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SYNTHESIS OF (±)HERITOL+

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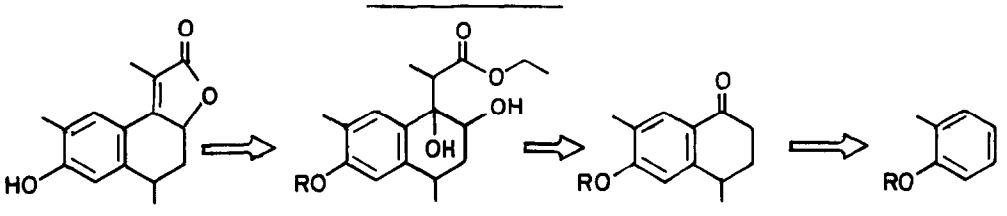
Abstract Synthesis of (±)heritol and epi-heritol is described. The key step is the osmylation of the unsaturated ester **9a**. Osmylation is used as a tool to construct the α,β-unsaturated γ-lactone system.

(+)Heritol (**1c**), a naturally occurring sesquiterpene was isolated from the sap of the mangrove plant Heritiera littoralis. It was shown to possess ichthyotoxicity in ppm quantities to Tilapia nilotica fingerlings. Miles[1] et al. have isolated the active toxin from the plant sap and its stereochemistry was established by a single crystal X-ray analysis. It was suggested that heritol is a potential biocompatible pesticide. Heritol possesses unusual oxygenation pattern not generally encountered in cadinane family.

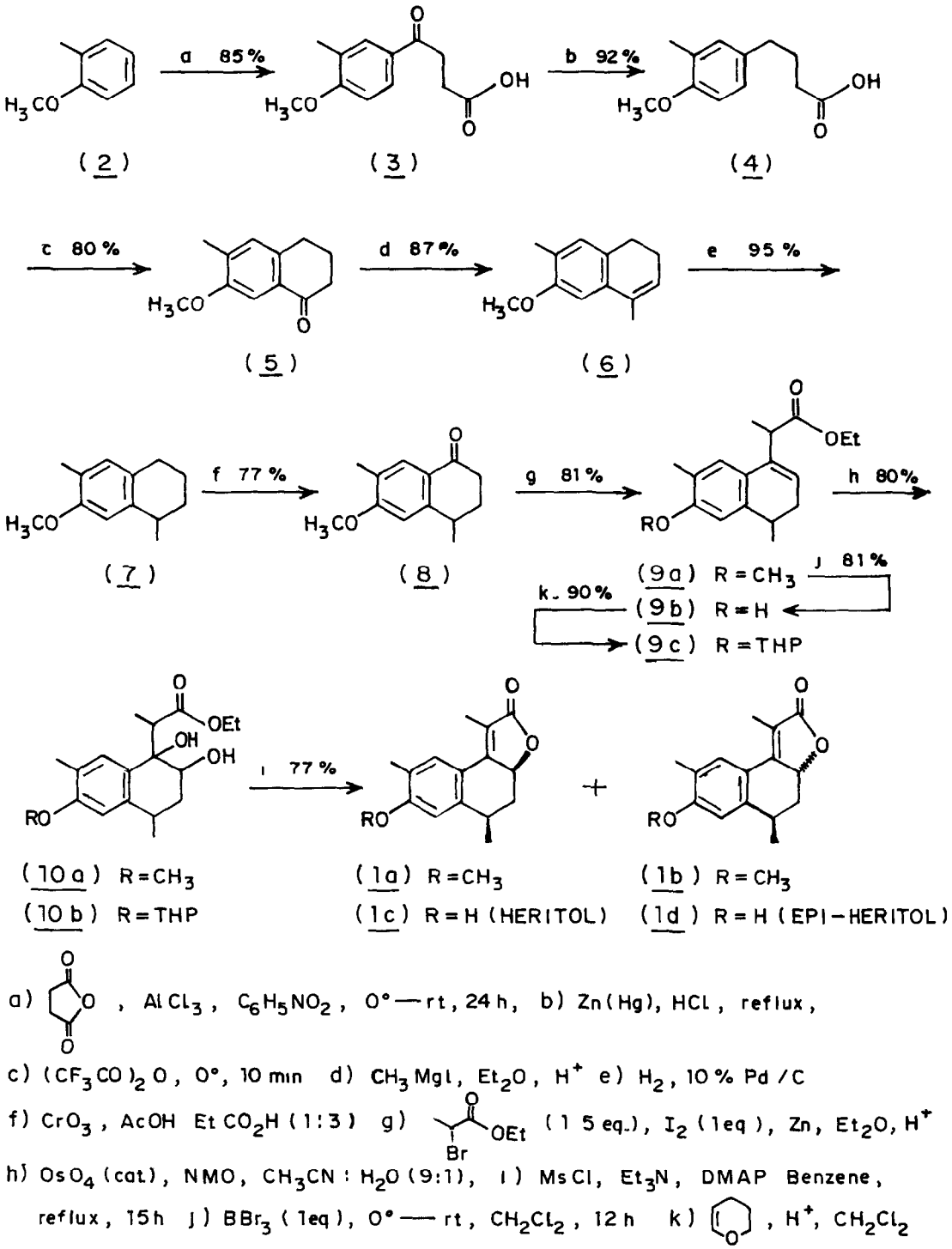
As a part of the ongoing programme in our laboratory and interest in the area of pesticides, we chose to undertake the synthesis of heritol and its analogues. At the time of communication of this work, Irie et al[2] reported the synthesis of (±)heritol and (±)epi-heritol employing a large number of steps including an intramolecular Wittig reaction to construct the butenolide moiety. It is pertinent to mention at this stage that both Irie's[2] and our strategy incorporates the same tetralone **8** intermediate. However, our method is shorter than Irie's and efficiently generates the butenolide moiety **1d** in high yields as against Irie's method, where poor yields are reported at the intramolecular Wittig reaction state.

Scheme-1



HERITOL

Scheme-2



a) , $AlCl_3$, $C_6H_5NO_2$, 0°—rt, 24 h, b) Zn(Hg), HCl , reflux,

c) $(CF_3CO)_2O$, 0°, 10 min d) CH_3MgI, Et_2O, H^+ e) H_2 , 10% Pd/C

f) CrO_3 , AcOH $EtCO_2H$ (1:3) g) (1.5 eq.), I_2 (1eq), Zn, Et_2O, H^+

h) OsO_4 (cat), NMO, $CH_3CN : H_2O$ (9:1), i) MsCl, Et_3N, DMAP Benzene, reflux, 15h j) BBr_3 (1eq), 0°—rt, CH_2Cl_2, 12 h k) , H^+, CH_2Cl_2

As is obvious from the antithetic analysis (Scheme-1), our strategy was to construct tetralin unit of heritol followed by the butenolide ring at later stage. The key intermediate ethyl 2-[(3,8-dimethyl-2-methoxy-7,8-dihydro)-5-naphthyl] propionate (**9a**) was easily accessible from ortho cresol methyl ether (**2**) by standard sequence of high yielding reactions. Accordingly, Friedel Crafts acylation of **2** with succinic anhydride furnished the corresponding keto acid **3** in 85% yield. Reduction of **3** under Clemmensen's conditions[3] furnished the butyric acid **4**, which on treatment with trifluoroacetic anhydride,[4] underwent smooth cyclisation to furnish the tetralone **5** in good yields. 1,4-Ketone transposition and introduction of the methyl group was successfully accomplished by the following set of reactions. Grignard reaction of **5** with methyl magnesium iodide furnished the corresponding carbinol which on treatment with acid, during work up, underwent dehydration to afford the dihydronaphthalene **6**. Catalytic reduction (H_2/10% Pd-C)[5] of **6** under pressure (40 psig) furnished the corresponding tetrahydronaphthalene **7** in excellent yields (95%). Benzylic oxidation of **7** was realised by chromium trioxide[6] to furnish the tetralone **8** as a high yielding step. The spectral data of **8** thus obtained corresponded well with those reported by Irie[2] employing a totally different approach. Reformatsky reaction[7] on **8** employing ethyl α-bromopropionate followed by acidic work up smoothly afforded the ester **9a** as a mixture of diastereomers. Since the stereochemistry at the newly incorporated methyl group would be destroyed at the later stages during the formation of butenolide moiety, its stereochemistry was of no consequence to us at this stage and hence no attempt was made to identify the diastereomers. No trace of α,β-unsaturated ester could be detected. Having observed the synthesis of the key intermediate **9a**, next task was to construct the butenolide moiety of heritol. The olefinic bond of **9a** was hydroxylated[8] by using osmium tetroxide. The resultant diol **10a** was obtained again as a mixture of diastereomers. Diol **10a** was further subjected to a reaction with methane sulphonyl chloride in the presence of catalytic amount of DMAP to furnish methyl ether of heritol **1a** (major product) along with methyl epi-heritol (**1b**) as a 3 2 diastereomeric mixture in 77% yield[9]. The noteworthy point under the reaction conditions employed is the occurance of two steps in one pot, lactonisation followed by concomitant loss of water to generate α,β-unsaturated lactone system.

The mixture of **1a** and **1b** was then subjected to demethylation with boron tribromide to give a mixture of heritol (**1c**) and epi-heritol (**1d**) as judged by the ^1H and ^{13}C NMR analysis of the mixture. Since it was not possible to separate the diastereomers **1c** and **1d** by column chromatography, it was decided to separate **1a** and **1b**. **1a** and **1b** also could not be

separated by column chromatography hence it was decided to separate them by fractional crystallisation.

Thus, heritol methyl ether (**1a**) and epi-heritol methyl ether (**1b**) were obtained in pure form by simple crystallisation from pet-ether. The epi-heritol ether (**1b**) was the first to fall out from the solvent. Recrystallisation of the mother liquor afforded pure heritol ether (**1a**). When pure **1a** and **1b** were separately subjected to demethylation employing boron tribromide, a mixture of **1c** and **1d** resulted. Since butenolides underwent isomerisation under the demethylating conditions, our attempts to obtain pure **1c** and **1d** met with failure. Hence an alternate and more efficient demethylating agent was employed. Thus, when **1a** was treated with $AlCl_3$- EtSH at room temperature, epi-heritol (**1d**), mp 262-63° (dec), was obtained as a white solid. It was gratifying to note that when identical conditions were employed, pure heritol (**1c**) was obtained from **1b** in 94 % yields as a white solid without any contamination of epi-heritol (**1d**) via isomerisation. Synthetic (±) heritol had identical spectral data as the ones reported in literature.[1] Both **1c** and **1d** had identical Rf values to that of the naturally occurring heritol (kindly provided to us by Prof. D.H. Miles[1]).

The synthesis of **1c** and **1d** was also achieved by first demethylating **9a**. Careful selective demethylation of **9a** with BBr_3 furnished the corresponding phenol **9b** in good yields. The **9b** thus obtained was protected as its **THP** ether **9c**. Osmylation[7] of **THP**-ether **9c** yielded the desired diol **10b**. When **10b** was refluxed with methane sulphonyl chloride in the presence of triethylamine and catalytic amount of DMAP, a mixture of diastereomeric isomers **1c** and **1d** resulted. Interestingly, the ratio of **1a** **1b** which was 3·2, was reversed in favour of **1b**, when saponified diol **10a** was cyclised under acidic conditions. In this case the ratio of **1a**:**1b** was 1 8. Using similar conditions epi-heritol (**1d**) was also synthesized from **10b**. However, when **10b** was saponified followed by acidic cyclization, epi-heritol (**1d**), mp. 262-263°C (dec) was isolated as the sole product after purification. We are currently working on the synthesis of optically pure heritol (**1a**) employing the strategy similar to the one outlined in Scheme-2.

EXPERIMENTAL

Melting points were determined in open capillaries and Kofler block instrument. All mps and bps are uncorrected. Infra red spectra (IR) (ν_{max} in cm^{-1}) were recorded as smears or nujol mulls (solids) or in solution on a Perkin Elmer 683 and with sodium chloride optics. ^1H NMR spectra were WH-90 or MSL-300 spectrometer in $CDCl_3$ containing TMS as an internal standard. All chemical shifts are reported in parts per million (δ)

downfield from TMS. Mass spectra were recorded on Finnigan-MAT 1020 automated GC/MS spectrometer using an ionisation potential of 70 eV. All solvents and reagents were purified and dried by standard techniques. Progress of the reaction was monitored by thin layer chromatography (tlc).

2-(4'-Methoxy-3'-methyl benzoyl) propionic acid (3):

To a stirred solution of 2-methyl anisole (2) (147 g, 1.21 mol) and succinic anhydride (131 g, 1.31 mol) in nitrobenzene (500 ml) at 0-5°C, aluminium chloride (349 g, 2.62 mol) was gradually added. The temperature of the reaction mixture was not allowed to exceed 5°C. After complete addition, a clear solution was obtained which was stirred at room temperature for 24 h. Ice-cold 50% HCl was added and the solid thus obtained was filtered, washed with ether and recrystallised from methanol to furnish the keto acid as colourless needles (236.5 g, 85% yield), m.p. 147°C. IR(nujol)· 3900(b), 1700(s), 1680(s), 1600(m), 1500(m), 1460(m), 1450(m), 1440(m), 1420(w), 1400(w), 1380(w), 1360(w), 1350(w), 1340(w), 1250(s), 1210(w), 1160(w), 1150(s), 1060(w), 1040(w), 1020(w) and 960(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90 MHz), δ 2.2 (s, 3H), 2.7 (t, 2H, J=7Hz), 3.24 (t, 2H, J=7Hz), 3.86 (s, 3H), 6.8 (d, 1H, J=8Hz), 7.8 (m,2H), Mass m/z 222 (M^+, 15%), 149(100), 135(20), 121(20), 91(38), 77(26), 65(5), 55(3). Analysis calulated for $C_{12}H_{14}O_4$· C, 64.8, H, 6.34; Found C, 64.51; H, 6.37.

4-(3'-Methyl-4'-methoxyphenyl) butyric acid (4):

A mixture of Zn (100 g), water (75 cc), conc. HCl (175 cc) and the keto acid 3 (40 g, 0.18 mol) was refluxed for 7 h. The reaction mixture was allowed to cool to room temperature and the solid separated was filtered, dried and recrystallised from pet. ether to furnish butyric acid 4 (34.5 g, 92% yield) as colourless needles, m.p. 98°C. IR (Nujol)· 2900(b), 1700(s), 1610(w), 1510(m), 1460(m), 1410(m), 1380(w), 1320(w), 1310(w), 1300(w), 1290(w), 1260(s), 1230(s), 1210(w) and 1190(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90MHz) δ1.93 (m, 2H), 2.57 (t, 2H, J=7Hz), 2.2 (s, 3H), 2.3 (t, 2H, J=7Hz), 3.77 (s, 3H), 6.77 (d, 1H, J=8Hz), 6.9 (m, 2H), Mass m/z. 208 (M^+, 63%) 146(55), 135(100). Analysis calculated for $C_{12}H_{16}O_3$, C, 69.23, H, 7.69 Found C, 68.98; H, 7.80.

6-Methyl-7-methoxytetral-1-one (5):

A 50 ml two-necked flask fitted with a guard tube is charged with 4-(3'-methyl-4'-methoxyphenyl) butyric acid (4). A mixture of trifluoroacetic acid (1 ml) and trifluoroacetic anhydride (10.94 g, 0.048 mol) are added dropwise at 0°C. After 10 min, the reaction mixture is poured slowly into ice-cold sodium bicarbonate solution. The aqueous layer is extracted with ether, dried (anhyd. Na_2SO_4), filtered and the solvent evaporated under

reduced pressure to furnish a residue which on distillation under reduced pressure furnished the tetralone 5 (7.3 g, 80% yield) as a white solid, m.p. 55-56°C. b.p. 200°C/6 mm. IR (Nujol): 1680(s), 1610(m), 1500(m), 1460(m), 1410(m), 1350(m), 1340(m), 1270(s), 1240(w), 1220(m), 1180(m), 1140(w), 1060(w), 1040(w), 980(w), 920(w), 910(w), 790(w), 690(w) and 650(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90MHz) δ 2.0 (m, 2H), 2.15 (s, 3H), 2.53 (t, 2H, J=6Hz), 2.7 (t, 2H, J=5Hz), 3.6 (s, 3H), 6.9 (s, 1H), 7.33 (s, 1H) Mass· m/z 190 (M^+, 100%), 175(22), 162(32), 148(20), 134(45). Analysis Calculated for $C_{12}H_{14}O_2$· C, 75.78, H, 7.36; Found: C, 75.56, H, 7.55.

3,8-Dimethyl-2-methoxy-5,6-dihydronaphthalene (6)·

To a methyl magnesium iodide [prepared from methyl iodide (2.98 g, 0.0101 mol) and Mg (0.624 g)] solution in ether (10 ml), tetralone 5 (2 g, 0.0105 mol) solution in ether (10 ml) was added dropwise and the resultant solution was stirred at room temperature. After completion of reaction (tlc), the solution was poured slowly into 50% ice-cold H_2SO_4. The oil which separated was extracted with pet.ether. Rotary evaporation of the solvent furnished a residue which was distilled under reduced pressure to furnish olefin 6 (1.715 g, 87% yield), b.p. 105°C/1 mm. IR (neat) 3000(s), 2940(s), 2900(m), 2820(m), 1620(m), 1580(m), 1500(m), 1470(m), 1460(m), 1440(w), 1410(m), 1380(m), 1370(m), 1350(w), 1310(w), 1270(s), 1260(m), 1220(s), 1200(s), 1150(s), 1050(s), 960(m), 890(m), 860(s), and 800(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90MHz): δ 2.0 (s, 3H), 2.15 (s, 3H), 2.12 (t, 2H, J=7Hz), 2.6 (m, 2H), 3.77 (s, 3H), 5.63 (t, 1H, J=4Hz), 6.6 (s, 1H), 6.8 (s, 1H), Mass· m/z 188 (M^+, 63%), 175 (100%), 160(20), 148(22), 128(15), 115(18), 91(19), 77(10), 65(5). Analysis Calculated for $C_{13}H_{16}O$ C,82.9, H,8.5, Found·C,82.5, H,8.3.

3,8-Dimethyl-2-methoxy-5,6,7,8-tetrahydronaphthalene (7)

A pressure bottle charged with olefin 6 (15 g, 0.008 mol), 10% Pd/C (0.15 g) and methanol (50 ml) is subjected to hydrogenation under pressure (40 psig) After 6 h, the catalyst was filtered and the filtrate rotary evaporated to furnish a residue which on distillation under reduced pressure afforded tetrahydronaphthalene 7 (1.49 g, 95% yield). b.p. 110°C/1 mm. IR (Nujol) 1630(m), 1580(w), 1520(s), 1480(m), 1420(m), 1380(w), 1340(w), 1320(w), 1310(w), 1260(s), 1220(s), 1190(m), 1180(w), 1140(w), 1100(s), 1060(m), 1050(m), 1000(w), 960(w), 950(w), 900(w), 800(w), and 790(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90MHz) δ1.24 (d, 3H, J=6Hz), 1.7 (m, 2H), 2.1 (s, 3H), 2.6 (t, 2H, J=3Hz), 3.0 (m, 1H), 3.7 (s, 3H), 6.6 (s, 1H, 6.7 (s, 1H), Mass m/z 190 (M^+, 65%), 175(100), 160(20), 148(22), 128(15), 115(18), 91(18), 77(10), 65(5). Analysis Calculated for $C_{13}H_{18}O$ C, 82.11, H, 9.47, Found· C, 82.31, H, 9.67.

4,7-Dimethyl-6-methoxy-tetral-1-one (8).

To a magnetically stirred solution of tetrahydronaphthalene (1.4 g, 7.4 mmol) in acetic acid (10 ml was added dropwise CrO_3 (3.36 g) in propionic

acid (5 ml) in 10 min. The temperature of the reaction mixture was maintained between 17-21°C by ice-bath. After completion of reaction (tlc, 4h), the reaction mixture was diluted with water (1 l) and extracted with ether (2 x 250 ml). The combined extracts were washed with water, saturated $NaHCO_3$ solution, dried (anhyd. Na_2SO_4), filtered and concentrated to furnish a yellow solid. Recrystallisation of the solid with pet. ether afforded pure tetralone 8 (1.16 g, 77% yield). m.p. 108°C, lit.[2] m.p. 107-109°C. IR (Nujol): 1680(s), 1610(m), 1580(s), 1510(s), 1470(m), 1410(w), 1390(w), 1360(m), 1340(m), 1300(m), 1280(m), 1270(m), 1250(m), 1220(w), 1180(m), 1160(m), 1120(w), 1070(w) and 1040(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 1.4 (d, 3H, J=7Hz), 1.8 (m, 2H), 2.6 (dd, 2H, J=12, 7Hz), 3.0 (m, 1H), 3.8 (s, 3H), 6.6 (s, 1H), 7.8 (s, 1H), Mass m/z 204 (M^+, 100%), 189(45), 176(72), 161(25), 148(28), 133(15), 115(7). Analysis: calculated for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84, Found· C, 76.10, H, 8.13%.

2-[(3,8-Dimethyl-2-methoxy-7,8-dihydro)-5-naphthyl] propionic acid ethyl ester (9a):

To a stirred solution of tetralone 8 (1 g, 4.9 mmol), α-bromoethyl propionate (1.1 g, 6 mmol) and activated zinc (0.5 g) in dry ether (20 ml), iodine crystals (1.5 g, 6 mmol) were added at such a rate to reflux ether gently. After 2 h, the reaction mixture was decomposed with 50% HCl-crushed ice. Organic layer was separated and the aqueous layer extracted with ether. Combined organic layers were washed with aq. $NaHCO_3$, sodium thiosulphate solution, dried (anhyd. Na_2SO_4), filtered and rotary evaporated to furnish a residue. Purification of the residue by chromatography (SiO_2) 5% ethyl acetate pet. ether furnished β,γ-ester 9a (1.15 g, 81% yield) as viscous yellow oil. IR (Neat)· 1740(s), 1620(m), 1580(m), 1510(m), 1470(s), 1460(m), 1410(m), 1390(m), 1350(m), 1330(w), 1310(m), 1280(s), 1250(w), 1200(m), 1150(m), 1140(m), 1110(m), 1090(m), 1060(m), 1050(m), 1020(w), 1000(w), 980(w), 900(m), 880(m) and 800(m) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 1.2 (t, 3H, J=7Hz), 1.4 (d, 3H, J=7Hz), 2.2 (s, 3H), 2.4 (m, 2H), 2.8 (m, 1H), 3.8 (s, 3H), 4.15 (q, 2H, J=7Hz), 5.8 (t, 1H, J=5Hz), 6.78 (s, 1H), 7.2 (s, 1H), ^{13}C-NMR ($CDCl_3$, 300 MHz)· δ 174.71(s), 156.41(s), 140.46(s), 135.035(s), 134.68(s), 125.31(d), 124.95(d), 123.18(d), 120.7(d), 120.46(d), 108.43(d), 108.27(d), 60.03(t), 54.86(q), 41.15(d), 32.30(d), 32.08(d), 30.59(t), 30.45(t), 19 73(q), 19.57(q), 16.68(q), 16.25(q), 15.63(q), 13.73(q), Mass m/e 288 (M^+, 35%), 221(5), 215(22), 191(61), 187(100), 186(50), 172(28), 155(9), 141(15), 128(11), 115(7), 102(3), 91(3), 77(2), 65(1), Analysis calculated for $C_{18}H_{24}O_2$· C, 75.06, H, 8.39, Found C, 75.44, H, 8.36%.

2[-(3,8-Dimethyl-2-methoxy-5,6-dihydroxy-7,8-dihydro)-5-naphthyl] propionic acid ethyl ester (10a):

A 20 ml test tube was charged with β,γ-unsaturated ester (**9a**) (0.5 g, 1.74 mmol), N-methyl morpholine oxide (0.351 g, 1.5 eq.) and acetonitrile-water mixture (9:1, 0.5 ml). Catalytic amount of osmium tetroxide (0.005 M) solution in toluene was syringed in the reaction mixture. The reaction mixture was allowed to stir for 12 h (tlc). $Na_2S_2O_5$ (0.5 g) was introduced into the reaction mixture and stirred for 0.5 h. The reaction mixture was filtered and the solid washed repeatedly with dichloromethane. The solvent was removed by rotary evaporation and the residue chromatographed (SiO_2) with 10% ethyl acetate pet ether to furnish the corresponding diol **10a** (0.455 g, 81% yield). IR (Neat): 3400-3500(s), 1740(s), 1620(m), 1580(w), 1510(s), 1460(m), 1440(m), 1380(m), 1340(m), 1260(m), 1190(m), 1150(w), 1120(w), 1070(m), 1060(m), 1030(m), 1000(w), 950(w), 900(w) and 870(w) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 90 MHz): δ 1.26 (t, 3H, J=6Hz), 1.3 (d, 3H, J=8Hz), 2.1 (s, 3H), 2.3 (m, 1H), 2.7 (m, 1H), 3.0 (m, 1H), 3.8 (s, 3H), 3.86 (dd, 1H, J=2Hz), 4.13 (q, 2H, J=6Hz), 6.6 (s, 1H), 7.26 (s, 1H); Mass: m/e 322 (M^+, 8%), 259(9), 221(100), 203(75), 175(30), 149(3), 77(3), Analysis: calculated for $C_{18}H_{26}O_4$: C, 67.5, H, 7.5, Found: C, 67.8, H, 7.28%.

(±)Methyl heritol (1a) and (±)methyl epi-heritol (1b):

To a solution of the diol (**10a**) (200 mg, 0.63 mmol) in benzene (10 ml) were added methane sulphonyl chloride (2 g) and triethylamine (5 ml) in one lot followed by DMAP (cat.). The reaction mixture was refluxed (15 h) and monitored by tlc It was then cooled to room temperature. The benzene layer was decanted and the residue was washed repeatedly with benzene. Removal of the solvent at reduced pressure followed by purification by chromatography (SiO_2) using ethylacetate pet. ether (10%) furnished the lactone (**1a** + **1b**, 125 mg) in 77% yield. Recrystallisation, of the solid thus obtained, in boiling pet-ether furnished epi-heritol methyl ether (**1b**) as a white needle shaped crystals m.p. 166°C, lit[2] 166-167°C. IR ($CHCl_3$): 1750(s), 1660(m), 1620(m), 1560(w), 1510(m), 1450(w), 1460(w), 1400(m), 1350(m), 1340(m), 1320(m), 1260(m), 1240(m), 1180(w), 1160(w), 1120(m), 1060(m), 960(w), 950(w), 900(m) and 880(m) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.43 (d, 3H, J=7.5Hz), 1.89 (m, 1H), 2.12 (d, 3H, J=1.7Hz), 2.24 (s, 3H), 2.4 (m, 1H), 3.3 (q, 1H, J=7,5Hz), 3.87 (s, 3H), 5.11 (ddq, 1H, J=12.1, 4.2, 1.6Hz), 6.69 (s, 1H), 7.4 (s, 1H), ^{13}C-NMR ($CDCl_3$, 300 MHz) 9.75 (q), 15.83(q), 23.68(q), 33.01(d), 36.01(d), 36.19(t), 55.21 (q), 75.37(d), 110.03(s), 116.23(s), 119.9(s), 125.61(s), 129.4(d), 142.62(s), 156.72(s), 159.33(s), 175.31(s). Mass: m/z 258 (M^+, 100%), 243(38), 229(26), 215(28), 199(39), 187(25), 172(34), 157(12), 141(19), 128(28), 115(23), 105(3), 91(3), Analysis: calculated for $C_{16}H_{18}O_3$ C, 74.4, H, 7.02, Found C, 74.16, H, 7.29%/ Concentration of the filtrate and recrystallisation of the resultant solid afforded pure heritol methyl

ether (1a) as a white solid. m.p. 109°C IR ($CDCl_3$)· 1750(s), 1660(s), 1620(m), 1570(w), 1560(w),1510(s), 1480(w), 1460(w), 1400(m), 1360(m), 1340(s), 1320(m), 1270(s), 1180(w), 1140(w), 110(m), 1060(s), 1010(w), 970(w), 950(w), 920(m) and 870(m) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 1.45 (d, 3H, J=7.5Hz), 2.13 (d, J=1.77Hz), 2.24 (s, 3H), 2.63 (m, 1H), 3.13 (m, 1H), 3.89 (s, 3H), 4.9 (ddq, 1H, J=12, 5, 1.7Hz), 6.85 (s, 1H), 7.41 (s, 1H). ^{13}C-NMR ($CDCl_3$, 300 MHz)·δ 9.75(q), 15.74(q), 21.53(q), 31.79(d), 38.51(t), 55.14(q), 77.95(d), 108.23(d), 115.63(s), 120.48(s), 125.53(s), 142.05(s), 156.50(s), 159.40(s), 175.31(s). Mass. m/z 258(M^+, 100%), 243(38), 229(26), 215(28), 199(39), 187(25), 172(24), 157(12), 141(19), 128(28), 23(115), 105(3), 91(7), 77(8), 65(5). Analysis·calculated for $C_{16}H_{18}O_3$: C, 74.4, H, 7.02, Found· C, 74.65; H, 7.17%.

(±)Heritol (1c)·

To a stirred solution of heritol methyl ether (1a) (20 mg, 0.078 mmol) and anhydrous aluminium trichloride (50 mg, 0.375 mmol) in dichloromethane (1 ml), at room temperature, was added ethane thiol (1 ml). The reaction mixture was allowed to stir for 12 h. Water was added to the reaction mixture and the solid thus separated was extracted with dichloromethane. The combined organic layer was dried (anhydrous Na_2SO_4), filtered and evaporated under reduced pressure, to furnish a white solid. Purification of the solid by chromatography (SiO_2) using 20% ethyl acetate pet. ether as the eluent afforded heritol (18 mg, 94% yield) as a white solid. m.p. 245-246°C, lit.[2] m.p. 245-246°C IR ($CHCl_3$): 3595(m), 2960(m), 2360(m), 1739(s), 1654(m), 1616(m), 1559(m), 1419(m), 1384(m), 1321(m), 1198(w) and 1047(s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.3(d, 3H, J=6.8Hz), 2.08 (s, 3H), 2.2 (d, 3H, J=1.8Hz), 2.58 (m, 2H), 3.0 (m, 1H), 4.98 (ddq, 1H, J=12.89, 4.75 and 1.74 Hz), 5.2 (s, 1H, D_2O exchangeable), 6.78 (s, 1H), 7.34 (s, 1H). Mass m/z 244 (M^+, 100%), 229(40), 215(22), 201(25), 185(25), 173(28), 158(20), 145(11), 128(20), 115(20), 91(10), 77(12), 55(11). Analysis calculated for $C_{15}H_{16}O_3$ C, 73.83, H, 6.61, Found: C, 73.51, H, 6.38%.

(±) epi- Heritol (1d):

Using the above mentioned procedure epi-Heritol (1d) was obtained from 1b in 90% yield as a white solid. m.p. 262°C (dec). IR ($CHCl_3$): 3593(m), 2362(m), 1739(s), 1655(m), 1617(m), 1495(w), 1321(m), 1218(s), 1160(w), 1065(w) and 1045(s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz)·δ 1.32 (d, 3H, J=7.4Hz), 1.82 (m, 1H), 2.0 (d, 3H, J=1.8Hz), 2.2 (s, 3H), 2.3 (m, 1H), 3.18 (m, 1H), 5.00 (ddq, 1H, J=11.5, 4.0 & 1.8Hz), 5.2 (s, 1H), 6.6 (s, 1H), 7.32 (s, 1H). Mass: m/z 244 (M^+, 100%), 229(38), 215(22), 201(28), 185(28), 173(28), 158(20), 145(11), 128(20), 115(20), 91(11), 77(12), 69(13), 55(14). Analysis calculated for $C_{15}H_{16}O_3$: C, 73.83, H, 6.61, Found C, 73.55, H 6.52%.

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