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CONTRIBUTION TO THE CHEMISTRY OF β-PIPITZOL

P. JOSEPH-NATHAN, M.P. GONZÁLEZ, L.U. ROMÁN,[1] J.D. HERNÁNDEZ,[1] A. FLORES-VELA, and R.L. SANTILLAN

Departamento de Química del Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, P.O. Box 14-740, México, D.F., 07000 México

ABSTRACT.—Exploration of the chemistry of β-pipitzol (**1a**) leads to the preparation of a series of new derivatives, thus allowing its correlation with *ent*-3-*epi*-α-cedrene (**18**) known as 3-*epi*-α-cedrene. Alcohol **2**, obtained by $LiAlH_4$ reduction of *O*-methyl-β-pipitzol (**1c**), undergoes 1-4 dehydration on acid treatment, giving the ketoalcohol **3**, which differs only in the stereochemistry at C-9 from the ketoalcohol **4a** obtained by Li/NH_3 reduction of **1c**, followed by acid treatment. Moreover, hydrolysis of 4-desoxo-β-pipitzol benzoate (**12**) and of 4,9-*bis*-desoxo-β-pipitzol benzoate (**15**) yields ketones **10** and **16**, respectively, which differ in the stereochemistry of the methyl group at C-6. Catalytic hydrogenation of ketoalcohol **3** followed by oxidation gave the diketone **9**, which is epimeric at C-6 with the diketone **10**, its stereochemistry being deduced from ord measurements. Spectroscopic data and stereochemical assignment for all compounds are provided.

The naturally occurring sesquiterpenes α- and β-pipitzol are two well-known cedranolides isolated from the roots of several species of *Perezia* (1), whose structures were elucidated in 1965 (1,2) from chemical transformations and spectroscopic studies. Moreover, it has been reported that an equimolar mixture of α- and β-pipitzol can be obtained by thermolysis of perezone (3-5), while stereoselective catalyzed transformations (6,7) lead to an excess of either one of the isomers, depending on the nature of the substrate and the reaction conditions.

Although the chemistry of α-pipitzol has been explored (8), mainly because of its close structural relationship to α-cedrene (9), almost no chemical transformations of the β-isomer have been reported (8). The present work describes a series of compounds derived from β-pipitzol (**1a**), which were obtained to investigate its stereochemical behavior. This allowed a correlation with the known 3-*epi*-α-cedrene (**18**) (10), more properly designated as *ent*-3-*epi*-α-cedrene.

The natural mixture of α- and β-pipitzol was separated by fractional crystallization of the derived benzoates followed by hydrolysis (2). An alternative procedure using medium pressure column chromatography allowed separations of small quantities of each of the pipitzols.

Treatment of β-pipitzol (**1a**) with an ethereal solution of CH_2N_2 gave *O*-methyl-β-pipitzol (**1c**), which was reduced with $LiAlH_4$ in THF to afford the oily enol ether **2**. Acid treatment of the ether **2**, to remove the methoxyl group, occurred with concomitant 1-4 dehydration to afford an α,β-unsaturated hydroxyketone, which shall be referred to as β-pipitzone (**3**). Its structure was readily adduced from its spectral data (see Experimental section).

On the other hand, Li/NH_3 reduction of *O*-methyl-β-pipitzol (**1c**), followed by treatment with HCl, afforded 9-*epi*-β-pipitzone (**4a**) with the same stereochemistry at C-9 as the diol obtained by Li/NH_3 reduction of β-pipitzol (2). Compound **4a** showed two doublets at 6.16 and 5.20 (J=2 Hz) for the vinylic hydrogens and a triplet at 4.36 (J=4.5 Hz) for the C*H*-OH group, which collapses into a doublet (J=4.5 Hz) upon equilibration with D_2O.

As far as stereochemical assignments of the hydroxyl group at C-9 in β-pipitzone

[1]Present address: Instituto de Investigaciones Químico Biológicas, Universidad Michoacana de San Nicolás de Hidalgo, Morelia, Mich., 58240 México.

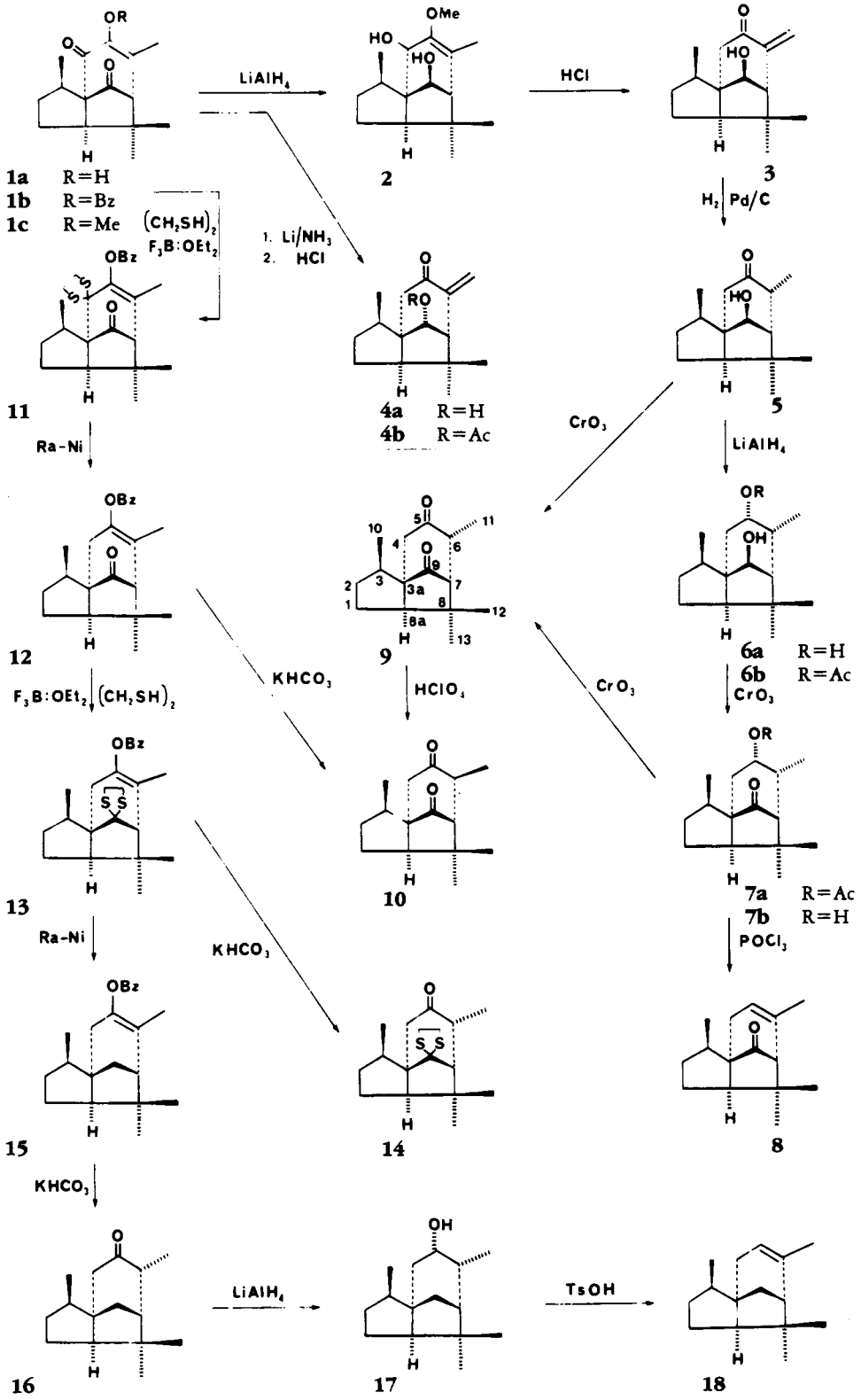

FIGURE 1. Synthetic route for the preparation of β-pipitzol derivatives

(**3**) and 9-*epi*-β-pipitzone (**4a**) are concerned, it seems evident that attack by $LiAlH_4$ at the C-9 carbonyl function in *O*-methyl-β-pipitzol (**1c**) proceeds from the less-hindered side of the molecule, which in this case is that opposed to the secondary methyl group (C-10), thus giving rise to **3**. On the other hand, Li/NH_3 reductions are not as dependent on steric factors (11), and, therefore, the reaction gives rise to the thermodynamically more stable alcohol, which is also the less-hindered one (**4a**). Furthermore, the stereochemistry at C-9 is chemically confirmed by the fact that β-pipitzone (**3**) does not form the corresponding acetate, while 9-*epi*-β-pipitzone (**4a**) does readily. Further evidence to support the stereochemistry at C-9 in compounds **3** and **4a** is evident after construction of the Dreiding models. Examination of the models reveals that the C-H-7 and C-H-9 bonds form an angle of about 80° in β-pipitzone (**3**), thus leading to a nonobservable coupling in the ^{1}H-nmr spectrum, according to Karplus-type relationships (12). These protons form an angle of approximately 45° in 9-*epi*-β-pipitzone (**4a**) corresponding to an observed coupling constant of 4.5 Hz, which is indeed seen.

Dihydro-β-pipitzone (**5**) was obtained by catalytic hydrogenation of β-pipitzone (**3**). The assignment of stereochemistry at the newly formed chiral center (C-6) is based on the positive Cotton effect in the ord curve (13) (see below).

As in the case of **3**, compound **5** failed also to acetylate after treatment with Ac_2O/Py on the steam bath for 3 h, further demonstrating the *cis*-relationship of the hydroxyl group and the C-10 secondary methyl group.

Reduction of dihydro-β-pipitzone (**5**) with $LiAlH_4$ gave diol **6a** which required 8 h on the steam bath to yield only the monoacetate **6b**, the other hydroxyl group remaining resistant to acetylation, as in the case of **5**. Oxidation of monoacetate **6b** with CrO_3 afforded the ketoester **7a**, which was hydrolyzed to yield the corresponding alcohol **7b**. This, in turn, was converted into the β,γ-unsaturated ketone **8**, by dehydration with $POCl_3$.

Jones oxidation of both **5** and **7b** gave a diketone (**9**) which is identical to the oxidation product of the diol obtained by Li/NH_3 reduction (2) of β-pipitzol (**1a**). Compound **9** is epimeric at C-6 with that obtained by hydrolysis of 4-desoxo-β-pipitzol benzoate (**12**) (2). Furthermore, the epimerization process of **9** at C-6 was followed by ^{1}H nmr in C_6D_6 solution by observing the variation in relative areas of the *gem*-dimethyl group signals. The singlets corresponding to diketone **9** absorb at 0.90 and 1.12 ppm, while those of **10** appear at 0.86 and 1.09 ppm. Thus, adding $HClO_4$ to diketone **9** shows that **9** and **10** were present in a 3:1 ratio after 10 min. A ratio of 1:2 of **9** and **10** was achieved at room temperature after 37 h. These results suggest that diketone **10** is thermodynamically more stable than **9**. Therefore, the methyl group at C-6 in compound **9** is more hindered than the same substituent in **10** where it has the *beta*-configuration.

The Cotton effects exhibited by each of the diketones (**9** and **10**) further confirmed the proposed stereochemistry. Diketone **9** shows a moderate positive Cotton effect (3500°) at 334 nm, while **10** shows a strong positive effect (7490°) at the same wavelength. These effects are in accordance with those predicted by the octant rule (13).

The α-equatorial configuration of the C-6 methyl group in **9** also explains the fact that reduction of dihydro-β-pipitzone (**5**) with$LiAlH_4$ give diol **6a**. Since the CH_3-11 in dihydro-β-pipitzone (**5**) is α-equatorial, the *endo*-side of the molecule is sterically hindered, and, therefore, hydride attack must proceed from the *exo*-side, thus generating an α-axial hydroxy group, which does not readily acetylate.

In an alternate sequence, removal of the two carbonyl groups in β-pipitzol benzoate (**1b**) was achieved by successive thioketalization-desulfuration (8), thus affording 4,9-*bis*-desoxo-β-pipitzol benzoate (**15**).

In contrast to desulfuration of compound **11** at neutral pH, a slightly basic medium (pH=8) afforded a mixture of the known (8) 4-desoxo-β-pipitzol benzoate (**12**) and ketoalcohol **7b**, as proved by direct comparison with the sample obtained from β-pipitzone (**3**).

Treatment of 4-desoxo-β-pipitzol benzoate (**12**) with $KHCO_3$ yielded diketone **10**, identical to the substance obtained by treatment of its epimer **9** with $HClO_4$. This was also tested by direct comparison. Under the same reaction conditions, thioketal **13** yielded a ketone (**14**) whose stereochemistry at C-6 is analogous to that of the hydrolysis product of 4,9-*bis*-desoxo-β-pipitzol (**15**) (see below). A common configurational assignment based on observation of coupling constants in the ^{1}H-nmr spectrum was not possible in this case due to an overlap of signals.

Removal of the benzoate residue in 4,9-*bis*-desoxo-β-pipitzol benzoate (**15**) with $KHCO_3$ yielded the corresponding ketone (**16**), the assignment of configuration at C-6 being based on ^{1}H-nmr evidence. It has been described previously (8) that $NaHCO_3$ hydrolysis of 4,9-*bis*-desoxo-α-pipitzol yields the known 5-isocedranone (14). The structures of 5-isocedranone and ketone **16** keep an enantiomeric relationship, except for the methyl group at C-3, as is evident from the spectral data. The ^{1}H-nmr chemical shifts for the hydrogens at C-10, C-11, C-12, and C-13 in ketone **16** are 0.90, 1.17, 1.00, and 0.93 ppm, respectively, while the same protons in 5-isocedranone appear at 0.85, 1.19, 1.00, and 0.97 ppm, respectively. Its configurational assignment at the C-5 hydroxyl group and C-6 methyl group is also attained by comparing the ^{1}H-nmr spectra of alcohol **17** and 5-neoisocedranol (14). The ^{1}H-nmr spectrum of **17** shows the C-5, C-10, C-11, C-12, and C-13 hydrogens at 3.94, 0.80, 1.14, 1.25, and 0.90, respectively, while the same protons in 5-neoisocedranol appear at 4.00, 0.82, 1.14, 1.30, and 0.95, respectively.

On the other hand, it seems reasonable to expect that attack by $LiAlH_4$ on ketone **16** occurs by the less-hindered side of the molecule, as in the case of keto alcohol **5**, thus leading to a C-5 *alpha*-hydroxyl group.

Finally, *ent*-3-*epi*-α-cedrene (**18**) was obtained by dehydration of **17** with *p*-toluenesulfonic acid, showing ^{1}H-nmr data in very good agreement with reported values (10).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Uv absorption spectra were determined on an Unicam SP-800 spectrophotometer using 95% EtOH. Rotations were taken on a Perkin-Elmer 141 M polarimeter in $CHCl_3$ or dioxane for ord measurements, unless otherwise specified. Ir spectra were measured on a Perkin-Elmer 421 spectrometer in $CHCl_3$ solution. ^{1}H-nmr spectra were recorded on Varian Associates A-60, EM-390, and XL-100A spectrometers using CCl_3D or CCl_4 as the solvent and TMS as internal reference. Microanalyses were performed by the Analytical Laboratories Elbach (Federal Republic of Germany). Melting points were determined on a Fisher-Johns apparatus and are uncorrected.

β-PIPITZOL (**1a**).—The natural mixture of α- and β-pipitzol (1 g, 4.0 mmol) was separated on 20 g of silica gel (230-400 mesh) using medium pressure chromatography. Elution with light petroleum ether (200 ml) afforded α-pipitzol), mp 146-147° [lit (2): 146-147°]. β-pipitzol (**1a**), mp 131-132° [lit (2): 131-132°] was obtained from the hexane fractions.

O-METHYL-β-PIPITZOL (**1c**).—A sample of β-pipitzol (**1a**) (5 g, 20.2 mmol) was dissolved in 50 ml of MeOH and treated with 200 ml of an ethereal CH_2N_2 solution (prepared from 14 g of *N*-nitroso-*N*-methylurea) at 4° for 8 days. The solution was partitioned with Et_2O-H_2O. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution and with H_2O, dried (Na_2SO_4), and evaporated. The residue was chromatographed on 50 g of alumina. The hexane-C_6H_6 (1:1) fractions were combined, evaporated, and recrystallized from hexane to afford 3.7 g (70% yield) of **1c** (needles), mp 72-74°; $[\alpha]D$ −165° (c, 1, $CHCl_3$); uv λ max (EtOH) 240, 271 nm (log ε=3.63, 3.63); ir ν max ($CHCl_3$) 1760 (5-membered ketone), 1675 and 1620 cm^{-1} (6-membered ring conjugated ketone); nmr (60 MHz, CCl_4) 3.72 (3H, s, OMe), 2.61 (1H, s, H-7), 2.03 (3H, s, CH_3-11), 1.26 (3H, d, J=6.5 Hz, CH_3-10), 1.04 (6H, s, CH_3-12 and CH_3-13) ppm. *Anal.* Found: C, 73.18; H, 8.48; O, 18.36%; calcd. $C_{16}H_{22}O_3$: C, 73.25; H, 8.45; O, 18.30%

ENOLETHER **2**.—*O*-Methyl-β-pipitzol (**1c**) (3.5 g, 13.4 mmol) was dissolved in 150 ml of THF and slowly added to 150 ml of a suspension of $LiAlH_4$ in THF (0.13 mmol) with stirring at room temperature. The reaction mixture was refluxed for 3 h and cooled to room temperature. The excess hydride was destroyed with EtOAc and H_2O, filtered, and the organic layer extracted with EtOAc. The combined EtOAc extracts were dried (Na_2SO_4) and concentrated, giving 1.42 g (40% yield) of **2** (oil), which were chromatographed on 50 g of alumina. The combined Et_2O fractions afforded enolether **2**, which was characterized by its ^{1}H-nmr spectrum; nmr (60 MHz, CCl_4 4.15 (1H, broad s, H-9), 3.83 (1H, q, J=1.5 Hz, H-4), 3.50 (3H, s, OMe), 1.61 (3H, d, J=1.5 Hz, CH_3-11), 1.28 (3H, d, J=6 Hz, CH_3-10), 1.18 (3H, s, CH_3-12), 0.93 (3H, s, CH_3-13) ppm.

β-PIPITZONE (**3**).—Enolether **2** (1.42 g, 5.3 mmol) was dissolved in 35 ml of MeOH, 2 ml of dilute HCl was added and the reaction mixture refluxed for 10 min. The solvent was evaporated and the product extracted with Et_2O. The organic layer was washed with cold H_2O, dried (Na_2SO_4), and concentrated. The residue was chromatographed on 40 g of alumina. The combined hexane-C_6H_6 (1:1) fractions afforded 1.06 g (85% yield) of β-pipitzone (**3**), recrystallized from hexane-Me_2CO, mp 115-116°; $[\alpha]_D$ +33° (c, 0.65, $CHCl_3$); uv λ max (EtOH) 242 nm (log ε=3.58); ir ν max 3605 (OH), 1695 and 1615 cm^{-1} (α,β-unsaturated ketone); ord (c, 0.22, dioxane) $[\phi]_{579}$ +85°, $[\phi]_{436}$ +250°, $[\phi]_{405}$ +530°, $[\phi]_{334}$ −630°, $[\phi]_{313}$ +125°, $[\phi]_{302}$ +680°, $[\phi]_{289}$ +140°, $[\phi_{280}$ +2450°; nmr (100 MHz, $CDCl_3$) 5.88 (1H, d, J=2 Hz, H-11), 5.07 (1H, d, J=2 Hz, H-11′), 4.12 (1H, s, H-9), 2.60 (1H, s, H-7), 2.59 and 2.23 (2H, J_{AB}=19 Hz, H_2-4), 1.28 (3H, s, CH_3-12), 1.17 (3H, d, J=6 Hz, CH_3-10), 0.85 (3H, s, CH_3-13) ppm; *Anal.* Found: C, 76.85; H, 9.37; O, 13.50%; calcd. $C_{15}H_{22}O_2$: C, 76.88; H, 9.46; O, 13.65%.

9-*EPI*-β-PIPITZONE (**4a**).—A vigorously stirred solution of **1c** (1 g, 3.8 mmol) in THF (8 ml), MeOH (8 ml), and liquid NH_3 (100 ml) was treated with Li (2.5 g) until a blue color persisted. Solid NH_4Cl (8 g) was added and the remaining NH_3 evaporated. The residue was acidified with dilute HCl and extracted with EtOAc. The organic layer was washed with H_2O, dried (Na_2SO_4), and concentrated. The reaction product was dissolved in 30 ml of MeOH adding 0.5 ml of diluted HCl solution, and the reaction mixture was refluxed for 10 min. Extraction with Et_2O-H_2O yielded after workup **4a**, which was chromatographed on 20 g of alumina. The hexane-C_6H_6 (1:1) fractions afforded, after recrystallization from a Me_2CO-hexane mixture, white needles (50 mg, 6% yield) of **4a**, mp 128-130°; $[\alpha]_D$ +5° (c, 1, $CHCl_3$); uv λ max (EtOH) 237 nm (log ε=3.62); ir ν max ($CHCl_3$) 3620 (OH), 1700 and 1620 cm^{-1} (α,β-unsaturated ketone), ord (c, 0.04, dioxane) $[\phi]_{577}$ +25°, $[\phi]_{546}$ +120°, $[\phi]_{436}$ +175°, $[\phi]_{405}$ +230°, $[\phi]_{365}$ +470°, $[\phi]_{334}$ −1000°, $[\phi]_{313}$ −1290°, $[\phi]_{302}$ −820°, $[\phi]_{289}$ −290°, $[\phi]_{265}$ +2200°; nmr (100 MHz, $CDCl_3$) 6.16 (1H, d, J=2 Hz, H-11), 5.20 (1H, d, J=2 Hz, H-11′), 4.36 (1H, t, J=4.5 Hz, H-9), 2.99 and 2.05 (2H, J_{AB}=18 Hz, J_{AX}=1 Hz, J_{BX}=0 Hz, H_2-4), 2.64 (1H, d, J=4 Hz, H-7), 1.08 (3H, d, J=6 Hz, CH_3-10), 1.04 (3H, s, CH_3-12), 0.86 (3H, s, CH_3-13) ppm.

9-*EPI*-β-PIPITZONE ACETATE (**4b**).—9-*epi*-β-Pipitzone (**4a**) (25 mg, 0.11 mmol) was acetylated by treatment with pyridine (1 ml) and Ac_2O (0.2 ml) on a steam bath for 1 h. After usual workup, 20 mg (69% yield) of **4b** (oil) was obtained. Ir ν max ($CHCl_3$) 1740 (ester), 1720 (6-membered ring ketone); nmr (60 MHz, CCl_4) 5.97 (1H, d, J=2 Hz, H-11), 5.03 (1H, d, J=2 Hz, H-11′), 5.08 (1H, d, J=4.5 Hz, H-9), 2.85 and 2.03 (2H, J_{AB}=18 Hz, H_2-4), 2.80 (1H, d, J=4.5 Hz, H-7), 1.92 (3H, s, OAc), 1.10 (3H, s, CH_3-12), 0.90 (3H, d, J=6 Hz, CH_3-10), 0.87 (3H, s, CH_3-13).

DIHYDRO-β-PIPITZONE (**5**).—A solution of 1.3 g (5.6 mmol) of **3** in 100 ml of EtOAc was stirred in the presence of 130 mg of prehydrogenated 10% Pd on activated charcoal at room temperature and atmospheric pressure until uptake of H_2 ceased. The catalyst was removed by filtration and the solvent evaporated to dryness, giving white needles (1.1 g, 84%) which were recrystallized from Me_2CO-hexane mp 115-116°; $[\alpha]_D$ +30° (c, 0.42, $CHCl_3$); ir ν max ($CHCl_3$) 3615 (OH), 1700 (6-membered-ring ketone); ord (c, 0.42); $[\phi]_{546}$ +94°, $[\phi]_{436}$ +200°, $[\phi]_{405}$ +260°, $[\phi]_{365}$ +370°, $[\phi]_{334}$ +770°, $[\phi]_{313}$ +1000°, $[\phi]_{302}$ +460°, $[\phi]_{297}$ +210°, $[\phi]_{289}$ −130°, $[\phi]_{280}$ −390°; nmr (60 MHz, CCl_4) 4.23 (1H, broad s, H-9), 2.5 (1H, J_{AB}=6 Hz, H-4), 1.30 (3H, s, CH_3-12), 1.13 (6H, d, J=6 Hz, CH_3-10 and CH_3-11), 1.01 (3H, s, CH_3-12) ppm. *Anal.* Found: C, 76.05; H, 10.02; O, 13.72%; calcd. $C_{15}H_{24}O_2$: C, 76.23; H, 10.24; O, 13.54.

DIOL **6a**.—A solution of 1.1 g (4.6 mmol) of **5** in 150 ml of THF was treated with 1.1 g (28.9 mmol) of $LiAlH_4$, and the mixture was refluxed for 1.5 h. The excess hydride was destroyed by slow addition of H_2O, the solution was filtered, dried (Na_2SO_4), and concentrated. The organic layer was extracted with EtOAc, the residue concentrated and chromatographed on 25 g of alumina. The combined hexane-C_6H_6 (1:1) fractions afforded diol **6a** which was recrystallized from Me_2CO-hexane (800 mg, 72%); mp 79-81°; $[\alpha]_D$ +22 (c, 0.88, $CHCl_3$); ir ν max ($CHCl_3$) 3610 (OH); nmr (60 MHz, CCl_4) 3.82 (1H, t, J=5 Hz, H-5), 3.53 (1H, broad s, H-9), 1.27 (3H, s, CH_3-13), 1.16 (6H, d, J=6 Hz, CH_3-10, CH_3-11), 1.16 (3H,

s, CH_3-12). *Anal.* Found: C, 75.76; H, 10.81; O, 13.54%; calcd. $C_{15}H_{26}O_2$: C, 75.58; H, 10.99; O, 13.42.

ACETATE **6b**.—Diol **6a** (800 mg, 3.4 mmol) was dissolved in 8 ml of pyridine adding 12 ml of Ac_2O, and the reaction mixture was allowed to react for 8 h on a steam bath. After workup, the residue was chromatographed on 20 g of alumina. The hexane-C_6H_6 fractions (3:1) afforded 517 mg (55% yield) of **6b** as white crystals which were recrystallized from MeOH, mp 98-101°; $[\alpha]_D$ +75 (c, 2.01, $CHCl_3$) ir ν max ($CHCl_3$) 3605 (OH), 1730, and 1260 (acetate); nmr (60 MHz, CCl_4) 5.00 (1H, t, J=6 Hz, H-5), 3.60 (1H, s, H-9), 2.01 (3H, s, OAc), 1.30 (3H, s, CH_3-12), 1.23 (3H, s, CH_3-13), 1.08 (6H, d, J=6 Hz, CH_3-10, CH_3-11). *Anal.* Found: C, 73.02; H, 10.16; O, 17.30%; calcd. $C_{17}H_{28}O_3$: C, 72.82; H, 10.06; O, 17.12%.

KETOESTER **7a**.—A solution of 755 mg (2.7 mmol) of **6b** in 15 ml of HOAc was treated with 700 mg of CrO_3 dissolved in 1 ml of H_2O and 10 ml of HOAc. After 1 h at room temperature, the mixture was diluted with H_2O and extracted with Et_2O. The organic layer was washed with H_2O saturated aqueous $NaHCO_3$ solution and H_2O again. The solution was dried over anhydrous Na_2SO_4, filtered, and evaporated to give 600 mg (80% yield) of **7a** (oil); $[\alpha]_D$ +66° (c, 0.84, $CHCl_3$); ir ν max ($CHCl_3$) 1740 (6-membered ketone and acetate); nmr (60 MHz, CCl_4) 5.08 (1H, t, J=5 Hz, H-7), 2.09 (3H, s, OAc), 1.37 (3H, s, CH_3-12), 1.15 (6H, d, J=6 Hz, CH_3-10, CH_3-11), 0.88 (3H, s, CH_3-13).

KETOALCOHOL **7b**.—Compound **7a** (600 mg, 2.2 mmol) was dissolved in 50 ml of EtOH, treated with 300 mg of KOH dissolved in 1 ml of H_2O and refluxed for 4 h. The reaction mixture was diluted with cold H_2O and extracted with Et_2O. The organic phase was washed with H_2O, dried (Na_2SO_4), and evaporated, giving 570 mg (95%) of white plates of ketoalcohol **7b**, which was recrystallized from MeOH; mp 112-113°; $[\alpha]_D$ +53° (c, 1.13, $CHCl_3$); ir ν max ($CHCl_3$) 3615 (OH), 1740 (5-membered ring ketone); ord (c, 0.054, $[\phi]_{577}$+150°, $[\phi]_{546}$+260°, $[\phi]_{435}$+390°, $[\phi]_{408}$+520°, $[\phi]_{366}$+1000°, $[\phi]_{313}$+2200°, $[\phi]_{302}$−130°, $[\phi]_{297}$−1180°, $[\phi]_{280}$−2000°, $[\phi]_{265}$−962°, $[\phi]_{254}$−350°; nmr (60 MHz, CCl_4) 3.91 (1H, t, J=4 Hz, H-5), 1.33 (3H, s, CH_3-12), 1.29 (6H, d, J=6 Hz, CH_3-10 and CH_3-11), 0.80 (3H, s, CH_3-13) ppm. *Anal.* Found: C, 76.44; H, 10.36; O, 13.67%; calcd. $C_{15}H_{24}O_2$: C, 76.23; H, 10.24; O, 13.54%.

KETONE **8**.—Ketoalcohol **7b** (285 mg, 0.12 mmol) was dissolved in 6 ml of pyridine and 7 drops of $POCl_3$ were added at 0°. The reaction mixture was allowed to stand in the dark at room temperature for 21 h. The solution was poured onto ice followed by extraction with Et_2O. The organic layer was washed with HCl, H_2O, $NaHCO_3$, and H_2O, concentrated and dried (Na_2SO_4) to give 171 mg (60% yield) of **8** (oil); ir ν max ($CHCl_3$) 1740 (5-membered ring ketone); ord (c, 1), $[\phi]_{579}$+52°, $[\phi]_{436}$+110°, $[\phi]_{405}$+120°, $[\phi]_{365}$+104°, $[\phi]_{334}$−270°, $[\phi]_{313}$−480°, $[\phi]_{302}$+1290°, $[\phi]_{280}$+2920°, $[\phi]_{254}$+3780°; nmr (60 MHz, CCl_4) 5.31 (1H, m, H-5), 1.70 (3H, q, J=2 Hz, CH_3-11), 1.27 (3H, d, J=6 Hz, CH_3-10), 1.11 (3H, s, CH_3-12), 0.88 (3H, s, CH_3-13). *Anal.* Found: C, 82.45; H, 9.96; O, 7.51; calcd. $C_{15}H_{22}O_2$: C, 82.52; H, 10.16; O, 7.33%.

DIKETONE **9**.—A solution of 100 mg (0.42 mmol) of **7b** was treated with 120 mg of CrO_3 following the procedure described for **7a**. After workup in the usual manner 30 mg (33% yield) of diketone **9** was obtained, which was recrystallized from an Me_2CO-hexane mixture, mp 59-61°; ir ν max ($CHCl_3$) 1740 cm^{-1} (5-membered ring ketone) 1710 cm^{-1} (6-membered ring α,β-unsaturated-ketone); nmr (60 MHz, CCl_4) 3.02 (1H, J_{AB}=16 Hz, H-4) 1.28 (3H, d, J=7 Hz, CH_3-11), 1.12 (3H, s, CH_3-12), 1.15 (3H, d, CH_3-10), 0.90 (3H, s, CH_3-13) ppm; ord (c, 1): $[\phi]_{334}$ (maximum) +3500°. This product was identical to the compound obtained by CrO_3 treatment of dihydro-β-pipitzone (**5**) as shown by comparison with the authentic sample. Moreover, the same diketone (**9**) can be obtained by oxidation of the diol obtained by Li/NH_3 reduction of β-pipitzol (2) (**1a**).

DIKETONE **10**.—A solution of 50 mg (0.15 mmol) of 4-desoxo-β-pipitzol benzoate (8) (**12**) in 25 ml of MeOH was treated with 100 mg $KHCO_3$ dissolved in 1 ml of H_2O and refluxed 1 h. After workup, 20 mg (58% yield) of diketone **15** was obtained mp 84-86°; $[\alpha]_D$ +92° (c, 1.56, $CHCl_3$); ir ν max ($CHCl_3$) 1740 (5-membered ring ketone), 1710 cm^{-1} (6-membered ring ketone); ord (c, 0.23, MeOH), $[\phi]_{579}$+274°, $[\phi]_{546}$+344°, $[\phi]_{435}$+810°, $[\phi]_{405}$+1200°, $[\phi]_{365}$+2390°, $[\phi]_{334}$+7490°, $[\phi]_{313}$+3690°, $[\phi]_{289}$−8136, $[\phi]_{265}$−7866°; nmr (60 MHz, CCl_4) 1.25 (3H, d, J=5 Hz, CH_3-11), 1.15 (3H, d, J=7 Hz, CH_3-10), 1.09 (3H, s, CH_3-12), 0.86 (3H, s, CH_3-13).

ETHYLENEDITHIOKETAL (**14**).—A solution of 50 mg (0.12 mmol) of **13** in 25 ml of MeOH was refluxed for 2 h with 100 mg of $NaHCO_3$ dissolved in the minimum amount of H_2O. Extraction with Et_2O in the usual manner afforded after concentration and crystallization from MeOH 30 mg (80% yield) of **14** (needles), mp 62-64°; ir ν max (CCl_4) 1706 cm^{-1}; nmr (90 MHz, $CDCl_3$) 3.94 (1H, m, H-6), 3.50-3.05

(4H, m, $(CH_2S)_2$), 1.43 (3H, s, CH_3-12), 1.22 (6H, d, J=6 Hz, CH_3-10, CH_3-11), 1.04 (3H, s, CH_3-13).

KETONE **16**.—A solution of 30 mg (0.11 mmol) of **15** in 40 ml of MeOH was treated with 80 mg of $KHCO_3$ dissolved in the minimum amount of H_2O and refluxed for 4 h. The solvent was evaporated and the residue partitioned with Et_2O-H_2O. After workup, the organic phase was dried (Na_2SO_4), concentrated, and chromatographed on silica gel. Elution with petroleum ether afforded 20 mg (83% yield) of **16**, mp 51-53°; $[\alpha]_D$ +1.0°; ir ν max (CCl_4) 1709 cm^{-1} (carbonyl); nmr (90 MHz, $CDCl_3$) 2.55 (1H, m, H-6), 1.19 (3H, d, J=7 Hz, CH_3-11), 1.00 (3H, s, CH_3-12), 0.93 (3H, s, CH_3-13), 0.92 (3H, d, J=6.5 Hz, CH_3-10).

ALCOHOL **17**.—Ketone **16** (30 mg, 0.14 mmol) was dissolved in 30 ml of Et_2O and 80 mg (2.1 mmol) of $LiAlH_4$ was added. The reaction mixture was stirred at room temperature for 24 h. The excess hydride was destroyed by careful addition of H_2O, and the product was filtered and concentrated. The residue was chromatographed on silica gel. The combined hexane-C_6H_6 (1:1) fractions afforded 20 mg (70% yield) of alcohol **17**; mp 70-72°; ir ν max (CCl_4) 3466 (OH); nmr (90 MHz, CCl_4) 3.94 (1H, t, J=5 Hz, H-5), 1.25 (3H, s, CH_3-12), 1.14 (3H, d, J=7 Hz, CH_3-11), 0.90 (3H, s, CH_3-13), 0.80 (3H, d, J=6 Hz, CH_3-10).

ENT-3-*EPI*-α-CEDRENE (**18**).—A solution of 20 mg (0.09 mmol) of **17** was treated with 1 mg of *p*-toluenesulfonic acid and the mixture refluxed for 2 h using a Dean-Stark apparatus. The organic phase was extracted with EtOAc, followed by washing with $NaHCO_3$ and H_2O. The residue was chromatographed on silica gel. Elution with light petroleum ether afforded 15 mg of *ent*-3-*epi*-α-cedrene; nmr (90 MHz, $CDCl_3$) 5.20 (1H, m, H-5), 2.32 (1H, m, H-4), 1.64 (3H, m, CH_3-11), 0.98 (3H, s, CH_3-13), 0.90 (3H, d, J=4.5 Hz, CH_3-12), 0.85 (3H, d, J=4.5 Hz, CH_3-10).

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