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SYNTHESIS OF DRIMANE SESQUITERPENES AN INTRAMOLECULAR DIELS-ALDER APPROACH

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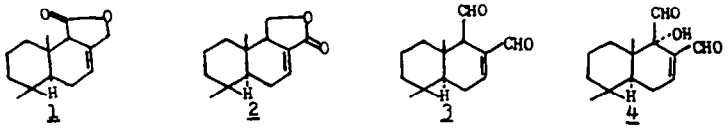
Abstract ------ Drimane sesquiterpenes, including drimenin 1, cinnamolide 2 and polygodial 3 in both racemic and optically active forms, were synthesized from β-ionone with intramolecular Diels-Alder reaction as the key step.

Recently there has been increasing interest in the synthesis of biologically active sesquiterpenes related to drimane. Among a number of different synthetic strategies leading to these molecules, the application of the Diels-Alder reaction to construct an appropriately functionalised decalin is especially attractive[1]. Up to now, there are quite a number of reports on the synthesis of drimane sesquiterpenes using Diels-Alder reaction. However, the construction of a decalin system using a more stereoselective and regioselective intramolecular Diels-Alder reaction has not yet been explored. Here we report in full on the synthesis of racemic and optically active drimane sesquiterpenes, namely drimenin 1, cinnamolide 2 and polygodial 3, with the intramolecular Diels-Alder reaction as the key step.



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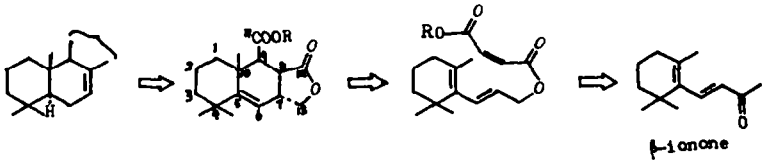
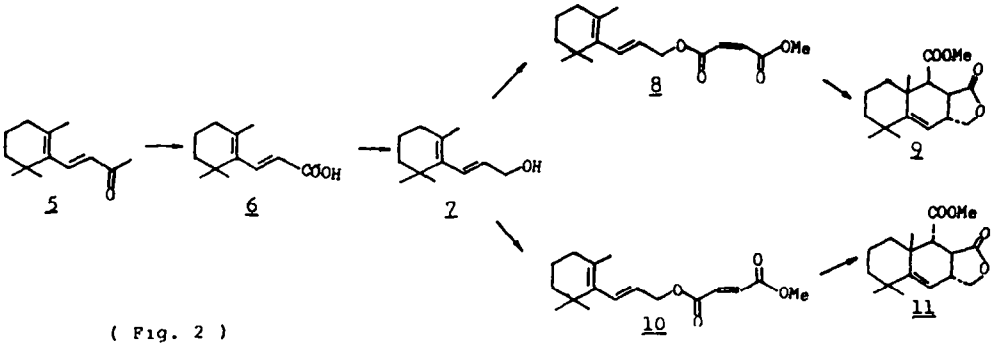
Our synthetic strategy employs maleic diesters as dienophiles to construct a drimane-like skeleton (Fig. 1). When R was methyl, it would give a racemic compound; when R was a chiral group, we hope it would effect an asymmetric induction to provide an optically active compound.



(Fig. 1)

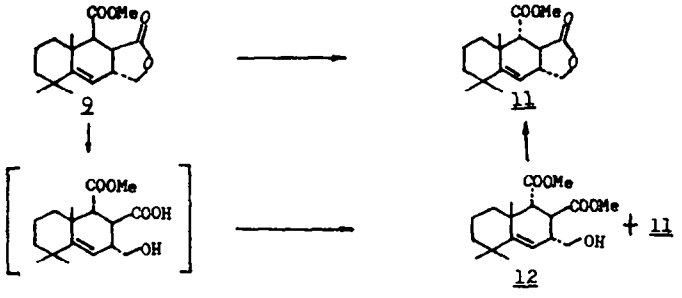
The preparation of the maleic diester required for the intramolecular Diels-Alder reaction started from β-ionone. β-Ionone was treated with sodium hypobromite to give 6, which was then reduced with lithium aluminium hydride to produce 7 in an overall yield of 71%[2]. Treatment of 7 with maleic anhydride afforded maleic acid mono-ester which was further converted into maleic diester 8 with diazomethane in 75% yield. With this ester in hand, its intramolecular Diels-Alder reaction was investigated. Cycloaddition of 8 in the presence of acid catalysts such as $ZnCl_2$, $AlCl_3$ and CF_3COOH didn't take place. Thermocyclization of 8 in a sealed tube at 150°C resulted in a messy reaction with very low yield of product. Finally, refluxing of 8 in xylene with a small amount of hydroquinone under nitrogen for 90 h, an excellent yield (88%) of Diels-Alder adduct 9 was obtained (Fig. 2).



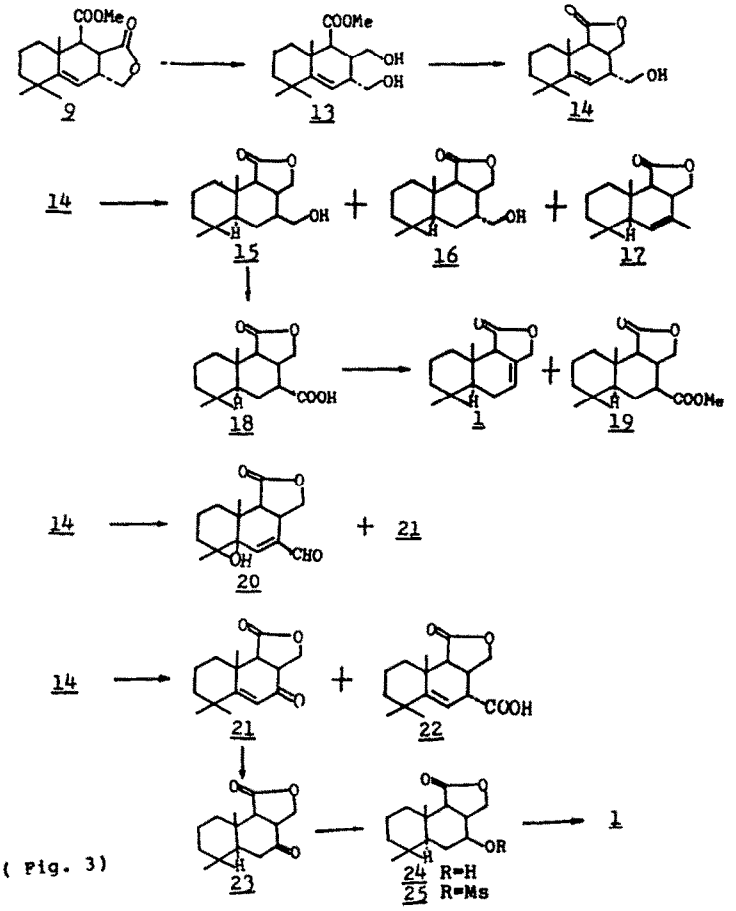
(Fig. 2)

The structure of this compound was deduced from spectral evidence. In particular, the assignment of the lactone ring stereochemistry in 9 rested on the observation that the coupling constant between 7-proton and 8-proton is 13.2 Hz, typical of a trans-diaxial arrangement of the protons. Therefore an exo cyclization has occurred and it was similar to previous report[3] when a γ-lactone was formed during the intramolecular Diels-Alder reaction.

Owing to compound 9 has one more carbon than drimane sesquiterpenes, so the next step was to open the lactone ring to liberate the primary hydroxy group and then to eliminate the 13-carbon. Treatment of 9 with sodium methoxide in methanol at room temperature gave an epimeric product quantitatively which was identical with compound 11 obtained from the intramolecular Diels-Alder thermocyclization of fumaric diester 10. Reaction of 9 with potassium hydroxide in methanol-water at room temperature also gave 11. Only under vigorous conditions (refluxing of 9 with potassium hydroxide in tetrahydrofuran-water) the lactone ring could be opened, and after very careful neutralization, treatment with diazomethane provided a small amount of dimethyl ester 12 along with epimeric product 11. 12 would cyclize to form 11 spontaneously on standing.



Attempts for hydrolysis of the lactone 9 were unsuccessful, so we turned our attention to selective reduction of the lactone ring in compound 9 under the coexistence of methyl ester moiety. Careful reduction of 9 with lithium aluminium hydride at 0°C gave the diol 13, which was treated with p-toluenesulfonic acid in benzene to provide 14 in 71% yield. Since compound 14 possessed lactone ring necessary for drimenin, we synthesized drimenin 1 from 14 through two routes (Fig. 3).

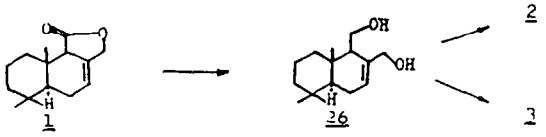


(Fig. 3)

Hydrogenation of 14 using 10% Pd-C in methanol gave 57% of the desired product 15, together with two other byproducts 16 and 17. Oxidation of 15 with Jones' reagent provided lactone acid 18. Finally, decarboxylation of 18 with iodosobenzene diacetate[4] in refluxing benzene gave 57% of drimenin 1 and 34% of 19. The spectral data of drimenin 1 were identical with those previously reported.[1c]

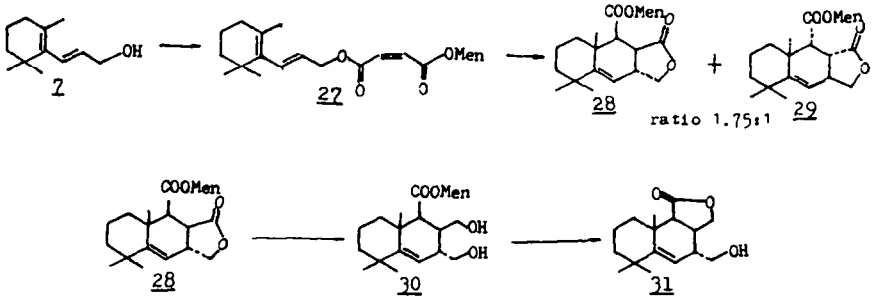
Since the presence of hydroxy group in 14 caused hydrogenolysis during hydrogenation, we tried to oxidize the hydroxy group in 14 first. However, oxidation of 14 with pyridinium dichromate in dimethylformamide gave an undesired unsaturated γ-hydroxy aldehyde 20 along with a small amount of unsaturated ketone 21 formed in 52% and 5% yield respectively. When 14 was oxidized with Jones' reagent, a good yield (64%) of 21 could be obtained and which could be easily transformed into drimenin. Hydrogenation of 21 with 10% Pd-C in methanol gave 23, which was reduced with sodium borohydride to provide 24. Treatment of 24 with methanesulfonyl chloride in pyridine gave mesylate 25 , which was heated in dimethyl sulfoxide at 100°C for 2 h to give drimenin 1 in 65.5% yield (24⟶1).[5]

Reduction of drimenin 1 with lithium aluminium hydride gave drim-7-ene-11,12-diol 26 in 89% yield. This diol is a key intermediate for other drimane sesquiterpenes synthesis. Oxidation of 26 with 10 equiv. of barium manganate[1c] furnished cinnamolide 2 in 95% yield. Swern oxidation[1c] of 26 at -50°C provided polygodial 3 in 97.6% yield. Their spectral data were identical with those previously reported.[1c] The preparation of warburganal 4 from 26 has also been reported.[1c,1f]



Having achieved the total synthesis of racemic drimane sesquiterpenes, we further synthesized optically active drimane compounds. As described at the beginning, our synthetic strategy was to introduce a chiral group in the substrate of intramolecular Diels-Alder reaction to effect an asymmetric induction.

Connection of 7 with maleic acid mono-l-menthyl ester using 1,3-bicyclohexylcarbodiimide gave maleic diester 27 in 58.4% yield. Refluxing of 27 in xylene containing hydroquinone under nitrogen afforded two diasteroisomers in 78.6% yield, and the ratio of 28:29 was 1.75:1 according to proton magnetic resonance spectra. Fortunately, these two isomers could be easily separated by recrystallization (petroleum ether-ethyl acetate) to give the desired product 28 in 43% yield from 27. 28 possesses an optical purity of 100% d.e. as revealed by ^{1}HNMR and its absolute configuration was confirmed by the CD spectrum.



Reduction of 28 with lithium aluminium hydride at 0°C gave diol 30, which was treated with p-toluenesulfonic acid in benzene to provide 31 in 75.5% yield, m.p. 110-112°C, $[\alpha]_D^{25}$ -165.8 (c 0.98 in $CHCl_3$), the spectral data (IR, MS and ^{1}HNMR) of this lactone were identical with those of racemic compound 14.

With this compound 31, through two synthetic routes described above, we obtained (-)-drimenin 1, m.p. 131-133°C, $[\alpha]_D^{23}$ -46.8, (lit[6]., m.p. 133°C, $[\alpha]_D^{25}$ -42), (-)-cinnamolide 2, m.p. 124-125°C, $[\alpha]_D^{26}$ -30.6 (c 0.34 in $CHCl_3$), (lit[7]., m.p. 125-126°C, $[\alpha]_D^{29}$ -29.4 (c 1.0 in $CHCl_3$)) and (-)-polygodial 3, m.p. 56.5-57°C, $[\alpha]_D^{26}$ -130.6 (c 0.26 in C_2H_5OH), (lit[8]., m.p. 57°C, $[\alpha]_D^{24}$ -131 (C_2H_5OH)).

In summary, the synthesis of racemic and natural drimane sesquiterpenes were accomplished starting from achiral β-ionone using usual and asymmetric intramolecular Diels-Alder reaction.

EXPERIMENTAL SECTION

All m.p. were uncorrected. IR spectra were measured as films for oils or as nujor mulls for solids on a Shimadzu 440 spectrometer. ^{1}HNMR spectra were recorded with TMS as an internal standard at 60 MHz on a EM 360A spectrometer or at 200 MHz on a Varian XL-200 spectrometer. MS spectra were obtained on a FINNIGAN 4021 GC-MS spectrometer. Optical rotations were measured on a Autopol polarimeter. All column chromatographies were performed on silica gel H (10-40u), and with petroleum ether-ethyl acetate system as eluent.

Compound 6. 17 g of NaOH was dissolved in water to make a 70 ml solution in a 250 ml conical flask with a magnetic stirrer. The alkali solution was then cooled in an ice bath and 17 g of Br_2 was added to the solution. After stirring for 1 h, 4.5 g of β-ionone in 10 ml of dioxane was dropped into the solution. The stirring was continued at room temperature for 4 h, then the excess hypobromite was destroyed with 10% aqueous sodium bisulfite and the solution was extracted with ether to remove any impurities. Acidification of the alkaline solution with concentrated HCl and usual work-up gave 4.1 g (90%) of 6 as a white solid. m.p. 105-107°C; IR: 3400, 1690, 1630 cm^{-1}; ^{1}HNMR ($CDCl_3$): 1.20(6H,s), 1.90(3H,s) 5.90(1H,d,J=15Hz), 7.60(1H,d,J=15Hz).

Compound 7. A solution of 4.1 g of 6 in 30 ml of ether was dropped to a suspension of 1.3 g of $LiAlH_4$ in 10 ml of ether under cooling with ice. The stirring was continued for 2 h, then the reaction was quenched with aqueous ammonium chloride. Usual work-up and chromatography gave an oil 7 (3 g, 79%). IR: 3350, 1650 cm^{-1}; ^{1}HNMR (CCl_4): 1.00(6H,s), 1.70(3H,s), 3.20(1H,OH), 4.10(2H,d), 5.50(1H,m), 6.00(1H,d,J=14Hz).

Compound 8. To a solution of 500 mg of the alcohol 7 and 0.4 ml of Et_3N in 50 ml of CH_2Cl_2 was added 400 mg of maleic anhydride and 20 mg of DMAP. After the reaction mixture had been stirred at room temperature under nitrogen for 3 h, it was diluted with CH_2Cl_2, washed with dilute aqueous HCl, water and brine, dried over Na_2SO_4 and evaporated to give a crude acid. Treatment of this acid with CH_2N_2 and purification by column chromatography provided 610 mg of 8 in 75% yield. IR: 1740, 1650 cm^{-1}; ^{1}HNMR (CCl_4): 0.90(6H,s), 1.55(3H,s), 3.60(3H, s), 4.50(2H,d), 5.40(1H,m), 6.05(2H,s), 6.10(1H,d,J=14Hz).

Compound 9. A mixture of compound 8 (100 mg) and hydroquinone (50 mg) in 30 ml of xylene was refluxed under nitrogen for 90 h. The mixture was concentrated in vacuum and separated by chromatography to afford 20 mg of unreacted starting material 8 and 70 mg of 9 (88%) as a white solid. m.p. 112-114°C; IR: 1780, 1740 cm^{-1}; ^{1}HNMR ($CDCl_3$): 1.14(3H,s), 1.20(6H,s), 2.26(1H,dd,J=6.6,13.2Hz), 2.88(1H,d,J=6.6Hz), 3.65(1H,m), 3.70(3H,s), 3.88(1H,dd,J=8.0,11.4Hz), 4.57(1H,t, J=7.2,7.9Hz), 5.91(1H,d,J=2.2Hz); MS m/z 292; Elemental Anal. Calcd for $C_{17}H_{24}O_4$ C, 69.83%, H, 8.27%; Found: C, 69.77%, H, 8.32%.

Compound 10. To a solution of 100 mg of 7 and 186 mg of DCC in 10 ml of CH_2Cl_2 was added 108 mg of fumaric acid mono-methyl ester and 10 mg of DMAP. The mixture was stirred at room temperature under nitrogen for 30 h, and then filtered and washed with CH_2Cl_2. Removal of the solvent gave a residue, which was purified by chromatography to give 100 mg (62%) of 10. IR: 1730, 1650 cm^{-1}; ^{1}HNMR (CCl_4): 0.90(6H,s), 1.55(3H,s), 3.65(3H,s), 4.55(2H,d), 5.40(1H,m), 6.10(1H,d), 6.65(2H,s).

Compound 11. 100 mg of compound 10 was dissolved in 30 ml of xylene and 50 mg of hydroquinone was added. The mixture was refluxed under nitrogen for 140 h. After evaporation of the solvent, the mixture was chromatographed to give 60 mg of starting material 10 and 40 mg of 11. m.p. 160-161°C; IR: 1780, 1730 cm^{-1};

^{1}HNMR ($CDCl_3$): 1.10(3H,s), 1.13(3H,s), 1.26(3H,s), 2.45(1H,d,J=12.5Hz), 3.20(2H, m), 3.73(3H,s), 3.86(1H,t,J=8.2Hz), 4.53(1H,t,J=8.2Hz), 5.43(1H,d,J=2.8Hz); MS m/z 292; Elemental Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.83%, H, 8.27%; Found: C, 70.12%, H, 8.44%.

Conversion of 9 to 11. To a solution of 500 mg of sodium in 2.5 ml of absolute methanol (0.5 M) was added 80 mg of 9. The mixture was stirred at room tempera-ture under nitrogen for 10 h. After neutralization with 10% HCl and usual work-up gave 80 mg of 11, m.p. 160-161°C. The spectral data (IR, ^{1}HNMR and MS) were identical with compound 11.

Compound 12. To a solution of 100 mg of 9 in 5 ml of THF and 4 ml of H_2O was added 180 mg of KOH. The mixture was refluxed under nitrogen for 1.5 h. Neutralization with 5% HCl and usual work-up gave a residue, which was treated with CH_2N_2 and purified by column chromatography to provide 30 mg of 11 and 10 mg of 12. IR: 3500, 1740 cm^{-1}; MS m/z 324.

Compound 14. To a solution of 1 g of 9 in 40 ml of ether was added 200 mg of $LiAlH_4$ at 0°C under nitrogen. After stirring at 0°C for 30 min, the reaction was quenched with aqueous ammonium chloride and usual work-up gave a diol 13.

To the diol 13 in 100 ml of benzene was added 300 mg of p-toluenesulfonic acid, and the mixture was then stirred under nitrogen at room temperature for 6 h. Dilution with ethyl acetate, washing with brine and evaporation in vacuum gave a residue which was separated by chromatography to provide 640 mg of 14 in 70.8% yield. m.p. 116-117°C; IR: 3450, 1760 cm^{-1}; ^{1}HNMR ($CDCl_3$): 1.15(6H,s), 1.16(3H,s), 2.30(1H,m), 2.38(1H,d,J=11.6Hz), 2.78(1H,m), 3.60(1H,dd,J=7.9,9.9Hz) 3.76(1H,dd,J=5.3,10Hz), 4.03(1H,t,J=9.3Hz), 4.62(1H,t,J=9.2Hz), 5.51(1H,d,J=2.1 Hz); MS m/z 264; Elemental Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69%, H, 9.15%; Found: C, 72.38%, H, 8.79%.

Diol 30 and lactone 31 were prepared by the same procedure.

Compound 15. 58 mg of 14 was dissolved in 8 ml of methanol and 20 mg of 10% Pd-C was added, and the mixture was then stirred under an atmosphere of hydrogen. After 12 h, the mixture was filtered and the solvent was removed to provide a crude product which was chromatographed to give 33 mg of 15 (57%), 10 mg of 16 (17%) and 10 mg of 17 (18%). 15: m.p. 118-120°C; IR: 3500, 1740 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.89(3H,s), 0.91(3H,s), 1.05(3H,s), 2.22(1H,m), 2.26(1H,d,J=9.4Hz), 2.62(1H,dddd,J=4.1,9.5Hz), 3.62(2H,m), 4.07(1H,t,J=9.5Hz), 4.34(1H,t,J=9.5Hz); MS m/z Calcd for $C_{16}H_{26}O_3$: 266.1882; Found: 266.1856. 16: m.p. 102-104°C; IR: 3500, 1770 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.88(3H,s), 1.12(3H,s), 1.48(3H,s),2.26(1H, d,J=6.8Hz), 2.41(1H,m), 3.65(2H,m), 4.09(1H,dd,J=4.5,8.5Hz), 4.25(1H,dd,J=0.8, 8.4Hz); MS m/z 266. 17: IR: 1770 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.74(3H,s), 0.93(3H,s), 0.94(3H,s), 1.72(3H,d,J=1.3Hz), 2.50(1H,m), 2.89(1H,d,J=10Hz), 3.06(1H,bq,J=0.9, 9.7Hz), 3.91(1H,dd,J=8.6,10.3Hz), 4.54(1H,dd,J=8.6,9.5Hz), 5.63(1H,dd,J=1.4,6.3 Hz); MS m/z 248.

Optically active compound (-)-15 was prepared by the same procedure, m.p. 96-97° C; $[\alpha]_D^{24}$ -38.6 (c 1.01 in CH_3OH).

Compound 18. To a solution of 70 mg of 15 in 3 ml of acetone was added dropwise Jones' reagent at 0°C. The stirring was continued for 2 h, and then excess Jones' reagent was destroyed with 2-propanol. Usual work-up gave 73 mg of 18 in 99% yield. m.p. 183-185°C; IR: 3200, 1720 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.82(3H,s), 0.84(3H,s), 0.98(3H,s), 1.98(1H,m), 2.18(1H,m), 2.33(1H,d,J=9.2Hz), 2.69(1H,m), 3.04(1H,dddd, J=4.1,9.0Hz), 3.94(1H,t, J=9.0,9.7Hz), 4.28(1H,t, J=8.8,8.9Hz); MS m/z Calcd for $C_{16}H_{24}O_4$: 280.1673; Found: 280.1683. (-)-18: m.p. 165-167°C; $[\alpha]_D^{25}$ -59.3 (c 1.04 in $CHCl_3$).

Compound 20. To a solution of 110 mg of 14 in 3 ml of dimethylformamide was

added 1.6 g of pyridinium dichromate, the reaction mixture was stirred at room temperature for 6 h. Dilution with water and extraction with ethyl acetate gave a crude product which was chromatographed to give 60 mg of 20 (51.8%) and 5 mg of 21 (4.8%). 20: m.p. 192-194°C; IR: 3500, 1760, 1680, 1665 cm^{-1}; ^{1}HNMR ($CDCl_3$): 1.05(3H,s), 1.12(3H,s), 1.14(3H,s), 2.06(1H,m), 3.22(1H,d,J=10.2 Hz), 3.51(1H,s), 3.85(1H,dd,J=9.4,10.2Hz), 4.93(1H,dd,J=9.4,10.1Hz), 7.10(1H,d, J=1.9Hz), 9.57(1H,s); ^{13}CNMR ($CDCl_3$): 193.54(d,13-C), 177.93(s,11-C), 150.19(d, 6-C), 141.95(s,7-C), 75.04(t,12-C), 70.60(d,9-C), 47.14(s), 40.31, 36.95, 35.06, 33.16, 30.99, 27.42, 24.44, 19.45, 17.39; MS m/z 278; Elemental Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04%, H, 7.92%; Found: C, 69.20%, H, 8.00%.

Compound 21. 50 mg of 14 was stirred with Jones' reagent in 5 ml of acetone at 0°C for 1 h, and then 2-propanol was added to destroy excess Jones' reagent. Usual work-up and chromatography gave 30 mg of 21 (64%) and 7 mg of 22 (13%). 21: m.p. 110-112°C; IR: 1765, 1660, 1590 cm^{-1}; ^{1}HNMR ($CDCl_3$): 1.12(3H,s), 1.27 (3H,s), 1.29(3H,s), 2.36(1H,m), 2.97(1H,d,J=11.2Hz), 3.49(1H,bq,J=10,11Hz), 4.21 (1H,dd,J=9.6,9.9Hz), 4.69(1H,dd,J=9.4,10.8Hz), 6.15(1H,s); MS m/z 248; Elemental Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55%, H, 8.13%; Found: C, 72.32%, H, 8.33%. (-)-21: m.p. 114-116°C; $[\alpha]_D^{23}$ -226.2 (c 0.98 in $CHCl_3$). 22: m.p. 161-164°C; IR: 3300-2500(COOH), 1760, 1710 cm^{-1}; ^{1}HNMR($CDCl_3$): 1.13(3H,s), 1.14(3H,s), 1.16 (3H,s), 2.30(1H,m), 2.42(1H,d,J=11Hz), 3.12(1H,dd,J=2.2,8.0Hz), 3.20(1H,m), 4.05 (1H,t,J=9.0Hz), 4.66(1H,t,J=9.1Hz), 5.91(1H,d,J=2Hz); MS m/z 278; Elemental Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04%, H, 7.97%; Found: C, 68.86%, H, 8.20%. (-)-22: m.p. 161-163°C; $[\alpha]_D^{23}$ -194.4 (c 0.58 in $CHCl_3$).

Compound 23. A mixture of 35 mg of 21 and 5 mg of 10% Pd-C in 3 ml of methanol was stirred under an atmosphere of hydrogen for 2h. Filtration and removal of the solvent gave 35 mg of 23. m.p. 97-99°C; IR: 1770, 1720 cm^{-1}; ^{1}HNMR($CDCl_3$): 0.83(3H,s), 0.89(3H,s), 0.90(3H,s), 2.28-2.56(3H,m), 2.80(1H,d,J=12Hz), 3.28(1H, m), 4.38(1H,t,J=9.7Hz), 4.51(1H,dd,J=6.7,9.6Hz); MS m/z Calcd for $C_{15}H_{22}O_3$: 250.1569; Found: 250.1554. (-)-23: m.p. 123-124°C; $[\alpha]_D^{22}$ -114 (c 0.88 in$CHCl_3$).

Compound 24. To a solution of 23 (20 mg) in 3 ml of methanol was added 10 mg of $NaBH_4$, and the mixture was stirred at room temperature for 1 h. Dilution with water and extraction with ethyl acetate gave 20 mg of 24 in 99% yield. m.p. 157-158°C; IR: 3450, 1760 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.89(3H,s), 0.94(3H,s), 1.07(3H,s), 2.18(1H,m), 2.26(1H,d,J=8.4Hz), 3.04(1H,m), 4.01(1H,m), 4.24(1H,dd,J=9.6,11.6Hz) 4.37(1H,t,J=9.0Hz); MS m/z 252; Elemental Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39%, H, 9.59%; Found: C, 71.37%, H, 9.48%. (-)-24: m.p. 157-159°C; $[\alpha]_D^{22}$ -68.2 (c 0.74 in $CHCl_3$).

Drimenin 1. Method A: A solution of 24 (170 mg) and methanesulfonyl chloride (0.5 ml) in 5 ml of pyridine was stirred at room temperature under nitrogen for 4 h. Then the solution was diluted with ethyl acetate, washed with 5% aqueous copper sulfate, brine, dried over sodium sulfate and evaporated to give a residue.

A solution of the residue in 5 ml of dimethyl sulfoxide was stirred under nitrogen at 100°C for 2 h, the reaction mixture was cooled, diluted with ethyl acetate and washed with water. Chromatography of the residue gave 104 mg of 1 in 65.5% yield.

Method B: A solution of 18 (60 mg) in 8 ml of dry benzene containing 8 mg of $Cu(OAc)_2$ and 8 mg of pyridine was heated under nitrogen. To this solution 140 mg of iodosobenzene diacetate was added in portions, 70 mg per hour, and the mixture was refluxed for 2.5 h. The mixture was then diluted with ethyl acetate, washed with brine and dried over sodium sulfate. Chromatography of the residue gave an unreacted starting material 18 (18 mg), methyl ester 19 (15 mg,

34%) and drimenin 1 (20 mg, 57%). They showed the following spectral properties. Drimenin 1: m.p. 94.5-96°C; IR: 1765 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.81(3H,s), 0.83(3H,s), 0.85(3H,s), 1.92(1H,m), 2.13(1H,m), 2.43(1H,m), 2.71(1H,bs), 4.60(2H m), 5.67(1H,m); MS m/z Calcd for $C_{15}H_{22}O_2$: 234.1620; Found: 234.1623. 19: m.p. 80-82°C; IR: 1770, 1730 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.85(6H,s), 1.01(3H,s), 2.16(1H,m), 2.38(1H,d,J=9.1Hz), 2.68(1H,m), 3.08(1H,dddd,J=4.0,9.1Hz), 3.70(3H,s), 3.96(1H, dd,J=9.0,9.7Hz), 4.30(1H,t,J=8.9Hz); MS m/z 294; Elemental Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36%, H, 8.90%; Found: C, 69.72%, H,9.10%.

Compound 26. To a solution of 22 mg of 1 in 1 ml of dry ether was added 20 mg of $LiAlH_4$, and the mixture was stirred at room temperature for 1 h. The solution was diluted with ether and washed with water and brine, dried over sodium sulfate. Removal of the solvent and chromatography gave 20 mg of 26 in 89.3% yield. m.p. 76-78°C; IR: 3300, 1665 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.76(3H,s), 0.87(3H,s), 0.88(3H,s), 1.8-2.2(5H,m), 3.73(1H,m), 3.90(1H,m), 4.00(1H,dd,J=2,12Hz), 4.37(1H,dd, J=2,12Hz), 5.81(1H,m); MS m/z 238; (-)-26: m.p. 72-74°C; $[\alpha]_D^{26}$ -7.6 (c 0.59 in $CHCl_3$).

Compound 27. To a solution of 2 g of 7 and 4.5 g of maleic acid mono-l-menthyl ester in 200 ml of CH_2Cl_2 was added 50 mg of DMAP and 3.8 g of DCC. After the reaction mixture had been stirred at room temperature under nitrogen for 2 h, it was filtered and washed with CH_2Cl_2. Removal of the solvent gave a residue, which was purified by chromatography to give 2.7 g of 27 in 58.4% yield. IR: 1730, 1680, 1640 cm^{-1}.

Compound 28. 6.2 g of 27 was dissolved in 600 ml of xylene and 500 mg of hydroquinone was added. The mixture was refluxed under nitrogen for 50 h. After evaporation of the solvent, the mixture was separated on silica gel to give 2 g of starting material 27 and 3.3 g of 28 and 29 (78.6%) in a ratio of 1.75:1. Recrystallization of this mixture of two isomers with petroleum ether-ethyl acetate gave 1.8 g of 28. m.p. 173-175°C; $[\alpha]_D^{25}$ -78.4 (c 1.10 in $CHCl_3$); CD λ_{max}(CH_3OH): 220nm ($\Delta\varepsilon$=+1.517); IR: 1780, 1730 cm^{-1}; ^{1}HNMR ($CDCl_3$): 0.71(3H,d,J=6.8 Hz), 0.83(3H,d,J=2.5Hz), 0.86(3H,d,J=3.0Hz), 1.05(3H,s), 1.12(3H,s), 1.19(3H,s), 2.16(1H,dd,J=6.2,13.0Hz), 2.75(1H,d,J=6.2Hz), 3.62(1H,m), 3.79(1H,dd,J=7.7,11.4 Hz), 4.49(1H,dd,J=7.0,7.6Hz), 4.66(1H,ddd,J=4.4,11.0Hz), 5.82(1H,d,J=2.1Hz); MS m/z 416; Elemental Anal. Calcd for $C_{26}H_{40}O_4$: C, 74.96%, H, 9.68%; Found: C, 75.23%, H, 10.01%.

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REFERENCES

1a. R.L. Snowden, Tetrahedron Lett., 1984, 25, 3835.
b. J.C. Loperfido, J. Org. Chem., 1973,38, 399.
c. S.P. Tanis & K. Nakanishi, J. Am. Chem. Soc., 1979, 101, 4398.
d. L.P. Burton & J.D. White, J. Am. Chem. Soc., 1981, 103, 3226.
e. M. Jalali-Naini, D. Guillerm & J.Y. Lallemand, Tetrahedron, 1983, 39, 749.
f. Ae. de Groot & T.A. van Beek, Rec. Trav. Chim., 1987, 106, 1.
2. P.J. Van Den Tempel & H.O. Huisman, Tetrahedron, 1966, 22, 293.
3. J.D. White & B.G. Sheldon, J. Org. Chem., 1981, 46, 2273.
4. J.I. Concepcion, C.G. Francisco, R. Freire, R. Hernandez, J.A. Salazar & E. Suarez, J. Org. Chem., 1986, 51, 402.
5. E. Wenkert & D.P. Strike, J. Am. Chem. Soc., 1964, 86, 2044.
6. H.H.Appel, J.D.Connolly, K.H.Overton & R.P.M.Bond, J.Chem.Soc., 1960, 4685.
7. L.Canonica, A.Corbella, G.Jommi, J.Krepinsky, Tetrahedron Lett.,1967, 2137.
8. C.S. Barnes & J.W. Loder, Aust. J. Chem., 1962, 15, 322.