25), 109 (43), 93 (20), 81 (25), 69 (41), 55 (21). Found C, 69.77; H, 8.89, Calcd for $C_{13}H_{20}O_3$ C, 69.61; H, 8.99 %.

(1RS,2S,3R)-2-Hydroxymethyl-3-methyl-2-prenylcyclopentanol **11**. To a suspension of LAH (3.9 g, 0.1 mol) in dry ether (600 ml), was added dropwise **8a** (20 g, 89.2mmol) in dry ether (100 ml) at 0-10°C and the mixture was stirred for 2 h. The mixture was treated with H_2O (1 ml), 15 % NaOH (1 ml) and H_2O (3 ml) and filtered. The filtrate was dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give (1R)-**11(11a)** and (1S)-**11(11b)** in a ratio 1 : 1 on a ^{1}H NMR analysis. (17.3 g, 98 %). **11a**; mp 65 °C $[\alpha]_D^{20}$-28.2 °(c=0.1, $CHCl_3$). IR ν_{max} 3350 (S), 2950 (s), 1440 (s), 1370 (m), 1050 (s). ^{1}H NMR δ 0.88 (3H, d, J=7.0 Hz), 1.20 (1H, m), 1.58 (1H, m), 1.69 (3H, s), 1.74 (3H, d, J=1.2 Hz), 2.00 (4H, m), 2.12 (1H, dd, J=8.0, 15.4 Hz), 2.33 (1H, dd, J=7.0, 14.0 Hz), 3.48 (1H, dd, J=10.1, 11.1 Hz)., 3.67 (1H, d, J=10.7 Hz), 4.23 (1H, t, J=6.5 Hz), 5.35 (1H, m). ^{13}C NMR δ 15.6 (q), 17.9 (q), 26.2 (q), 29.3 (t), 30.1 (t), 31.7 (t), 38.9 (d), 50.3 (s), 66.5 (t), 78.8 (d), 121.1 (d), 134.0 (s); MS m/z 198 (M^+, 1), 180 (41), 155 (23), 149 (65), 138 (26), 124 (35), 111 (49), 93 (78), 81 (77), 69 (74), 55 (100). Found C, 72.72; H, 11.06, Calcd for $C_{12}H_{22}O_2$ C, 72.68; H, 11.19 %. **11b** ; n_D^{20} 1.4881 $[\alpha]_D^{20}$-4.6°(c=0.2, $CHCl_3$). IR ν_{max} 3350 (m), 2950 (s), 1440 (m), 1370 (m), 1050 (m). ^{1}H NMR δ 0.98 (3H, d, J=6.7 Hz), 1.44 (1H, m), 1.67 (3H, s), 1.73 (3H, d, J=1.2 Hz), 1.75 (3H, m), 1.97 (1H, dddd, J=0.8, 1.6, 3.7, 7.9 Hz), 2.13 (1H, dd, J=11.2, 14.4 Hz), 2.32 (1H, dd, J=11.2, 14.4 Hz), 2.85 (2H, m), 3.54 (1H, dd, J=6.7, 11.2 Hz), 3.90 (1H, dd, J=4.0, 11.2 Hz), 4.04 (1H, m), 5.27 (1H, m). ^{13}C NMR δ 14.6 (q), 17.8 (q), 26.2 (q), 29.7 (t), 31.5 (t), 32.2 (t), 38.3 (d), 49.3 (s), 64.4 (t), 80.5 (d), 120.2 (d), 134.2 (s). MS m/z 198 (M^+, 8), 180 (47), 155 (28), 149 (78), 138 (33), 124 (43), 111 (58), 95 (93), 81 (92), 69 (87), 55 (100). Found C, 72.50; H,11.14, Calcd for $C_{12}H_{22}O_2$ C, 72.68; H, 11.19 %.

(1R,3aRS,7aS)-1,5,5-Trimethyl-7a-prenyl-4,6-dioxahexahydrindane **12**. A mixture of **11**(13.1 g, 66.2 mmol), p-TsOH(0.5 g) and 2,2-dimethoxypropane (300 ml) was refluxed for 6-8 h. After being cooled, the mixture was washed with sat $NaHCO_3$, brine and dried over $MgSO_4$. Organic layer was concentrated and the residue was chromatographed over Florisil(100-200 mesh) to give **12** (14.2 g,90 %). **12**; n_D^{24}1.4610 $[\alpha]_D^{24}$-16.3°(c=0.1, $CHCl_3$). IR ν_{max} 2950 (s), 1740 (m), 1630 (m), 1450 (m), 1380 (s), 1370 (s), 1050(m), 850 (m). ^{1}H NMR δ 0.86 (3H, d, J=7.4 Hz), 0.92 (3H, d, J=6.9 Hz), 1.30 (3H, s), 1.35 (3H, s), 1.65 (3H, s), 1.72 (3H, s), 1.75 (1H, m), 2.18 (2H, dddd, J=7.8, 8.0, 18.4, 22.7 Hz), 3.25 (1H, d, J=11.3 Hz), 3.62 (1H, d, J=11.3 Hz), 3.82 (1H, dd, J=10.7, 11.3 Hz), 3.87(1H, d, J=4.2 Hz), 5.17 (1H, m). ^{13}C NMR δ 14.2(q), 18.5 (q), 23.0(q), 26.5 (q), 28.0 (q), 32.4 (t), 33.6 (t), 34.9 (t),

40.8 (d), 48.6 (s), 61.7 (d), 78.8 (d), 98.4 (s), 120. (d), 134.1 (s). MS m/z 238 (M^+, 4), 223 (11), 180 (49), 165 (17), 147 (30), 136 (29), 121 (48), 111 (45), 93 (74), 79 (85), 69 (100), 55 (73). Found, C, 75.63; H,10.78, Calcd for $C_{15}H_{26}O_2$ C,75.58; H,11.00 %.

(1R,3aRS,7aS)-7a-Hydroxyethyl-1,5,5-trimethyl-4,6-dioxahexahydrindane **13**. To a soln of **12** (14.0 g, 58.8 mmol) in dry MeOH (100 ml), was introduced O_3 until the color becoming brue at -78°C. To this soln was added $NaBH_4$(2.22 g, 60 mmol) portionwise and the mixture was stirred overnight. MeOH was evaporated and ether (300 ml) and brine (50 ml) were added to the residue. Organic layer was washed with brine several times, dried over $MgSO_4$ and concentrated. The residue was chromatographed over Florisil to give **13** (10.1 g, 80 %). **13**; n_D^{26}1.4645 $[\alpha]_D^{26}$ -15.7°(c=0.27, $CHCl_3$), IR ν_{max} 3450 (s), 2950 (s), 1370 (s), 1230 (m), 1050 (m). ^1H NMR δ 0.94 (3H, d, J=6.4 Hz), 1.32 (3H, s), 1.39 (3H, s), 1.79 (7H, m), 3.40 (1H, d, J=11.4 Hz), 3.65 (1H, d, J=11.4 Hz), 3.76 (1H, dddd, J=1.2, 6.4, 6.6, 11.6 Hz), 3.85 (1H, dddd, J=5.9, 6.0, 7.7, 11.9 Hz), 3.98 (1H, d, J=4.2 Hz). ^{13}C NMR δ 13.4 (q), 23.3 (q), 26.0 (q), 32.4 (t), 33.2 (t), 41.5 (t), 43.6 (d), 47.6 (s), 59.9 (t), 61.6 (t), 77.7 (d), 98.7 (s). MS m/z 199 (M^+-15, 11), 156 (6), 138 (446), 108 (55), 93 (82), 79 (87), 67 (81), 59 (100), 55 (82), 53 (67). Found C, 67.04; H, 10.04, Calcd for $C_{12}H_{22}O_3$ C, 67.26; H, 10.35 %.

(1R,3aRS,7aS)-7a-Methoxyethyl-1,5,5-trimethyl-4,6-dioxahexahydrindane **14**. To a suspension of 60 % NaH (3.6 g, 90 mmol) in dry THF (500 ml), was added dropwise **13** (9.70 g, 45.3 mmol) in dry THF (500 ml) at 40-50°C and the mixture was refluxed for 5 h. After being cooled, CH_3I (13.4 g, 90 mmol) was added dropwise to the mixture and this mixture was stirred for overnight. The mixture was poured into ice-water (50 ml) and extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **14** (9.81 g, 95 %). **14**; n_D^{22}1.4581 $[\alpha]_D^{22}$ -18.2° (c=0.215, $CHCl_3$). IR ν_{max} 2950 (s), 1450 (m), 1365 (m), 1220 (s), 1115 (s). ^1H NMR δ 0.95 (3H, d, J=7.0 Hz), 1.30 (3H, s), 1.36 (3H, s), 1.65 (4H, m), 1.78 (2H, m), 1.85 (1H, ddd, J=5.5, 6.4, 8.0 Hz), 3.33 (3H, s), 3.37 (1H, d, J=10.6 Hz), 3.49 (2H, m), 3.64 (1H, d, J=10.6 Hz), 3.92 (1H, d, J=3.8 Hz). ^{13}C NMR δ 14.2 (q), 22.9 (q), 26.4 (q), 32.2 (t), 33.5 (t), 37.1 (t), 41.6 (d), 47.2 (s), 58.6 (q), 61.4 (t), 69.7 (t), 78.9 (d), 98.5 (s). MS m/z 228 (M^+, 1), 213 (30, 170 (14), 152 (59), 138 (34), 121 (34), 121 (44), 107 (37), 93 (95), 79 (100), 67 (73), 59 (72). 55 (72), 53 (66). Found C, 68.38; H, 10.54, Calcd for $C_{13}H_{24}O_3$: C,68.38; H, 10.59 %.

(1RS,2S,3R)-2-Hydroxymethyl-2-methoxyethyl-3-methylcyclopentan-1-ol **15**. **14** (7.80 g, 34.2 mmol) was dissolved in 100 ml of 70 % CH_3COOH soln and the mixture was stirred for 1-2 h. To this mixture was added 30-50 % KOH soln to be neutralized. The mixture was extracted with ether. The ether layer was washed with sat $NaHCO_3$, brine and dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **15**(6.11 g, 95 %). **15**; n_D^{20}1.4698 $[\alpha]_D^{20}$-14.6° (c=0.2, $CHCl_3$). IR ν_{max} 3450 (s), 2950 (s), 1120 (m). ^1H NMR δ 0.86 (3H, d, J=7.1 Hz), 1.43 (1H, m), 1.57 (2H, m), 1.76 (2H, m), 1.92 (1H, ddd, J=3.1, 6.7, 15.1 Hz), 2.03 (1H, m), 3.39 (3H, s), 3.50 (1H, brs), 3.55 (1H, dd, J=1.7, 11.7 Hz), 3.62 (1H, m), 3.67 (1H, dddd, J=3.6, 3.6, 6.7, 6.7 Hz), 3.77 (1H, dddd, J=3.1, 3.1, 8.7, 8.7 Hz), 3.96 (2H, dd, J=1.0, 11.6 Hz). ^{13}C NMR δ 14.3 (q), 28.7 (t), 30.1 (t), 37.5 (t), 41.1 (d), 47.1 (s), 58.6 (q), 63.9 (t), 70.5 (t), 81.8 (s). MS m/z 152 (M^+-36), 140 (2), 138 (9), 120 (18), 107 (25), 97 (39), 95 (37), 81 (45), 79 (56), 67 (66), 55 (100), 53 (76). Found C, 63.55; H, 10.49, Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71 %.

(2S,3R)-2-Formyl-2-methoxyethyl-3-methylcyclopentanone**16**,; (2S,3R)-2-methoxyethyl-3-methyl-2-(3-oxo-1-butenyl)-cyclopentanone **17** and (2S,3R)-2-methoxyethyl-3-methyl-2-(3-oxo-1-pentenyl)cyclopentanone **18**. To a soln of $(COCl)_2$ (6.1 ml, 70 mmol) in dry CH_2Cl_2 (100 ml), was added a soln of DMSO (9.15 ml, 140 mmol) in dry CH_2Cl_2 at -78°C. To the mixture was added **15** (6.0 g, 31.9 mmol) in dry CH_2Cl_2 soln and the mixture was stirred for 15 min at -78°C. To the mixture, was added Et_3N (45 ml) and stirred for 1 h at -78 °C and up to room temp. The mixture was poured into ice-water(30 ml) and organic layer was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Brine (10 ml) was added to a residue and organic layer was extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated to give crude **16**. **16** was employed for the next step without further purification. **16**; IR ν_{max} 2950 (s), 2750 (m), 1740 (s), 1705 (s), 1450 (m), 1110 (s). ^1H NMR δ (C_6D_6) 0.86 (3H, d, J=7.1 Hz), 1.43 (1H, m), 1.52 (1H, m), 1.78 (1H, m), 1.88 (2H, m), 2.07 (1H, m), 2.13 (1H, ddd, J=2.3, 8.6, 19.8 Hz), 2.96 (3H, s), 3.18 (1H, m), 3.31 (1H, m), 9.35 (1H, d, J=1.0 Hz). ^{13}C NMR δ (C_6D_6) 14.5 (q), 20.0 (t), 30.6 (t), 37.7 (t), 39.7 (t), 58.0 (q), 67.0 (s), 68.3 (t), 199.9 (d), 214.0 (s).

The mixture of **16** and triphenylphosphoranylideneacetone (60 g, 0.15 mol) in dry benzene was refluxed for 48 h under Ar. Benzene was evaporated and the residue was chromatographed over SiO_2 to give **17** (2.57 g, 72 %). **17**; n_D^{24}1.4703 $[\alpha]_D^{24}$+60.6°(c=0.135, MeOH). IR ν_{max} 2950 (s), 1740 (s), 1665 (s), 1615 (s), 1360 (s), 1260 (m), 1120 (s). ^1H NMR δ 1.07 (3H, d, J=6.9 Hz), 1.55 (1H, m), 1.80 (1H, ddd, J=5.7, 6.0, 14.4 Hz), 2.08 (1H, m), 2.10 (1H, m), 2.23 (3H, s), 2.30 (1H, m), 2.35 (2H, m), 3.25 (3H, s), 3.40 (2H, dddd, J=1.2, 1.4, 4.2, 9.6 Hz), 6.03 (1H, d, J=16.3 Hz), 6.70 (1H, d, J=16.3 Hz). ^{13}C NMR δ 14.9 (q), 27.3 (t), 28.0 (q), 32.9 (t), 37.1 (t), 39.2 (d), 57.1 (s), 58.5 (q), 68.6 (t), 131.1 (d), 143.8 (d), 197.3 (s), 217.9 (s). MS m/z 224 (M^+, 15), 209 (10), 182 (26),

166 (17), 149 (36), 137 (75), 123 (69), 109 (74), 91 (68), 79 (100), 77 (83), 65 (66), 55 (72), 53 (79). Found C, 69.59; H, 9.01, Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99 %.

18 was prepared from **15** (5.8 g, 31.7 mmol) in the same manner described above(2.64 g, 72 %). **18**; n_D^{22}1.4822 $[\alpha]_D^{22}$ +50.5°(c=0.45, ether). IR ν_{max} 2950 (s), 1740 (s), 1680 (s), 1620 (s), 1460 (m), 1120 (s), 990 (m). ^{1}H NMR δ 1.06 (3H, d, J=6.9 Hz), 1.08 (3H, t, J=7.3 Hz), 1.56 (1H, m), 1.82 (1H, ddd, J=5.6, 6.2, 14.3 Hz), 2.06 (1H, m), 2.09 (1H, dt, J=5.3, 7.2 Hz), 2.28 (2H, m), 2.38 (1H, ddd, J=2.3, 8.8, 19.2 Hz), 2.53 (2H, q, J=7.3 Hz), 3.26 (3H, s), 3.40 (2H, dt, J=5.9, 7.3 Hz), 6.04 (1H, d, J=16.2 Hz), 6.73 (1H, d, J=16.2 Hz). ^{13}C NMR δ 7.9 (q), 14.8 (q), 27.3 (t), 32.8 (t), 34.6 (t), 37.2 (t), 39.1 (d), 57.1 (s), 58.5 (q), 68.6 (t), 130.1 (d), 142.5 (d), 199.8 (s), 218.1 (s). MS m/z 238 (M^+, 7), 207 (54), 182 (32), 153 (72), 137 (58), 128 (56), 109 (64), 95 (69), 81 (80), 57 (100), 55 (97). Found C, 70.10; H, 9.26 Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30%.

(2S,3R)-2-Methoxyethyl-3-methyl-2-(3-oxobutyl)cyclopentanone **19** and (2S,3R)-2-methoxyethyl-3-methyl-2-(3-oxopentyl)cyclopentanone **20**. A mixture of **17**(2.5 g, 21 mmol) and Pd-C (10 %) (50 mg) in MeOH (30 ml) under H_2 atomosphere was stirred for 1 h at room temp. The mixture was filtered to remove a catalyst and the filtrate was concentrated to give **19**. **19** was employed for the next step without further purification. **19**;n_D^{22}1.4662 $[\alpha]_D^{22}$+45.0°(c=0.49, $CHCl_3$). IR ν_{max} 2950 (s), 1730 (s), 1720 (s), 1360 (m), 1160 (m), 1115 (s). ^{1}H NMR δ 1.05 (3H, d, J=6.9 Hz), 1.51 (2H, dddd, J=0.9, 1.7, 4.6, 6.5 Hz), 1.62 (1H, dt, J=1.4, 10.3 Hz), 1.75 (1H, ddd, J=6.2, 9.2, 15.2 Hz), 1.98 (2H, m), 2.12 (3H, s), 2.18 (2H, m), 2.33 (2H, dq, J=1.7, 8.7 Hz), 2.44 (1H, m), 3.24 (3H, s), 3.30 (2H, dt, J=1.3, 7.2 Hz). ^{13}C NMR δ 14.0 (q), 23.1 (t), 26.8 (t), 30.1 (q), 31.8 (t), 37.0(t), 37.3 (t), 38.1 (d), 51.6 (s), 58.5 (q), 68.9 (t), 208.3 (s), 221.7 (s). MS m/z 168 (M^+-58), 153 (100), 123 (39), 109 (39), 95 (52), 79 (63), 67 (84), 53 (98). Found C, 68.48; H, 9.70, Calcd for $C_{13}H_{22}O_3$: C,68.99; H, 9.80 %.

20 was prepared from **18** in the same manner (72%). **20**; n_D^{22}1.4650 $[\alpha]_D^{22}$+44.8°(c=0.485, ether). IR ν_{max} 2950 (s), 1730 (s), 1710 (s), 1450 (m), 1400 (m), 1360 (m), 1110 (s). ^{1}H NMR δ 1.03 (3H, t, J=7.4 Hz), 1.04 (3H, d, J=6.9 Hz), 1.49 (1H, m), 1.53 (1H, m), 1.63 (1H, m), 1.76 (1H, m), 1.98 (1H, m), 2.00 (1H, m), 2.12 (1H, m), 2.22 (1H, m), 2.32 (1H, ddd, J=1.5, 8.7, 8.9 Hz), 2.39 (2H, d, J=7.3 Hz), 2.40 (2H, m), 3.24 (3H, s), 3.30 (2H, dd, J=5.9, 6.0 Hz), ^{13}C NMR δ 7.8 (q), 14.0(q), 23.1 (t), 26.7 (t), 31.7 (t), 36.0 (t), 36.1 (t), 37.0 (t), 38.0 (d), 51.6 (s), 58.5 (q), 68.9 (t), 211.1 (s), 221.8 (s). Found C, 69.74; H, 9.96, Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06 %.

(1R,7aS)-7a-Methoxyethyl-1-methyl-5,6,7,7a-tetrahydrindan-5-one **21** and (1R,7aS)-7a-methoxyethyl-1,4-dimethyl-5,6,7,7a-tetrahydrindan-5-one **22**. **19** (5.25 g, 21.9 mmol) was dissolved in 2 % KOH in MeOH soln (30 ml) under Ar at room temp and the mixture was refluxed for 6-8 h. MeOH was evaporated to give a residue and the residue was extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **21**(3.40 g, 70 %). **21**; $n_D^{20.5}$1.5049 $[\alpha]_D^{20.5}$+44.2°(c=0.35, ether). IR ν_{max} 2950 (s), 1665 (s). ^{1}H NMR δ 0.87 (3H, d, J=7.1 Hz), 1.40 (1H, m), 1.70 (1H, ddd, J=1.0, 6.8, 14.0 Hz), 1.87 (3H, m), 2.15 (1H, m), 2.25 (1H, m), 2.37 (1H, dddd, J=0.8, 2.4, 14.0, 17.9 Hz), 2.52 (3H, m), 3.32 (3H, s), 3.46 (2H, dd, J=6.8, 7.0 Hz), 5.86 (1H, s). ^{13}C NMR δ 17.0 (q), 26.9 (t), 29.8 (t), 30.5 (t), 33.3 (t), 34.5 (t), 39.3 (d), 47.3 (s), 58.7 (d), 69.7 (t), 122.6 (d), 178.2 (s), 199.4 (s). MS m/z 208 (M^+, 3), 150 (58), 135 (36), 121 (28), 105 (49), 91 (100), 79 (59), 77 (72), 65 (37), 53 (37). Found C, 74.68; H, 9.64, Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68 %.

22 was prepared from **20** in the same manner(3.2 g, 72 %). **22**;n_D^{20}1.5072 $[\alpha]_D^{20}$+41.0°(c=0.44, ether). IR ν_{max} 2950 (s), 1650 (s), 1440 (m), 1370 (m), 1320 (s), 1290 (m), 1110 (s). ^{1}H NMR δ 0.82 (3H, d, J=7.2 Hz), 1.48 (1H, ddt, J=1.7, 3.7, 8.5 Hz), 1.70 (3H, brs), 1.71 (1H, ddt, J=1.0, 6.5, 14.5 Hz), 1.78 (1H, t, J=6.0 Hz), 1.85 (2H, dt, J=2.7, 6.2 Hz), 2.16 (1H, m), 2.22 (1H, ddd, J=2.3, 6.0, 10.0 Hz), 2.38 (1H, ddd, J=2.0, 4.0, 6.9 Hz), 2.51 (2H, m), 2.54 (1H, m), 3.32 (3H, s), 3.44 (2H, dd, J=6.7, 6.9 Hz). ^{13}C NMR δ 11.5 (q), 17.0 (q), 26.7 (t), 28.4 (t), 30.2 (t), 33.4 (t), 34.2 (t), 39.5 (d), 47.9 (s), 58.7 (q), 70.1 (t), 128.6 (s), 171.1 (s), 198.8 (s). MS m/z 222 (M^+, 8), 164 (100), 149 (88), 135 (71), 121 (53), 105 (66), 91 (98), 77 (98), 67 (48), 55 (93). Found C, 75.47; H, 9.75, Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97 %.

(1R,3aS,7aS)-7a-Methoxyethyl-1,4,4-trimethylhexahydrindan-5-one **28**. To a soln of metallic Li (1.08 g, 0.12 mol) in liquid NH_3 (100 ml), was added a soln of **22** (440 mg, 2 mmol) in dry THF (10 ml) at -33°C and the mixture was stirred for 1 h. To the mixture, was added dropwise CH_3I (1.49 g, 10 mmol) and then the mixture was warmed up to room temp. The mixture was diluted with brine (10 ml) and was extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **28** (262 mg, 55 %). **28** ; n_D^{20}1.4850 $[\alpha]_D^{20}$-49.8°(c=0.485, ether). IR ν_{max} 2950 (s), 1705 (s), 1460 (m), 1380 (m), 1120 (s). ^{1}H NMR δ 0.83 (3H, d, J=6.9 Hz), 0.99 (3H, s), 1.24 (2H, m), 1.30 (3H, s), 1.48 (1H, m), 1.72 (3H, m), 1.87 (1H, ddd, J=3.8, 9.6, 14.4 Hz), 1.98 (2H, m), 2.16 (1H, dddd, J=2.0, 2.8, 5.3, 13.0 Hz), 2.20 (1H, dt, J=3.8, 5.3 Hz), 2.76 (1H, dt, J=6.1, 14.4 Hz), 3.37 (3H, s), 3.51 (1H, dt, J=5.8, 9.3 Hz), 3.57 (1H, dt, J=5.5, 9.3 Hz). MS m/z 238 (M^+, 8), 223 (19), 179 (29), 162 (62), 161 (30), 149 (25), 121 (44), 109 (30), 107 (51), 95 (55), 93 (59), 81 (50), 79 (68), 67 (74), 55 (100).

(1R,3aS,7aS)-7a-Hydroxyethyl-1,4,4-trimethylhexahydrindan-5-one **34**. To a mixture of **28**(220 mg, 0.91 mmol), NaI (420 mg, 3 mmol) and 15-Crown-5 (250 mg, 1.2 mmol) in dry CH_2Cl_2 (60 ml), was added BBr_3(0.1 ml, 1.2 mmol) at -30°C under Ar and the mixture was stirred for 4 h. The mixture was poured into sat $NaHCO_3$(20 ml) and extracted with CH_2Cl_2. CH_2Cl_2 layer was washed with sat $Na_2S_2O_3$ several times, sat $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **34**. **34** contained 15-Crown-5 but was employed for the next step without further purification. **34**; IR ν_{max} 3450 (brs), 2950 (s), 1705 (s), 1450 (m), 1370 (m), 1020 (m). MS m/z 224 (M^+, 22), 194 (23), 192 (91), 160 (60), 128 (56), 109 (23), 96 (39), 95 (30), 81 (30), 73 (25), 64 (100), 55 (34).

(1R,3aS,7aS)-1,4,4-Trimethyl-7a-tosyloxyethylhexahydrindan-5-one **35**. To a mixture of crude **34** and DMAP (10 mg) in dry pyridine (5 ml), was added p-TsCl (190 mg, 1 mmol) at 0-5°C and the mixture was stirred overnight. The reaction mixture was poured into ice-water(10 ml) and extracted with ether(50 ml x 3). The ether was washed with sat $CuSO_4$, H_2O, sat $NaHCO_3$, brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **35**. **35** was employed for the next step without further purification. IR ν_{max} 2950 (s), 1700 (s), 1360 (m), 1170 (s).

(1R,2R,5S)-2,6,6-Trimethyltricyclo[6,2,1,$0^{1,5}$]undecan-7-one **36**. To a soln of **35** in dry THF (20 ml) under Ar, was added t-BuOK (112 mg, 1 mmol) at -20 °C and the mixture was stirred for 30 min. The mixture was poured into water (5 ml) and extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **36**(184 mg, 70 % from **28**). **36**; n_D^{22}1.4794 $[\alpha]_D^{22}$-7.5°(c=0.1, $CHCl_3$) IR ν_{max} 2950 (s), 1705 (s). ^{1}H NMR δ 0.90 (3H, d, J=6.8 Hz), 1.06 (3H, s), 1.18 (3H, s), 1.22 (2H, m), 1.40 (1H, ddd, J=1.8, 2.5, 12.2 Hz), 1.55 (1H, m), 1.58 (3H, m), 1.70 (1H, m), 1.82 (2H, m), 1.97 (2H, m), 2.73 (1H, dd, J=4.6, 7.7 Hz). ^{13}C NMR δ 14.6 (q), 24.7 (q), 26.1 (q), 29.7 (t), 30.8 (t), 31.5 (t), 31.8 (t), 33.3 (t), 38.9 (d), 44.0 (s), 50.3 (d), 53.7 (s), 57.5 (d), 220.2 (s). MS m/z 206 (M^+, 80), 191 (7), 178 (44), 163 (12), 150 (10), 135 (70), 121 (35), 107 (84), 94 (100), 82 (56), 69 (50), 55(25), 41 (100). HR-MS 206.1632 $C_{14}H_{22}O$.

(-)-5-Epiprezizanol **5**. To a soln of **36** (140 mg, 0.44 mmol) in dry ether(4 ml), was added CH_3Li (1 ml, 1.28 M ether soln, 1.28 mmol) at -78°C under Ar. The mixture was stirred at -78°C for 5 min and up to room temp for 10 min. The mixture was poured into ice-water (5 ml) and extracted with ether. The ether layer was washed with brine several times, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **5** (77 mg, 80 %). **5**; mp 30°C; $[\alpha]_D^{21}$-53.0°(c=0.2, $CHCl_3$); IR ν_{max} 3500 (s), 2950 (s), 1450 (m), 1375 (m), 1080 (m). ^{1}H NMR δ 0.83 (3H, d, J=6.4 Hz), 0.85 (3H, s), 1.12 (1H, m), 1.14 (3H, s), 1.22 (3H, s), 1.30 (2H, m), 1.40 (3H, m), 1.58 (4H, m), 1.80 (2H, m), 1.98 (2H, dd, J=4.4, 4.9 Hz). ^{13}C NMR δ 14.3 (q), 24.4 (t), 25.6 (q), 26.5(t), 29.7 (q), 30.1 (q), 30.2 (t), 30.6 (t), 30.9 (t), 38.2 (s), 38.4 (d), 50.5 (d), 52.8 (s), 59.8 (d), 76.6 (s). MS m/z 222 (M^+, 44), 179 (88), 161 (18), 137 (28), 109 (60), 95 (53), 83 (60), 71 (100), 43 (58). Found C, 80.76; H, 11.71, Calcd for $C_{15}H_{26}O$: C, 81.02; H,11.78 %.

(-)-5-Epiprezizaene **6**. To a soln of **5** (31.3 mg, 0.14 mmol), Et_3N (2 ml) in dry CH_2Cl_2 (3 ml), was added MsCl (0.1 ml) at 0°C under Ar. The mixture was stirred for 10 min, poured into ice-water and extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over neutral SiO_2 to give **6** (21 mg, 73 %). **6** ; n_D^{20}1.4986 $[\alpha]_D^{20}$-53.0°(c=0.05, $CHCl_3$) IR ν_{max} 2950 (s), 1630 (s), 1370 (s), 890 (s). ^{1}H NMR δ 0.83 (3H, d, J=7.0 Hz), 1.04 (3H, s), 1.17 (3H, s), 1.45 (2H, m), 1.52-1.85 (10H, m), 2.75 (1H, m), 4.61 (1H, d, J=1.8 Hz), 4.67 (1H, d, J=1.8 Hz). ^{13}C NMR δ 14.3 (q), 26.0 (t), 28.7 (q), 29.7 (t), 30.0 (q), 30.5 (t), 31.5 (t), 32.7 (q), 35.7 (s), 36.3 (d), 38.9 (t), 46.1 (d), 59.3 (d), 105.2 (t), 162.7 (s). MS m/z 204 (M^+, 13), 189 (35), 175 (10), 161 (23), 147 (22), 134 (42), 133 (100), 119 (40), 108 (35), 91 (35), 93 (32), 81 (25), 67 (12), 69 (12), 55 (15), 41 (10). Found C, 87.78; H, 11.67, Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84 %. HR-MS; 204.1852.

(1R,5R,7aS)-7a-Methoxyethyl-1-methyl-5,6,7,7a-tetrahydrindan-5-ol **40**. To a soln of **21**(2.08 g, 10.0 mmol) in MeOH, was added portionwise $NaBH_4$(450 mg, 12 mmol) at -20°C and the mixture was stirred for 1 h. MeOH was evaporated and to the residue, was added ether(100 ml) and brine (20 ml). Organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over neutral SiO_2 to give a mixture of **39** (1.75 g, 86.2 %) and **40** (0.28 g, 13.3 %) **39**; n_D^{20}1.5010 $[\alpha]_D^{20}$-25.2°(c=0.35, ether) IR ν_{max} 3450 (s), 2950 (s), 1460 (m), 1110 (s). ^{1}H NMR δ 0.75 (3H, d, J=7.1 Hz), 1.16 (1H, m), 1.50 (1H, dt, J=2.3, 7.0 Hz), 1.68 (2H, m), 1.98 (4H, m), 2.15 (2H, m), 2.30 (1H, m), 3.25 (3H, s), 3.41 (2H, t, J=7.0 Hz), 4.56 (1H, brt, J=7.0 Hz), 5.77 (1H, s). ^{13}C NMR δ 17.8 (q), 26.7 (t), 28.1 (t), 30.2 (t), 30.3 (t), 36.2 (t), 39.0 (d), 46.1 (s), 58.5 (q), 67.7 (d), 70.1 (t), 124.6 (d), 149.4 (s). MS m/z 192 (M^+-18, 21), 147 (16), 134 (91), 117 (69), 105 (34), 91 (100), 77 (19), 65 (13). Found C, 73.92; H, 10.20, Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54 %. **39** was converted to **40** by the method of Mitsunobu.[19] To a soln of **39** (1.75 g, 8.33 mmol) in dry benzene(30 ml), was added Ph_3P (2.18 g, 8.33 mmol), benzoic acid (1.02 g, 8.33 mmol) and DEAD (1.45 g, 8.33 mmol) and the mixture was stirred for 1 h at room temp. Benzene was evaporated and the residue was chromatographed over SiO_2 to give benzoate of **40**, which was employed

for the next step without further purification (containing DEAD and it is unable to separate DEAD and benzoate). Benzoate of **40**; IR νmax 2950 (s), 1780 (s), 1710 (s), 1440 (m), 1260 (s), 1120 (s), 750 (s). MS m/z 314 (M^+, 1), 254 (13), 192 (58), 147 (10), 134 (34), 119 (14), 105 (100), 91 (33), 77 (20). To a soln of benzoate in MeOH, was added K_2CO_3 (8 g) and the mixture was stirred for 1 h. MeOH was evaporated and the resiue was extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over neutral SiO_2 to give **40** (1.44 g, 73 %). **40** ; $n_D^{18.5}$1.5015 $[\alpha]_D^{18.5}$+107.5°(c=0.35, ether) IR ν_{max} 3450 (s), 2950 (s), 1460 (m), 1110 (s). ^{1}H NMR δ (C_5D_5N) 0.75 (3H, d, J=7.1 Hz), 1.13 (1H, m), 1.52 (1H, ddd, J=3.9, 4.0, 13.0 Hz), 1.66 (1H, ddd, J=1.0, 6.8, 14.2 Hz), 1.78 (2H, m), 1.95 (2H, m), 2.06 (2H, m), 2.21 (1H, m), 2.36 (1H, m), 3.28 (3H, s), 3.40 (2H, t, J=6.4 Hz), 4.42 (1H, s), 4.90 (1H, s), 5.83 (1H, brs). ^{13}C NMR δ 17.6 (q), 22.6 (t), 28.7 (t), 29.3 (t), 30.6 (t), 35.6 (t), 39.6 (d), 45.8 (s), 58.4 (q), 63.5 (d), 70.1 (t), 122.8 (d), 124.0 (s). MS m/z 192 (M^+-18, 20), 147 (17), 134 (100), 117 (64), 105 (29), 91 (88). Found C, 73.92; H, 10.31, Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54 %.

(1R,3aS,5R,7aS)-7a-Methoxyethyl-1-methylhexahydrindan-5-ol **41**. According to the method by Amma *et al.*[19] and Brown *et al.*,[20] [Rh(NBD)(DIPHOS-4)]ClO_4 in THF soln was prepared from $RhCl_3$, $AgClO_4$, NBD and 1,4-bis(diphenylphosphino)butane. To an autoclave (100 ml scale), was added **40**(1.06 g, 5.53 mmol), THF (30 ml) freshly distilled under N_2, and 5 % mol eq of THF soln of catalyst under N_2, and H_2 was introduced to this mixture. The mixture was hydrogenated (55 atm, room temp, 2.5 h) to give **41** (1.02 g, 95 %). **41**; n_D^{18}1.4900 $[\alpha]_D^{18}$+1.2°(c=0.35, $CHCl_3$); IR ν_{max} 3450 (s), 2950 (s), 1460 (m), 1120 (s), 690 (s). ^{1}H NMR δ 0.82 (3H, d, J=7.2 Hz), 1.15-1.25 (3H, m), 1.30 (1H, dt, J=3.0, 15.0 Hz), 1.65 (8H, m), 1.98 (3H, m), 3.35 (3H, s), 3.38 (2H, t, J=7.2Hz), 4.10 (1H, m). ^{13}C NMR δ 18.5 (q), 24.3 (t), 27.4 (t), 27.5 (t), 29.0 (t), 30.7 (t), 33.1 (t), 37.7 (d), 38.2 (d), 44.0 (s), 58.7 (q), 66.5 (d), 70.1 (t). MS m/z 194 (M^+-18), 180 (38), 162 (33), 152 (31), 135 (100), 107 (41), 94 (59), 79 (37), 45 (33). Found C, 73.78; H, 11.15, Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39 %.

(1R,3aS,7aS)-7a-Methoxyethyl-1-methylhexahydrindan-5-one **42**. To a soln of **41** (930 mg, 4.8 mmol) in acetone (50 ml), was added Jones reagent(15 ml) at 0-5°C and the mixture was stirred for 30 min. Isopropyl alcohol was added to the mixture to decompose excess of Jones reagent and organic layer was extracted with ether. The ether layer was washed with sat $NaHCO_3$, brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **42**(906 mg, 90 %). **42**; n_D^{18}1.4883 $[\alpha]_D^{18}$+26.0°(c=0.1, $CHCl_3$). IR ν_{max} 2950 (s), 1715 (s), 1460 (m), 1120 (s). ^{1}H NMR δ 0.84 (3H, d, J=7.2 Hz), 1.31 (1H, m), 1.38 (2H, m), 1.57 (1H, ddt, J=1.3, 5.3, 13.4 Hz), 1.68 (1H, m), 1.77 (1H, ddd, J=1.0, 6.4, 13.4 Hz), 1.98 (2H, m), 2.10 (1H, m), 2.18 (1H, m), 2.38 (4H, m), 3.36 (3H, s), 3.48 (2H, m), ^{13}C NMR δ 18.4 (q), 27.4 (t), 28.0 (t), 28.2 (t), 31.6 (t), 37.1 (d), 37.4 (t), 42.4 (t), 43.8 (s), 45.4 (d), 58.8 (q), 69.7 (t), 211.7 (s). MS m/z 210 (M^+, 48), 178 (37), 150 (95), 135 (46), 121 (40), 108 (65), 93 (80), 81 (59), 67 (45), 55 (40), 45 (100). HR-MS 210.1651 ; $C_{13}H_{22}O_2$.

(1R,3aS,7aS)-7a-Hydroxyethyl-1-methylhexahydrindan-5-one **44**. **44** was prepared from **42** (792 mg, 3.77 mmol) in the same manner described above. **44**; IR ν_{max} 3450 (br), 2950 (s), 1710 (s). ^{1}H NMR δ 0.83 (3H, d, J=7.2 Hz), 1.35 (3H, m), 1.58 (1H, ddt, J=1.3, 5.5, 8.5 Hz), 1.67 (3H, m), 1.79 (1H, ddd, J=2.1, 6.4, 8.5 Hz), 1.95 (2H, m), 2.13 (1H, ddd, J=1.3, 6.4, 8.5 Hz), 2.19 (1H, m), 2.40 (4H, m), 3.80 (2H, m). MS m/z 196 (M^+, 40), 151 (56), 133 (50), 123 (81), 110 (100), 93 (94), 81 (90), 67 (73), 55 (80).

(1R,3aS,7aS)-1-Methyl-7a-tosyloxyethylhexahydrindan-5-one **45** and (1R,2R,5S)-7-oxo-2-methyltricyclo[6,2,1,0,^{1,5}]-undecane **46**. **45** was prepared from crude **44** in the same manner described above. **45**; IR ν_{max} 1710 (s), 1360 (s). ^{1}H NMR δ (100 MHz) 0.80 (3H, d, J=7.0 Hz), 1.25 (1H, t, J=7.0 Hz), 1.50 (3H, m), 1.62 (2H, d, J=3.8 Hz), 2.00 (4H, m), 2.34 (4H, dt, J=6.0, 12.0 Hz), 2.47 (3H, s), 4.20 (2H, t, J=7.0 Hz), 7.35 (2H, d, J=7.5 Hz), 7.80 (2H, d, J=7.5 Hz). **45** was chromatographed over SiO_2 and was employed for the next step without further purification. **46** was prepared from **45** in the same manner described above(360 mg, 70 % from **42**). **46**; n_D^{18}1.5006 $[\alpha]_D^{18}$+115.2°(c=0.1, $CHCl_3$) lit. $[\alpha]_D^{25}$+115°(c=0.1, $CHCl_3$). IR ν_{max} 2950 (s), 1705 (s), 1450 (m), 1120 (m). ^{1}H NMR δ 0.92 (3H, d, J=7.2 Hz), 1.30 (1H, m), 1.38 (2H, m), 1.65 (1H, m), 1.66 (2H, dd, J=0.9, 12.5 Hz), 1.75 (1H, m), 1.81 (1H, dd, J=4.4, 11.5 Hz), 1.93 (2H, m), 2.06 (2H, m), 2.19 (1H, ddd, J=0.7, 12.8, 13.6 Hz), 2.36 (1H, dd, J=5.7, 14.8 Hz), 2.67 (1H, dd, J=5.5, 5.7 Hz). ^{13}C NMR δ 19.7 (q), 27.7 (t), 28.1 (t), 32.1 (t), 32.6 (t), 38.5 (t), 39.3 (d), 41.4 (t), 45.4 (d), 51.2 (d), 53.4 (s), 214.7 (s). MS m/z 178 (M^+, 93), 134 (100), 121 (75), 108 (80), 93 (97), 81 (60), 67 (70), 55 (35), 44 (10). Found C, 80.53; H, 10.04, Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18 %.

(-)-7-Oxo-2,6,6-trimethyltricyclo[6,2,1,0^{1,5}]undecane **47**. To a suspension of KH (278 mg, 20 % in mineral oil, 1.56 mmol) in dry THF (30 ml), was added dropwise **46** (260 mg, 1.45 mmol) in dry THF (2 ml) and the mixture was stirred for 1 h under Ar. To the mixture, was added CH_3I (excess) dropwise and the mixture was refluxed for 8 h. After being cooled, the mixture was poured into ice-water(20 ml) and organic layer was extracted with ether. The ether was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give **47** (267 mg, 91 %) **47**; n_D^{18}1.5018 $[\alpha]_D^{18}$+13.1°(c=0.1, $CHCl_3$) IR ν_{max} 2950 (s), 1705 (s), 1460 (m), 1070 (s). ^{1}H NMR δ 0.92 (3H, d, J=7.2 Hz), 1.71 (3H,s), 1.08 (3H, s), 1.25 (1H, m), 1.38 (1H, ddt, J=1.2, 4.4, 7.2 Hz), 1.60

(4H, m), 1.73 (1H, m), 1.83 (1H, ddd, J=1.2, 9.1, 10.5 Hz), 1.92 (2H, m), 2.08 (2H, m), 2.78 (1H, dd, J=4.2, 6.9 Hz). ^{13}C NMR δ 19.9 (q), 22.5 (t), 24.4 (q), 27.6 (t), 28.8 (q), 32.0 (t), 32.1 (t), 37.9 (t), 39.9 (d), 52.2 (d), 53.7 (s), 54.1 (d), 167.2 (s), 219.6 (s). MS m/z 206 (M^+, 100), 191 (50), 150 (40), 135 (82), 107 (71), 82 (60), 69 (55), 67 (40), 55 (22). Found C, 81.59; H, 10.95, Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75 %.

(-)-Prezizanol **1.** **1** was prepared from **47** (247 mg, 1.20 mmol) in the same manner described above(240 mg, 90 %). **1**; mp 34° $[\alpha]_D^{20}$-49.5°(c=0.1, $CHCl_3$) IR ν_{max} 3450 (br), 2950 (s), 1460 (m), 1370 (m), 1130 (m), 910 (m), 890 (m). ^1H NMR δ 0.87 (3H, s), 0.88 (3H, d, J=7.3 Hz), 1.01 (3H, s), 1.12 (2H, m), 1.22 (3H, s), 1.38 (2H, dd, J=4.7, 11.2 Hz), 1.45-1.60 (5H, m), 1.75 (1H, m), 1.84 (1H, dd, J=1.0, 2.2 Hz), 1.86 (1H, d, J=2.3 Hz), 1.98 (2H, m). ^{13}C NMR δ 19.4 (q), 19.6 (q), 23.5 (t), 24.9 (t), 27.5 (d), 27.5 (t), 28.6 (q), 32.5 (t), 33.4 (t), 38.1 (t), 39.7 (d), 40.3 (s), 52.0 (d), 53.0 (d), 53.1 (s). MS m/z 222 (M^+, 40), 204 (20), 189 (36), 179 (100), 137 (38), 123 (30), 109 (62), 95 (47), 82 (72), 71 (90), 55 (20), 43 (38). Found C, 81.19; H, 11.73, Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78 %.

(-)-Prezizaene **2.** **2** was prepared from **1** (100 mg, 0.45 mmol) in the same manner described above(67 mg, 73 %). **2**; n_D^{20}1.4992 $[\alpha]_D^{20}$-49.0°(c=0.105, $CHCl_3$) IR ν_{max} 2950 (s), 1630 (s), 1375 (m), 1360 (m), 890 (s). ^1H NMR δ 0.87 (3H, d, J=7.2 Hz), 1.07 (3H, s), 1.11(3H, s), 1.15 (1H, m), 1.25 (2H, dt, J=1.1, 8.3 Hz), 1.50-1.60 (5H, m), 1.79 (2H, m), 1.95 (2H, m), 2.81 (1H, dd, J=4.8, 6.3 Hz), 4.60 (1H, dd, J=1.8, 18.2 Hz), 4.71 (1H, dd, J=1.8, 18.2 Hz), ^{13}C NMR δ 20.0 (q), 22.9 (t), 27.1 (q), 30.0 (t), 31.4 (t), 32.2 (q), 32.6 (t), 37.6 (s), 40.4 (d), 41.1 (t), 48.0 (d), 53.6 (s), 54.3 (d), 105.5 (t), 163.1 (s). MS m/z 204 (M^+, 20), 189 (43), 161 (30), 133 (100), 108 (74), 91 (45), 79 (21), 55 (20). Found C, 87.88; H, 11.63, Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84 %.

(-)-Allokhusiol (-)-**3.** To a soln of **2** (30 mg, 0.15 mmol) in THF-H_2O, was added $Hg(OAc)_2$ (64 mg, 0.2 mmol) and the mixture was stirred for overnight at room temp. To this mixture was added gradually a soln of 3M $NaBH_4$ in 3M NaOH soln (1 ml). The mixture was diluted with water, filtered and extracted with ether. The ether layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over SiO_2 to give recovered (-)-**2** (15 mg, 50 %) and (-)-**3** (13 mg, 85 %, ~50 % conversion). (-)-**3**; n_D^{20}1.5015 $[\alpha]_D^{20}$-62°(c=0.1, $CHCl_3$) IR ν_{max} 3450 (s), 2950 (s), ^1H NMR δ 0.906 (3H, d, J=7.2 Hz), 0.910 (3H, s), 0.926 (3H, s), 1.08 (2H, m), 1.27 (2H, dd, J=4.6, 11.1 Hz), 1.44 (1H, dq, J=3.0, 9.1 Hz), 1.52 (2H, m), 1.58 (2H, m), 1.75 (4H, m), 1.95 (1H, m), 2.05 (2H, dd, J=4.6, 6.7 Hz). ^{13}C NMR δ 19.8, 21.3, 23.5, 23.8, 26.3, 27.3, 32.0, 33.1, 36.0, 39.8, 40.3, 50.7, 51.8, 52.7, 76.7. MS m/z 222 (M^+, 42), 204 (30), 189 (47), 179 (100), 161 (41), 137 (44), 109 (72), 95 (55), 82 (75), 71 (92), 43 (45). Pound: C, 81.20; H, 11.74 Calcd for $C_{15}H_{26}O$; C,81.02; H, 11.78 %.

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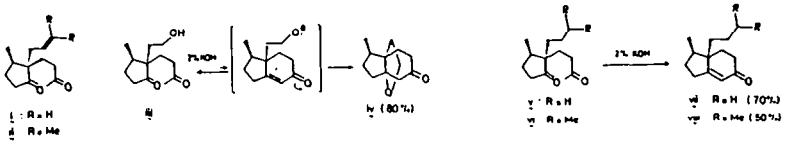
The yield of the annulation reaction was remarkably affected by changing substituent at the angular position. Unsaturated substituent i, ii caused recovery of starting material or low yield (~10 %) of product. Hydroxy group iii afforded propelane iv in high yield probably because the formation of oxolane ring forced equilibration to the right side. Diketone with saturated chain v, vi also gave annulation product in good yield. Thus, a smaller substituent gave better result and the methoxyethyl group was selected as the candidate.



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