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NEW DITERPENES FROM SALVIA TEXANA. CHEMICAL AND BIOGENETIC ASPECTS

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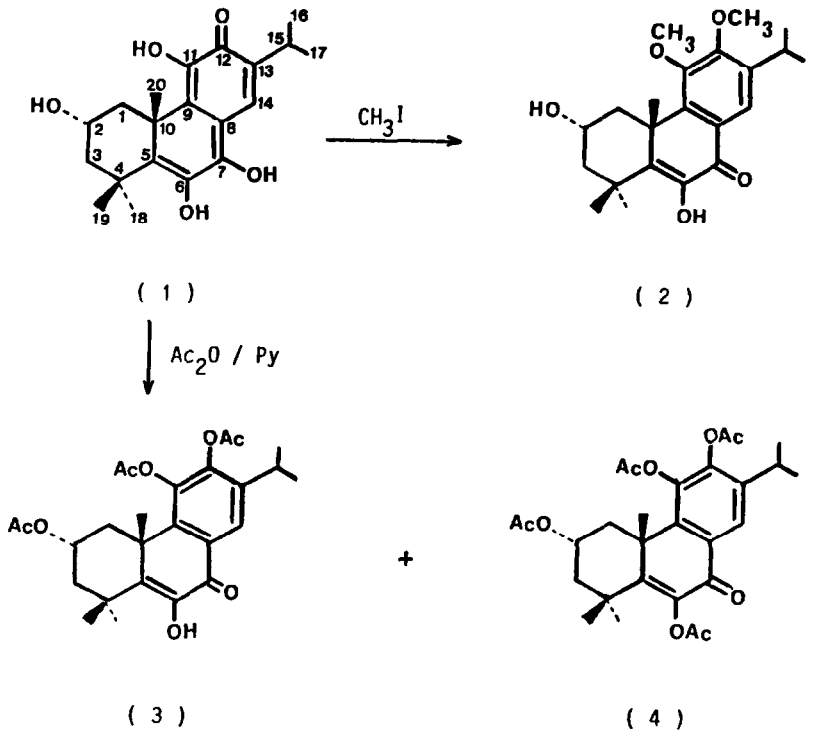
Abstract - Two new diterpenes, the quinone methide 5,6-dehydro-2α,7-dihydroxytaxodone (**1**) and 2α-hydroxysalvicanaric acid (**5b**) were isolated from the roots of Salvia texana Torr Their structure was established by spectroscopic and chemical means. Transformation of **1** into **5b** points to **1** being an intermediate in the biogenesis of **5b**

A member of the Labiatae family, the genus Salvia consists of some five hundred species found worldwide Since ancient times, many species of this genus have been credited with medicinal properties[1,2] and, therefore, reward investigation As part of an intensive study of the chemical composition of the flora used in Latin American popular medicine, following the recent isolation[3] of four diterpene methylene quinones, new 6,7-dehydrosalviol and two secoditerpenes[4] from the roots of Salvia texana Torr. collected in Mexico, we are now reporting the isolation and structure determination of two minor constituents, a quinone methide, **1**, and a hemiacetal diterpenic acid, **5b**, as well as touching on some of the chemical and biogenetic aspects involved

The structure of **1** was established as 5,6-dehydro-2α,7-dihydroxytaxodone from the following Low resolution m.s showed the molecular ion M^+ at m/z 346 (molecular formula $C_{20}H_{24}O_5$ by h r m s) The i r spectrum had bands for phenols and alcohols (3580, 3520 cm^{-1}) and for a methylene quinone grouping (1600 and 1570 cm^{-1}), which was confirmed by the u v spectrum (λ_{max} 345, 290 and 255 nm) In the ^1H n m.r spectrum, signals for an isopropyl group on an aromatic ring and three angular methyls were observed In the low-field region of the spectrum one proton at δ 7 14, interchangeable with deuterium oxide, could be assigned to the phenolic hydroxy group on C-11 while only one proton of the quinone methide system,

the 14-H, was observed Its low chemical shift (δ 7 72) indicated the presence of a coplanar hydroxy group on C-7, which was corroborated when the 14-H signal appeared at δ 8.25 when the spectrum was run in py-d_5[5] The $CDCl_3$ spectrum showed the proton geminal to the alcohol group as a very broad multiplet centred at δ 4.45; in this type of diterpene, the breadth and multiplicity of this signal is compatible only with a 2-Hβ and the stereochemistry of the alcohol group was thus determined as 2α. No signals were observed for the 5-H[3] or for protons allylic to any unsaturated function so the remaining oxygen atom must be part of a C_3–C_4 enolic system By means of double resonance and n.O e. difference experiments and a comparison of the ^{1}H n.m.r. spectra of **1** taken in $CDCl_3$ and py-d^5, the chemical shifts of all the protons and methyl groups could be ascertained All the above data are in agreement with the structure given for compound **1**



(1) (2)

(3) (4)

SCHEME 1

Chemical proof for structure **1** for this new compound was forthcoming as treatment of **1** with methyl iodide and potassium carbonate in acetone gave the dimethylether derivative **2** (Scheme 1) which, in its low resolution m s , showed the molecular ion M^+ at m/z 374 (molecular formula $C_{22}H_{30}O_5$ by h r m s) The i r spectrum had bands for enols and alcohols (3590 and

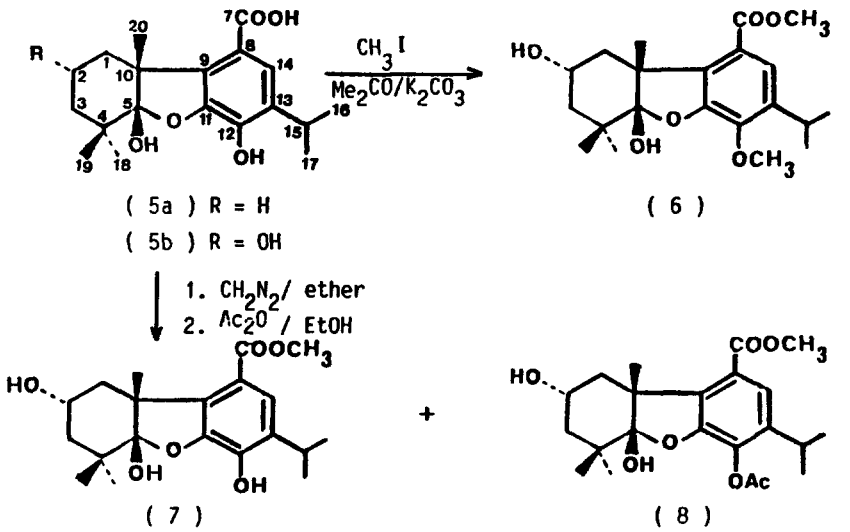
3370 cm^{-1}) and for a conjugated carbonyl (1620 cm^{-1}) The ^1H n m r spectrum, in addition to the signals for methyl groups and for the 2-Hβ as a multiplet centred at δ 4 43, showed two methoxy groups as three-proton singlets at δ 3 84 and 3.92, one proton singlet at δ 7 10, interchangeable with deuterium oxide, assigned to 6-O<u>H</u> and the aromatic proton 14-H as a singlet at δ 7 90, a chemical shift characteristic of this type of diterpene when there is a carbonyl group on C-7[4-7] These data agree with structure **2** which was formed from **1** by tautomerization in basic medium followed by methylation of the phenol groups Treatment of **1** with acetic anhydride in pyridine gave a mixture of two products which were separated by preparative t l c on silica gel The major product was **3** (Scheme 1), low resolution m s showed the molecular ion [M^+] at m/z 472 (molecular formula $C_{24}H_{32}O_8$ by h r m s) In its ^1H n m.r spectrum, signals appeared for one aliphatic and two aromatic acetates, the 14-H aromatic proton at δ 8 16, consonant with a ketone group on C-7, and a proton singlet interchangeable with D_2O at δ 7 05 assignable to 6-O<u>H</u> The minor product, compound **4**, (Scheme 1), had the molecular ion [M^+] at m/z 514 (molecular formula $C_{28}H_{34}O_9$ by h r m s) In the ^1H n m r , signals appeared for one aliphatic and three aromatic acetates In the low-field region of the spectrum, only the H-14 aromatic proton was observed, as a singlet at δ 8 11 These data are in accordance with structures **3** and **4** for the acetylderivatives of **1**.

2α-Hydroxysalvicanaric acid (**5b**) was isolated as a foam that could not be crystallized H r m s gave the molecular formula, $C_{19}H_{24}O_5$ Bands for acid and aromatic groups and a conjugated carbonyl (1685 cm^{-1}) were seen in i r In the ^1H n m r spectrum in py-d_5, signals for an isopropyl group on an aromatic ring and three angular methyls were observed In the low-field region of the spectrum one proton at δ 6 53, interchangeable with deuterium oxide, was assigned to a phenol group and a one-proton singlet at δ 7 75 to the aromatic 14-H The proton geminal to the 2α-hydroxy group appeared as a very broad multiplet centred at δ 4 47

Treatment of **5b** with diazomethane and then with acetic anhydride and ethanol (Scheme 2) gave a mixture of the methyl ester **7** and the acetoxy methyl ester **8**

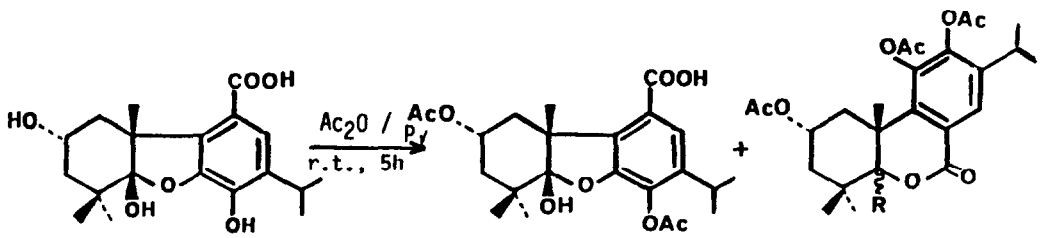
The main difference between the ^1H n m r spectra of **7** ($C_{20}H_{28}O_6$ by h r m s) and **5b** was the appearance of a carbomethoxy group as a three-proton singlet at δ 3 86 There were signals for only one aromatic acetate group, as a three-proton singlet at δ 2 32, in the ^1H n m r spectrum of **8** ($C_{22}H_{30}O_7$ by h r m s) Treatment of **5b** with methyl iodide

and potassium carbonate in acetone (Scheme 2) gave the dimethoxy derivative **6** ($C_{21}H_{30}O_4$ by h r m.s.) the ^1H n.m.r of which is very close to that of **7** with one extra signal for a methoxy group as a three-proton singlet at δ 3 98



SCHEME 2

When **5b** was treated with acetic anhydride in pyridine for five hours (Equation 1), t l c. detected a mixture of two products, **9** and **10** When the reaction was prolonged overnight, only **10** was obtained The i r spectrum of **9** ($C_{23}H_{30}O_8$ by h.r.m.s.) showed bands for alcohol, carboxylic acid and ester groups In the ^1H n.m r spectrum, signals were observed for one aromatic and one aliphatic acetate group as singlets at δ 2 34 and δ 1 96, respectively The 2-Hβ appeared as a broad multiplet centred at δ



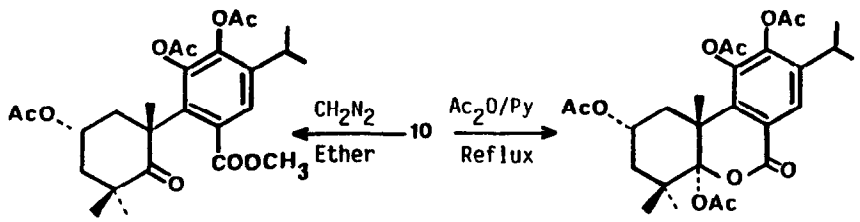
Equation 1

5 13 No geminal proton was observed for the non-acetylated alcohol group, demonstrating its tertiary nature The hemiacetalic nature of the B ring and consequently of the remaining oxygen atom in the molecule could be deduced

from the ^{13}C n m r spectrum of **5b** where a singlet at 114.9 ppm must be attributed to C-5 This spectrum is very similar to that of salvicanaric acid (**5a**), previously isolated from Salvia canariensis[8], except for the chemical shifts of the C-1, C-2 (in **5b**, a doublet at 63.1 ppm) and C-3 These data all accord with the structure of 2α-hydroxysalvicanaric acid for **5b**.

Chemical proof for structure **5b** was provided by **10** being formed when **5b** was acetylated ^1H n m r. of **10** showed it to be a mixture of **10a** and **10b** which behave as one on g c ($C_{28}H_{32}O_9$ by h r m s.) The ^1H n.m.r spectra of the two isomers showed signals for an aliphatic acetate and two aromatic acetates in each The i r. of the mixture did not have any carboxylic acid absorptions but did have a signal for an alcohol group as well as a lactone at 1750 cm^{-1} The alcohol group had to be tertiary, since it did not acetylate under the usual conditions and no protons geminal to the hydroxy were observed in ^1H n m.r. The chemical shift of the aromatic 14-H to δ 8 03 (in **10a**) and to δ 8 08 (in **10b**) places the lactone group carbonyl on C-7 All these data indicate a lactol structure for **10**, which must have been formed by the opening of **5b** to its ketophenol tautomer and subsequent acid group attack on the ketone.

Reflux of **10** with acetic anhydride in pyridine (Equation 2) gave the tetracetoxy derivative **11** ($C_{28}H_{34}O_{10}$ by h r.m s) The ^1H n m r spectrum had



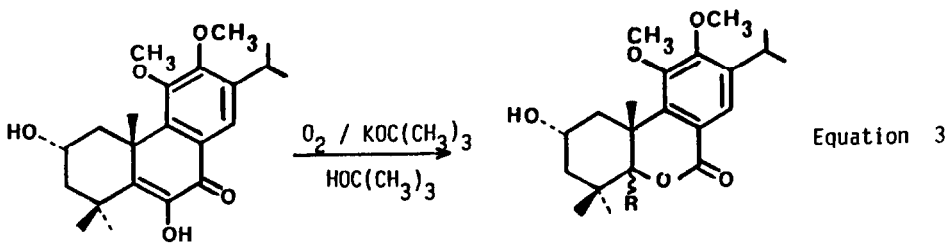
(12) Equation 2 (11)

signals for two aliphatic and two aromatic acetate groups; the aromatic 14-H appeared as a singlet at δ 8 02. When **10** was treated with diazomethane in ether, the ketotriacetoxymethyl ester **12** was obtained as sole product Compound **12** ($C_{24}H_{34}O_9$ by h.r.m.s) had i r signals characteristic of a cyclohexanone and conjugated carboxylate groups In the ^1H n.m r spectrum signals were seen for one aliphatic and two aromatic acetate groups, and also for a carbomethoxy group as a three-proton singlet at δ 3 83 All these data accord with the structure **12** which must have been formed via the tautomeric keto-acids of **10**

Comparison of the ^{1}H n.m.r. spectra of **10a** + **10b** run in $CDCl_3$ and py-d_5 shows that the minor isomer is **10b** with a 5β-OH. In the spectrum run in $CDCl_3$, the 19-Me and 20-Me appear at δ 1 20 and 1.30, respectively, and when taken in py-d_5, at δ 1.44 and 1.59 These shifts were not observed for the major isomer, **10a**

The cis nature of the A/B ring junction in **5b** was established from the following: in the ^{1}H n.m.r. spectrum of **5b**, the C-20 methyl appears as a three-proton singlet at δ 1.68; when the same spectrum was run in py-d_5 it appeared at δ 2 20 in accordance with the cis coplanarity with C_5-OH In a n O e difference experiment, irradiation of C-20 methyl produced a strong n O e effect on both the H-2β and the C-19 methyl, which agrees with the stereochemistry shown for **5b**

In a previous paper[8], we postulated the biogenetic origin of salvicanaric acid (**5a**) from the biosynthetic oxidation of demethylcryptojaponol To

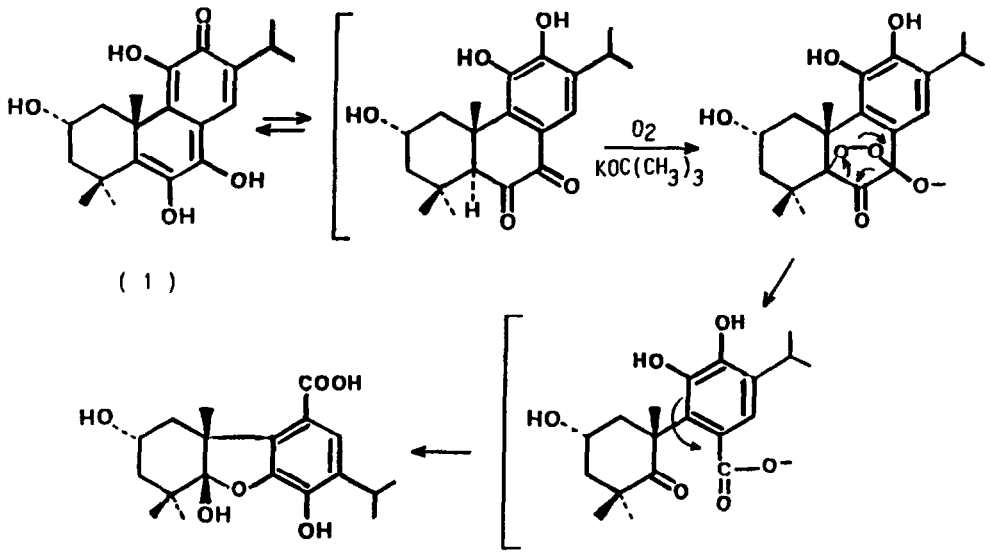


(2) Equation 3

(13a) R = α-OH
(13b) R = β-OH

confirm this, **1** was auto-oxidated with molecular oxygen in t-butanol and potassium t-butoxide, and an intractable mixture was obtained Under identical conditions, the dimethoxy derivative **2** (Equation 3) gave a product which showed one spot on t l.c but in ^{1}H n m r proved to consist of a mixture of the lactols **13a** and **13b** ($C_{21}H_{30}O_4$ by h r.m s) with **13b** as the major product Comparison of the ^{1}H n m r spectra of **13b** and **13a** taken in $CDCl_3$ and py-d_5 show a great downfield chemical shift of the 18-, 19- and 20-Me for the major isomer which must, therefore, have an A/B cis junction An unusual cis ring junction in a similar lactol has already been described[9] The aromatic 14-H protons appeared at δ 7 79 in **13b** and at δ 7 80 in **13a** If the phenol groups are free, cyclization after auto-oxidation should give **5b** (Scheme 3) When **1**, dissolved in n-hex-EtOAc, was irradiated with u v light (240 nm) for 1/2 hr, two spots were observed on t l c the less polar being unreacted starting material When the solution was left to stand, the more polar product slowly evolved to give **5b** Heating the

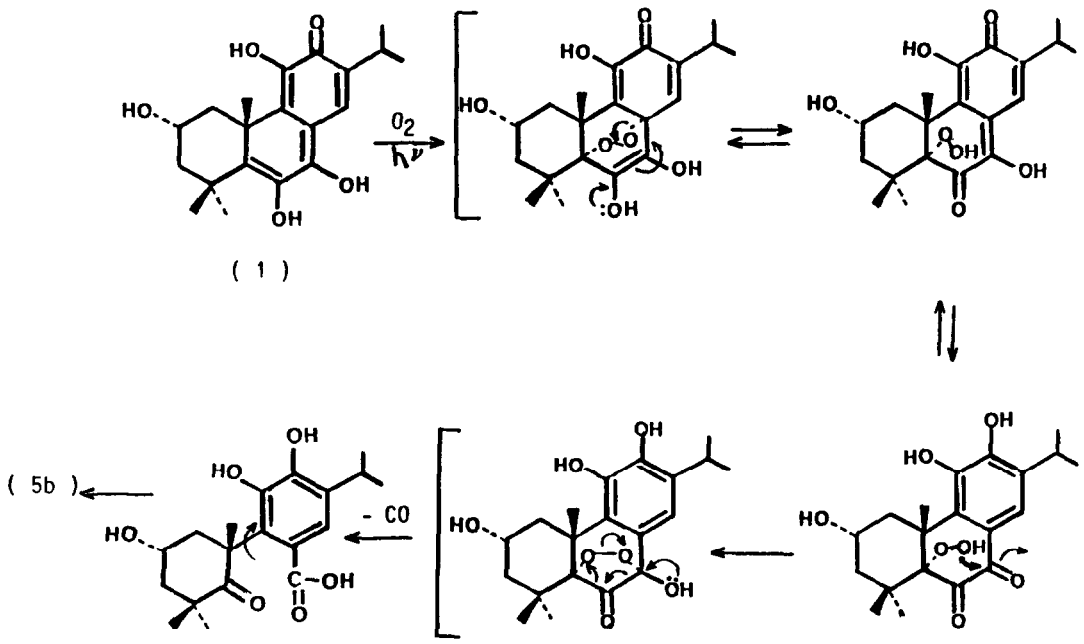
SCHEME 3



(1)

(5b)

solution accelerated the process. Scheme 4 outlines the proposed mechanism via oxygen singlet activation of the substrate as autosensitizer No intermediate could be isolated.



(1)

(5b)

SCHEME 4

Compound **1** was stable after 24 hr when a solution in n-hex-EtOAc was stirred under oxygen atmosphere, alone or with silica gel added It was also stable under silica gel chromatography. The above reactions suggest that **5b** may have been formed by the biosynthetic oxidation of **1**.

EXPERIMENTAL

Gas chromatography was carried out on a Perkin-Elmer 900 with a flame ionization detector ^1H and ^{13}C n.m r. were collected on Bruker AC80 and WP-200SY (200MHz) spectrometers with $CDCl_3$, Py-d_5 or CD_3OD as solvents and TMS as internal standard The i r spectra were taken on a Perkin-Elmer 681 spectrophotometer with sodium chloride cells (0.1 mm) and $CHCl_3$ as solvent UV spectra were recorded on a Perkin-Elmer 550SE spectrophotometer with quartz cells (1 and 5 mm) and EtOH as solvent. Mass spectra and accurate mass measurements were determined on a VG-Micromass ZAB-2F at an ionizing potential of 70 Kev. Dry column chromatography used silica gel (0 05-0 2 mm) Preparative t.l.c was developed on precoated Schleicher & SchÜll foils, F-1500/LS 254 Voucher plant specimens are lodged with the Herbarium of the Dept of Botany, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Mexico

The finely-cut roots of Salvia texana Torr (3 kg) were extracted with cold MeOH (5 l) Filtration and evaporation of the solvent with a rotavapor in vacuo gave a reddish-brown extract (48 g) which was chromatographed on Sephadex using a mixture of n-hexane-$CHCl_3$-MeOH (1 1 2) as solvent 500 ml fractions were collected Only Fractions 40-58 were studied After repeated chromatography on silica gel using mixtures of n-hexane-EtOAc as solvent, the following compounds were isolated -

5,6-Dehydro-2α,7-Dihydroxytaxodone (**1**) was isolated from the more polar fractions of the chromatography and purified by repeated crystallization in $CHCl_3$ (Found M^+, 346 1781 $C_{20}H_{26}O_5$ requires M 346 1782). ν_{max} ($CHCl_3$) cm^{-1}, 3580s, 3520s, 3000m, 2960s, 2920s, 1600 vs, 1570w, 1470m, 1370w, 1350vs and 1270m; λ_{max} (EtOH) nm, 345, 290 and 255, δ^H (200 MHz, $CDCl_3$, TMS) 1 28, 1 32 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 41, 1 65 (2H, m, 1-H_α and 3-H_α), 1 46 (3H, s, 19-Me), 1 54 (3H, s, 20-Me), 1 58 (3H, s, 18-Me), 2 30 (1H, dd, J 6 2, 15Hz, 3-H_β), 3.05 (1H, hept, J 7Hz, 15-H), 3 74 (1H, dd, J 7 2, 13 4Hz, 1-H_β), 4 45 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7.14 (1H, s, Ar-OH), 7 72 (1H, s, 14-H), δ^H (200 MHz, Py-d_5, TMS), 1 29, 1 30 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 71 (3H, s, 19-Me), 1 95 (3H, s, 20-Me), 2 00 (3H, s, 18-Me), 2 02 (2H, m, 1-H_α and 3-H_α), 2 54 (1H, dd, J 6 2, 16Hz, 3-H_β), 3 66 (1H, hept, J 7Hz, 15-H), 4 62 (1H, dd, J 7 3, 13Hz, 1-H_β), 4 87 (1H, br m, $W_{1/2}$ 33Hz, 2-Hβ), 8 25 (1H, s, 14-H), m/z (e i) 346 (M^+, 6%), 328(4), 313(7), 303(4), 290(40), 285(11), 272(42), 261(20) and 247(94)

Treatment of **1** with Methyl Iodide in Acetone **1** (10 mg), dissolved in dry acetone (7 ml), was chilled to 5° and potassium carbonate (400 mg) and methyl iodide (1 ml) were then added The reaction mixture was stirred at room temp for 8 hr, filtered and taken to dryness and after preparative chromatography gave **2**. (Found: M^+, 374 2102 $C_{22}H_{30}O_5$ requires M 374 2111), ν_{max} ($CHCl_3$) cm^{-1}, 3590m, 3370m, 3000w, 2960s, 2920s, 1620s, 1595m, 1470m, 1425w, 1330vs, 1270w and 1040s; λ_{max} (EtOH) nm, 352, 325, 283 and 255, δ^H (200 MHz, $CDCl_3$, TMS) 1 24, 1 27 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 47 (3H, s, 19-Me), 1 54 (3H, s, 20-Me), 1 56 (3H, s, 18-Me), 1.60 (2H, m, 1-H_α and 3-H_α), 2 29 (1H, dd, J 7, 14Hz, 3-H_β), 3 30 (1H, hept, J 7Hz, 15-H), 3 56 (1H, dd, J 7.5, 16Hz, 1-H_β), 3 84, 3.92 (each 3H, s, 2xOMe), 4 43 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 10 (1H, s, 6-OH), 7 90 (1H, s, 14-H); m/z (e i) 374 (M^+, 17%), 356(12), 341(19), 331(8), 325(12), 318(32), 313(17), 303(12), 287(100) and 275(99)

Acetylation of **1** Treatment of **1** (3 mg) with Ac_2O (0 1 ml) in py (0 2 ml) at room temp after 4 hr gave a mixture of **3** and **4**, separated by preparative plate chromatography using benzene-EtOAc (5 5) as eluent **3** was the major product (Found M^+, 472 2086. $C_{26}H_{32}O_8$ requires M 472 2097), δ^H (200 MHz, $CDCl_3$, TMS) 1 24, 1 28 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 48 (3H, s, 19-Me), 1 51 (3H, s, 20-Me), 1 54 (3H, s, 18-Me), 2 01 (3H, s, 2-OAc_α), 2 32, 2 39 (each 3H, s, 2xAr-OAc), 2 94 (1H, hept, J 7Hz, 15-H), 5 35 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 05 (1H, s, 6-OH), 8 16 (1H, s, 14-H), m/z (e i) 472 (M^+, 4%), 430(2), 412(16), 402(2), 370(82), 328(100) and 300(8) The minor product **4**· (found· M^+, 514 2169 $C_{28}H_{34}O_9$ requires M 514 2202), δ^H (200 MHz, $CDCl_3$, TMS) 1 24, 1 25 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 43 (3H, s, 19-Me), 1 52 (3H, s, 20-Me), 1 57 (3H, s, 18-Me), 2 00 (3H, s, 2-OAc_α), 2 31, 2 36 (each 3H, s, 2xAr-OAc), 2 34 (3H, s, 6-OAc), 3 00 (1H, hept, J 7Hz, 15-H), 5 31 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 8 11 (1H, s, 14-H), m/z (e i) 514 (M^+, 4%), 472(6), 454(17), 412(68), 388(3), 370(100), 328(85) and 272(20)

2α-Hydroxysalvicanaric Acid (**5b**) was isolated as a foam that would not crystallize (Found M^+, 350 1732 $C_{19}H_{26}O_6$ requires M 350 1735), ν_{max} (film) cm^{-1}, 3700-2300vs, 1685vs, 1620m, 1590w, 1470w, 1425vs, 1370m, 1238s, 1090m, 1045m, 1015m, 960w and 910w, λ_{max} (EtOH) nm, 330, 290 and 250; δ^H (200 MHz, $CDCl_3$, TMS) 1 23, 1 26 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 25, 1 27 (each 3H, s, 18-Me, 19-Me), 1 68 (3H, s, 20-Me), 1 80 (1H, dq, 1-H_α), 2 80 (1H, dq, 1-H_β), 3 25 (1H, hept, J 7Hz, 15-H), 4 07 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 45 (1H, s, 14-H), δ^H (200 MHz, Py-d_5, TMS), 1 24 (3H, s, 18-Me), 1 30, 1 33 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 49 (3H, s, 19-Me), 2 07 (1H, dq, 1-H_α), 2 24 (3H, s, 20-Me), 3 68 (1H, hept, J 7Hz, 15-H), 3 74 (1H, dq, 1-H_β), 4 52 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 84 (1H, s, 14-H), δ^H (200 MHz, Py-d_5+D_2O, TMS), 1 25, 1 28 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 32 (3H, s, 18-Me), 1 43 (3H, s, 19-Me), 2 10 (1H, dq, 1-H_α), 2 23 (3H, s, 20-Me), 3 62 (1H, hept, J 7Hz, 15-H), 3 78 (1H, dq, 1-H_β), 4 50 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 78 (1H, s, 14-H), δ^H (200 MHz, CD_3OD, TMS), 1 19 (6H, d, J 7Hz, 16-Me, 17-Me) 1 28 (3H, s, 18-Me) 1 59 (3H, s, 19-Me), 1 90 (3H, s, 20-Me), 2 68 (1H, dq, 1-H_β), 3 85 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 6 90 (1H, s, 14-H), δ_C (50MHz, Py-d_5), 18 9 (q, C-20), 22 97 (q, C-16), 23 03 (q, C-17), 25 8 (q, C-18), 27 3 (q, C-19), 27 4 (d, C-15) 39 6 (s, C-4), 48 1 (t, C-3), 49 2 (t, C-1), 52 4 (s, C-10), 63 1 (d, C-2), 114 9 (s, C-5), 120 7 (s C-9), 122 0 (d C-14), 135 2 (s, C-8), 139 3 (s, C-11), 144 5 (s, C-13), 145 3 (s, C-12) and 170 4 (s, C-7), m/z (e i) 350 (M^+, 4%), 332(3), 322(3), 304(2), 288(5), 273(3), 250(38), 237(28), 219(15), 189(11), 161(8), 119(16) and 55(100)

Treatment of **5b** with Diazomethane **5b** (8 7 mg), dissolved in ether (5 ml), was treated with an ether soln of CH_2N_2 (2ml, 0 4M) After 20 min the reaction was halted by the addition of Ac_2O and the excess eliminated by addition of EtOH Evaporation of the soln in rotavapor in vacuo gave a mixture of **7** and **8**, separated by preparative t l c **7**: (found M^+, 364 1903 $C_{20}H_{28}O_4$ requires M 364 1920), ν_{max} ($CHCl_3$) cm^{-1}, 3670m, 3590m, 3550m, 3000m, 2950m, 2920m, 1710vs, 1610m, 1600m, 1440m, 1420s, 1370m, 1335m, 1210vs, 1100s and 1040m, δ^H (200 MHz, $CDCl_3$, TMS) 1 23, 1 27 (each 3H, d, J 7Hz, 16-Me and 17-Me), 1 24, 1 25 (each 3H, s, 18-Me, 19-Me), 1 60 (3H, s, 20-Me), 1 76 (1H, dq, 1-H_α), 2 72 (1H, dq, 1-H_β), 3 25 (1H, hept, J 7Hz, 15-H), 3 86 (3H, s, -COOMe), 4 03 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 5 30 (1H, br s, ArOH), 7 29 (1H, s, 14-H), m/z (e i) 364 (M^+, 18%), 346(16), 333(3), 315(12), 305(1), 302(16), 287(10), 264(100), 249(37) and 221(38) **8** (found M^+, 406 1998 $C_{22}H_{30}O_7$ requires M 406 2005), δ^H (200 MHz, $CDCl_3$, TMS) 1 19, 1 21 (each 3H, s, 18-Me, 19-Me), 1.21 (6H, d, J 7Hz, 16-Me, 17-Me), 1 60 (3H, s, 20-Me), 1 72 (1H, dq, 1-H_α), 2 32 (3H, s, Ar-OAc), 2 72 (1H, dq, 1-H_β), 3 10 (1H, hept, J 7Hz, 15-H), 3 59 (3H, s, -COOMe), 4 02 (1H, br m, $W_{1/2}$ 33Hz, 2-Hβ), 7 26 (1H, s, 14-H), m/z (e i) 406 (M^+, 11%), 364(12), 346(1), 333(1), 315(2), 306(53), 302(1), 287(5), 278(10) and 264(100)

Acetylation of **5b** Treatment of **5b** (10 mg) with Ac_2O (0 3 ml) in py (0 6 ml) at room temp for 5 hr gave **9** + **10** If the reaction was left to stand overnight only **10** was obtained

9 (found M^+, 434 1943 $C_{25}H_{30}O_8$ requires M 434 1946), ν_{max} ($CHCl_3$) cm^{-1}, 3670w, 3020w, 2860m, 2820w, 1750m, 1735vs, 1420s, 1370s, 1250vs, 1190s, 1095m and 1020m, δ^H (200 MHz, $CDCl_3$, TMS) 1 20 (6H, s, 18-Me, 19-Me), 1 22, 1 26 (each 3H, d, J 7Hz, 16-Me, 17-Me), 1 68 (3H, br s, 20-Me), 1 96 (3H, s, 2-OAc_α), 2 34 (3H, s, Ar-OAc), 2 70 (1H, dq, 1-H_β), 3 06 (1H, hept, J 7Hz, 15-H), 5 13 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 42 (1H, s, 14-H), δ^H (200 MHz, Py-d_5, TMS) 1 15, 1 17 (each 3H, d, J 7Hz, 16-Me, 17-Me), 1 46, 1 59 (each 3H, s, 18-Me, 19-Me), 1 97 (3H, s, 2-OAc_α), 2 14 (3H, s, 20-Me), 2 37 (3H, s, Ar-OAc), 3 12 (1H, hept, J 7Hz, 15-H), 3 31 (1H, dq, 1-H_β), 5 30 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 7 67 (1H, s, 14-H), m/z (e i) 434 (M^+, 1%), 392(3), 332(3), 314(2), 292(17), 279(10), 265(4), 250(25), 167(20) and 149(100) **10** (found M^+, 476 2059 $C_{28}H_{32}O_9$ requires M 476 2072), ν_{max} ($CHCl_3$) cm^{-1}, 3660m, 3580m, 3000s, 2960s, 2920s, 1780vs, 1750vs, 1620w, 1380m, 1325m, 1250s, 1195s, 1180m, 1100m and 1040s, δ^H (200 MHz, $CDCl_3$, TMS) **10a** 1 20 (3H, s, 18-Me), 1 23 (6H, d, J 7Hz, 16-Me, 17-Me), 1 36 (3H, s, 19-Me), 1 51 (3H, s, 20-Me), 2 05 (3H, s, 2-OAc_α), 2 27, 2 31 (each 3H, s, 2xAr-OAc), 2 67 (1H, dd, 1-H_β), 2 95 (1H, hept, J 7Hz, 15-H), 3 26 (1H, br s, 5-OH), 5 24 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 8 03 (1H, s, 14-H), **10b** 1 20 (3H, s, 18-Me), 1 20 (3H, s, 19-Me), 1 22 (6H, d, J 7Hz, 16-Me, 17-Me), 1 30 (3H, s, 20-Me), 1 97 (3H, s, 2-OAc_α), 2 31, 2 32 (each 3H, s, 2xAr-OAc), 2 67 (1H, dd, 1-H_β), 2 95 (1H, hept, J 7Hz, 15-H), 3 21 (1H, br s, 5-OH), 5 24 (1H, br m, $W_{1/2}$ 33Hz, 2-H_β), 8 08 (1H, s, 14-H), δ^H (200 MHz, Py-d_5, TMS) **10a** 0 94, 0 96 (each 3H, d, J 7Hz, 16-Me, 17-Me), 1 36 (6H, s, 18-Me, 19-Me), 1 45 (3H, s, 20-Me), 2 09 (3H, s, 2-OAc_α), 2 37, 2 39 (each 3H, s, 2xAr-OAc), 2 56 (1H, dq, 1-H_α), 2 97 (1H, hept, J 7Hz, 15-H), 3 13 (1H, dq, 1-Hβ), 5 42 (1H,br m, $W_{1/2}$ 33Hz, 2-H_β), 8 28 (1H, s, 14-H), **10b** 1 06, 1 10 (each 3H, d, J 7Hz, 16-Me, 17-Me), 1 36 (3H, s, 18-Me), 1 44 (3H, s, 19-Me), 1 59 (3H, s, 20-Me), 2 01 (3H, s, 2-OAc_α), 2 37, 2 40 (each 3H s, 2xAr-OAc), 2 56 (1H, dq, 1-H_α), 2 97 (1H, hept, J 7Hz, 15-H), 3 13 (1H, dq, 1-H_β), 5 42 (1H,br m, $W_{1/2}$ 33Hz, 2-H_β), 8 35 (1H, s, 14-H),m/z (e i) 476 (M^+, 1%), 416(4), 374(6), 356(8), 314(47), 303(21), 292(33), 285(8), 270(6), 264(12), 247(23), 203(59) and 55(100)