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# SALVICANARIC ACID, A NEW DITERPENE FROM *SALVIA CANARIENSIS*

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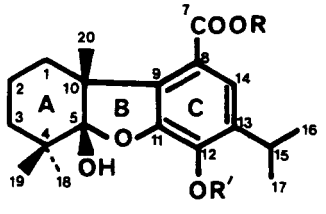
ABSTRACT.—From the $Me_2CO$ extract of *Salvia canariensis*, the new diterpene salvicanaric acid [**4**] was isolated, and its structure determined by spectroscopic and chemical means. The new diterpenes **1** and **2**, possible artifacts of **4**, were separated from a pre-acetylated and methylated fraction. The structure of **2** was elucidated by X-ray analysis.

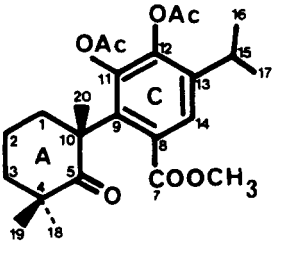
A previous paper (1) reported the new diterpenes deoxocarnosol-12-methyl ether, salvicanol, and 6 α-hydroxydemethylcryptojaponol, plus sugiol and demethylcryptojaponol, isolated from the roots of *Salvia canariensis* L. (Labiatae).

A later study of the more polar fraction of the root, which had previously been acetylated with $Ac_2O$ in pyridine and methylated with $CH_2N_2$, yielded the new products salvicanaric acid acetate methyl ester [**1**] and methyl (*R*)-2-(1,3,3-trimethyl-2-oxocyclohexyl)-3,4-diacetoxy-5-isopropyl-benzoate [**2**].

The evidence for structure **2** is as follows. Hrms indicated the molecular formula $C_{24}H_{32}O_7$. In ir there were signals characteristic of cyclohexanone and conjugated carboxylate groups. The $^1$H-nmr parameters are given in Table 1; signals for two aromatic acetates appear as singlets at δ 2.17 and 2.25, an isopropyl on the aromatic ring as two three protons doublets each at δ 1.17 and 1.19 and one proton as a heptet at 2.90, a methoxy group as a singlet at δ 3.86, an aromatic proton at δ 7.24, and three angular methyls. $^{13}$C-nmr parameters are given in Table 2. All the data are in accord with a bicyclic diterpene structure such as **2**.




| | R | R′ |
|---|---|---|
| **1** | $CH_3$ | Ac |
| **3** | $CH_3$ | H |
| **4** | H | H |




**2**

The conclusions drawn from spectroscopic analysis were corroborated by the molecular structure obtained by single X-ray diffraction. Figure 1 shows an ORTEP view of molecules B and A showing the atomic numbering. The asymmetric unit consists of two independent molecules that are related by a pseudo-binary axis. The two molecules do not show large variations.

A comparison of the two independent molecular geometries was carried out with a half-normal probability plot (2) with all intramolecular distances less than 1.80 Å, bond angles and torsion angles. The plots for bond distances and bond angles are nearly linear, but there are great differences in torsion angles.

TABLE 1. $^1$H-nmr Chemical Shifts (δ) and Coupling Constants (Hz, in parentheses) for **1-4**[a]

| H | Compounds | | | | | |
|---|---|---|---|---|---|---|
| | **1**[b] | **1**[c] | **2**[b] | **3**[b] | **3**[c] | **4**[b] |
| 1α | | | | 1.40 m | | 1.38 m |
| 1β | 2.35 d | 2.57 d | 2.38 | 2.37 bd | 2.73 bdd | 2.42 bd |
| 2α | | | | | | |
| 2β | | | | | | |
| 3α | 1.32-1.76 *m* | 1.22-1.78 m | | 1.4-1.7 m | 1.67 bd (some of them) | 1.4-1.7 m |
| 3β | | | | | | |
| 14 | 7.22 s | 7.58 s | 7.24 s | 7.25 s | 7.57 s | 7.45 s |
| 15 | 3.00 hep (7.0) | 3.10 hep (7.0) | 2.90 hep (7.0) | 3.22 hep (7.0) | 3.62 hep (7.0) | 3.25 hep (7.0) |
| 16,17 | 1.19 d (7.0), 1.19 d (7.0) | 1.14 d (7.0), 1.15 d (7.0) | 1.17 d (7.0), 1.19 d (7.0) | 1.18 d (7.0), 1.21 d (7.0) | 1.28 d (9.4), 1.32 d (9.4) | 1.22 d (7.0), 1.24 d (7.0) |
| 18 | 0.85, 1.14[d] | 1.48 s | 0.99 s | 1.20 s | 1.18 s | 1.23 s |
| 19 | 1.14 1.14[d] | 1.36 s | 1.14 s | | 1.36 s | 1.26 s |
| 20 | 1.50 s | 1.85 s | 1.36 s | 1.52 s | 1.93 s | 1.62 s |
| $CO_2Me$ | 3.87 s | 3.83 s | 3.86 s | 3.83 s | 3.82 s | |
| Ar-OH | | | | 5.44 bs | | |
| Ar-oAc | 2.30 s | 2.36 s | 2.17 s 2.25 s | | | |
| Alq-OH | 2.63 bs | | | 2.85 bs | 2.71 bs | |

[a]All spectra are recorded at 200 MHz.
[b]In $CDCl_3$.
[c]In pyridine-$d_5$.
[d]$CDCl_3$ at 50°.

The average of the C-C bond lengths for molecules A and B are 1.536 and 1.537 Å, respectively. The range in the single C-C bond lengths in molecule A (1.6498-1.4604 Å) is greater than in molecule B (1.594-1.484 Å). The standard derivations are not significantly different with the achieved precision. The C-C-C angles present similar correlations between molecules A and B; the averages of the C-C-C angles are 110.3° and 110.5° for molecules A and B, respectively, close to the tetrahedral value 109.5° for the

TABLE 2. $^{13}$C-nmr Chemical Shifts (δ), ($CDCl_3$)

| Carbon Atom | Compounds | | |
|---|---|---|---|
| | **2** | **3** | **4** |
| 1 . . . . . | 39.5 t | 38.8 t | 38.5 t |
| 2 . . . . . | 18.2 t | 17.9 t | 17.8 t |
| 3 . . . . . | 37.2 t | 37.8 t | 37.8 t |
| 4 . . . . . | 45.9 s | 38.0 s | 38.1 s |
| 5 . . . . . | 170.6 s | 115.1 s | 115.2 s |
| 7 . . . . . | 169.5 s | 167.5 s | 171.0 s |
| 8 . . . . . | 134.0 s | 134.2 s | 134.3 s |
| 9 . . . . . | 131.1 s | 119.5 s | 118.0 s |
| 10 . . . . . | 52.5 s | 51.4 s | 51.6 s |
| 11 . . . . . | 140.5 s[a] | 136.9 s | 138.0 s |
| 12 . . . . . | 142.0 s[a] | 142.5 s[a] | 143.3 s[a] |
| 13 . . . . . | 142.7 s[a] | 143.0 s[a] | 143.4 s[a] |
| 14 . . . . . | 125.1 d | 122.3 d | 123.5 d |
| 15 . . . . . | 27.8 d | 27.4 d | 27.4 d |
| 16 . . . . . | 22.7 q[b] | 22.5 q[b] | 22.5 q[b] |
| 17 . . . . . | 22.8 q[b] | 22.6 q[b] | 22.6 q[b] |
| 18 . . . . . | 25.5 q[c] | 24.6 q[c] | 24.6 q[c] |
| 19 . . . . . | 26.6 q[c] | 26.5 q[c] | 26.5 q[c] |
| 20 . . . . . | 29.1 q | 17.6 q[c] | 17.8 q[c] |

[a,b,c]Chemical shifts with the same letter can be interchanged.

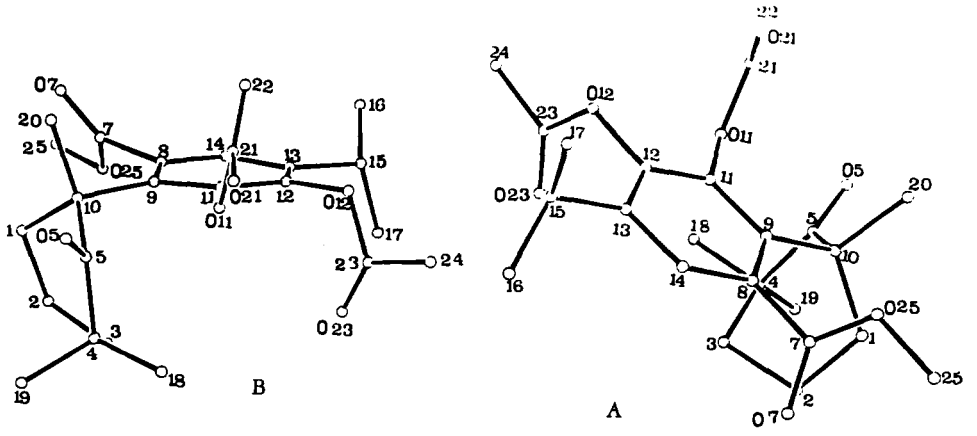
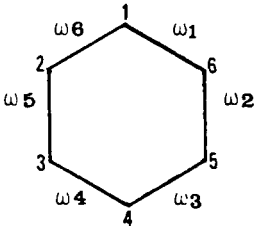



FIGURE 1. ORTEP view of molecules B and A with the atomic numbering

cyclohexane ring. The torsion angles for the cyclohexane ring in Table 3 show that there are slight differences between A and B. Table 4 shows the Cremer (3) and Duax (4) parameters, which define the conformation of the cyclohexane ring. It can be observed that in both molecules this ring shows similar planarity ($Q$ value); molecule A has a conformation close to a boat, while molecule B has a conformation between a boat and a twist ($\phi$ and $\theta$ values). On the other hand, the asymmetry parameter indicates that in molecule A the dominant symmetry is a mirror plane, while a rotational symmetry is dominant in molecule B.

TABLE 3. Torsion Angles (O) for the Cyclohexane Ring Molecules A and B

| Molecule | $w_1$ | $w_2$ | $w_3$ | $w_4$ | $w_5$ | $w_6$ |
|---|---|---|---|---|---|---|
| A | −60.8 | 51.8 | 8.3 | −57.3 | 45.5 | 13.5 |
| B | −64.5 | 47.6 | 10.2 | −51.9 | 36.1 | 24.9 |




The two independent molecules are related in the crystal by a pseudo-twofold rotation axis. The relative orientations of the ring system are shown below:

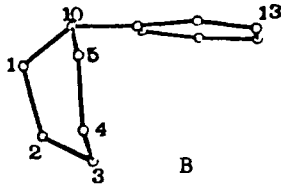
The methyls C18, C19, and C20 have the configuration α, β, and β, respectively, for both molecules.

No relevant intermolecular contacts closer than the sum of the Van der Waals radii were found.

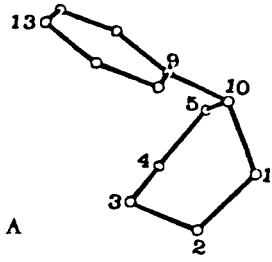
The structure of salvicanaric acid acetate methyl ester [**1**] was established as follows. It was isolated as an oil that would not crystallize; hrms indicated the molecular formula $C_{22}H_{30}O_6$, while ir showed signals characteristic of an alcoholic group, an aromatic acetate, and a conjugated carboxylate group. $^1$H-nmr parameters are given in Table 1. Treatment with $Ac_2O$ in pyridine gave unaltered starting material, demonstrating the tertiary nature of the alcohol group. Hydrolysis of compound **1** with KOH

TABLE 4. Conformational and Asymmetry Parameters for the Cyclohexane Ring for Molecules A and B

| Molecule | ϕ | θ | Q | |
|---|---|---|---|---|
| A | 172.0° | 91.7° | 0.81 | Ds (C4-C5 (0.66 Å) |
| B | 164.6 | 94.4 | 0.76 | D2 (C2) (0.08 Å) |




B



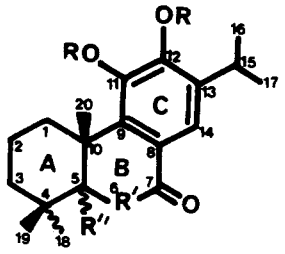

A

in MeOH gave **3**, which could not be crystallized. Hrms gave a molecular formula, $C_{20}H_{28}O_5$. $^1$H-nmr parameters are set out in Table 1 and $^{13}$C-nmr in Table 2. In the latter, C-5 appears at 115.1 ppm suggesting a hemiketalic nature (4). These data all accord with structures **1** and **3** for the acetate and the phenol, later confirmed chemically. Thus, treatment of **2** with KO-*t*-Bu in DMSO at reflux gives a single product with spectral data totally superimposable upon those of **3**; its acetate was superimposable upon **1**.

The molecular rotations of product **1**, natural and synthetic, were in agreement, indicating that the nature of the A and B ring junction is the same in both cases. This junction was established at A/B *cis* on the basis of the following: when $^1$H-nmr spectra of **1** and **3** taken in $CDCl_3$ were compared with those taken in pyridine-$d_5$, the latter showed a shift of 0.35 and 0.41 ppm, respectively, towards the lower field of the C-10 methyl signal (H-20), only explicable if this methyl is facing the hydroxyl group on C-5 (5). Again, in the $^1$H-nmr spectrum of **1** (Table 1) the 18-Me is shielded, appearing at δ 0.85 as a broad singlet which is sharpened and shifted to δ 1.14 when the spectrum is taken at 50°. This is apparently due to the possibility of two chair conformations for ring A with a moderate energy barrier between. In the chair form with the aromatic ring and the axial 18-Me, the latter lies over the former and is strongly shielded. This required a *cis* A/B ring juncture (6,7).

From a more polar fraction of the original column, salvicanaric acid [**4**] was isolated as an oil that would not crystallize. Hrms gave the molecular formula $C_{19}H_{26}O_5$. The ir shows an acid group and aromatic signals. The $^1$H-nmr spectrum is given in Table 1 and the $^{13}$C-nmr spectrum in Table 2. As can be seen, both spectra are very similar to those of **3**, the principal difference being the absence of the methoxy of the methyl ester. This is in agreement with structure **4** for salvicanaric acid. Treatment of **4** with $Ac_2O$ in pyridine gave a mixture of diacetates [**5a**,**5b**] which behaved as one on tlc and gc. This mixture does not present any carboxylic acid absorptions in the ir but does show an alcoholic group which must be tertiary, since protons geminal to the hydroxyl are not seen in $^1$H nmr. Hrms gave a molecular formula $C_{23}H_{30}O_7$. All these data indicate the lactol structure **5** which must have been formed by the opening of **4** to its ketophenol tautomer and subsequent acid group attack on the ketone. Treatment of **5a** plus **5b** with $CH_2N_2$ gives a single product, the physical and spectral data of which are completely superimposable on those of **2** and which must have been formed via the tautomeric keto-acids of **5a** plus **5b**.

Detailed study of the $^1$H-nmr and $^{13}$C-nmr parameters of **5a** plus **5b** shows that it




| | R | R′ | R″ | A/B |
|---|---|---|---|---|
| **5a** | Ac | O | OH | *cis* |
| **5b** | Ac | O | OH | *trans* |
| **6** | H | O | OH | *cis* |
| **7** | H | $CH_2$ | H | *trans* |

is indeed a mixture of the two epimers at C-5 in the proportion **5b**:**5a** = 2:1, and so $^1$H-nmr at 25° show two groups of three methyls each with relative intensities 2:1; the H-15 signals which appear as heptets centered at 2.80 δ and 2.90 δ and the H-1 β broad singlets at 3.23 and 3.29 δ are almost duplicated. One of the methyls of the minor product [**5a**] is shielded, appearing at 0.70 δ as a broad singlet. When the spectrum is taken at 50°, this signal and those of H-15 at 2.60 δ and of H-1 β at 3.23 δ are sharpened, indicating that in **5a** both chair forms of ring A must be present with an apprec-

TABLE 5. Atomic Coordinates of Molecule B

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O5 | 0.4392(3) | 0.2750(7) | 0.6188(15) |
| O7 | 0.4368(3) | −0.0235(8) | 1.0147(16) |
| O11 | 0.5117(2) | 0.2209(6) | 0.6817(13) |
| O12 | 0.5755(2) | 0.1728(6) | 0.7867(11) |
| O21 | 0.5234(4) | 0.1117(8) | 0.5057(14) |
| O23 | 0.5730(3) | 0.2953(8) | 0.9297(18) |
| O25 | 0.4581(3) | 0.0218(8) | 1.2485(18) |
| C1 | 0.4179(4) | 0.1782(12) | 0.9645(28) |
| C2 | 0.4304(5) | 0.2386(14) | 1.1011(25) |
| C3 | 0.4594(5) | 0.3067(12) | 1.0516(22) |
| C4 | 0.4525(4) | 0.3392(11) | 0.8755(22) |
| C5 | 0.4484(4) | 0.2635(11) | 0.7594(22) |
| C7 | 0.4567(5) | 0.0207(10) | 1.0885(23) |
| C8 | 0.4863(4) | 0.0747(9) | 1.0114(19) |
| C9 | 0.4820(4) | 0.1331(8) | 0.8877(16) |
| C10 | 0.4449(4) | 0.1676(11) | 0.8343(24) |
| C11 | 0.5138(3) | 0.1602(8) | 0.8135(16) |
| C12 | 0.5466(3) | 0.1370(9) | 0.8751(19) |
| C13 | 0.5507(4) | 0.0827(9) | 1.0101(20) |
| C14 | 0.5195(4) | 0.0506(8) | 1.0746(19) |
| C15 | 0.5876(3) | 0.0619(12) | 1.0683(20) |
| C16 | 0.5901(5) | −0.0325(12) | 1.1229(27) |
| C17 | 0.5979(4) | 0.1216(12) | 1.2027(25) |
| C18 | 0.4836(5) | 0.3972(10) | 0.8170(30) |
| C19 | 0.4183(5) | 0.3980(12) | 0.8660(27) |
| C20 | 0.4320(4) | 0.1042(10) | 0.6938(25) |
| C21 | 0.5172(5) | 0.1880(11) | 0.5335(22) |
| C22 | 0.5155(6) | 0.2571(12) | 0.4124(21) |
| C23 | 0.5483(5) | 0.2572(12) | 0.8190(31) |
| C24 | 0.6105(4) | 0.2898(12) | 0.6889(26) |
| C25 | 0.4342(6) | −0.0365(13) | 1.3371(23) |

iable barrier between them, only possible, as shown by Dreiding models, if the A/B juncture is *cis* (6,7). When heated, the molecule will adopt the more stable conformation of ring A, with the 18-Me and the aromatic ring axial (in this conformation there

TABLE 6. Atomic Coordinates of Molecule A

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O5 | 0.8349(2) | 0.1491(7) | 0.7476(13) |
| O7 | 0.7785(3) | 0.5067(7) | 0.4547(18) |
| O11 | 0.7690(2) | 0.1287(5) | 0.5702(11) |
| O12 | 0.7042(2) | 0.1308(5) | 0.4336(12) |
| O21 | 0.7801(3) | 0.0679(7) | 0.3252(15) |
| O23 | 0.6845(3) | 0.1703(7) | 0.6782(14) |
| O25 | 0.8146(3) | 0.4276(8) | 0.2923(15) |
| C1 | 0.8287(4) | 0.3618(10) | 0.6725(25) |
| C2 | 0.8025(6) | 0.3975(10) | 0.8043(26) |
| C3 | 0.7737(6) | 0.3221(15) | 0.8615(24) |
| C4 | 0.7947(4) | 0.2429(10) | 0.8870(21) |
| C5 | 0.8158(4) | 0.2123(10) | 0.7400(19) |
| C7 | 0.7877(5) | 0.4362(10) | 0.3896(29) |
| C8 | 0.7682(3) | 0.3527(9) | 0.4166(19) |
| C9 | 0.7811(4) | 0.2782(8) | 0.5002(16) |
| C10 | 0.8168(3) | 0.2732(9) | 0.5955(21) |
| C11 | 0.7578(3) | 0.2082(9) | 0.4885(16) |
| C12 | 0.7251(3) | 0.2080(8) | 0.4253(15) |
| C13 | 0.7119(3) | 0.2801(9) | 0.3481(19) |
| C14 | 0.7343(3) | 0.3532(8) | 0.3441(21) |
| C15 | 0.6752(4) | 0.2836(10) | 0.2698(23) |
| C16 | 0.6553(4) | 0.3658(13) | 0.3131(31) |
| C17 | 0.6778(4) | 0.2687(15) | 0.0895(27) |
| C18 | 0.7680(5) | 0.1685(14) | 0.9354(23) |
| C19 | 0.8179(5) | 0.2409(18) | 1.0315(23) |
| C20 | 0.8449(4) | 0.2399(10) | 0.4677(18) |
| C21 | 0.7814(4) | 0.0650(9) | 0.4695(23) |
| C22 | 0.7933(4) | −0.0121(9) | 0.5664(22) |
| C23 | 0.6853(4) | 0.1195(10) | 0.5714(20) |
| C24 | 0.6645(3) | 0.0374(8) | 0.5622(19) |
| C25 | 0.8335(5) | 0.5096(13) | 0.2617(26) |

are fewer 1,3-diaxial interactions). This is consonant with the 18-Me being found at 0.70 δ in the $^1$H-nmr at 50°, when shielded by the aromatic ring. Moreover, in the $^{13}$C-nmr of **5a** plus **5b**, although many signals of the carbons of both products are superimposed, those corresponding the C-5 are well differentiated, in **5a** appearing as a singlet at 105.6 ppm and in **5b** at 107.2 ppm, while C-14 appears in **5a** as a doublet at 127.3 ppm and in **5b** as a doublet at 127.0 ppm, maintaining the same ratio of intensity as in the $^1$H-nmr.

Therefore, salvicanaric acid [**4**] would appear to be a natural product with **1** and **2** as artifacts of the acetylation and methylation of the first fraction studied. However, there is also a possibility of **4** having been formed from **6** which in its turn could be a biosynthetic oxidation product of demethylcryptojaponol [**7**].

## EXPERIMENTAL

The plant material was collected in Montaña Cardones, Arucas (Gran Canaria), Spain, during May 1983. A voucher specimen is lodged with the Departamento de Botánica, Facultad de Biología, Universidad de La Laguna, Tenerife, Spain.

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were determined of a Kofler apparatus and are un-

corrected. Optical activities were measured on a Perkin-Elmer 241 polarimeter. Ir spectra were recorded on a Perkin-Elmer 681. Mass spectra were taken on a VG Micromass LTD-ZAB-2F spectrometer operating at 70 eV in the electron impact mode. Uv spectra were taken on a Perkin-Elmer 550 SE spectrophotometer. $^1$H-nmr spectra were obtained with Brüker WP-200 SY and Perkin-Elmer R-12E spectrometers. Chemical shifts are expressed as units δ. $^{13}$C-nmr were taken on a Brüker WP-200 SY. Gc was carried out on a Hewlett-Packard 5790A with an OV-1 micro-capillary column.

ISOLATION OF THE CONSTITUENTS.—The powdered roots of *S. canariensis* (3 kg) were exhaustively extracted with $Me_2CO$ at room temperature. Evaporation of the solvent afforded 25.8 g of crude extract that was subjected to Si gel (0.063-0.2 mm) column separation. The column was eluted with a gradient of *n*-hexane and EtOAc, beginning with *n*-hexane, and fractions of 150 ml were collected.

Under tlc the fractions eluted with 20% EtOAc yielded two products with very close Rf which could not be purified by repeated Si gel chromatography. When the ir and nmr showed no signals for acetate or methyl groups, the substances were acetylated with $Ac_2O$ in the usual way and then dissolved in $Et_2O$ and treated with $CH_2N_2$. The 760.9 mg of crude material obtained was chromatographed on Si gel (0.063-0.2 mm) columns with 8% *n*-hexane/EtOAc collected in 5-ml fractions and yielded **1** (196.3 mg) and **2** (295.7 mg).

The fractions eluted with 30% EtOAc yielded **4** (130 mg) when subjected to further Si gel (0.063-0.2 mm) chromatography.

METHYL (*R*)-2-(1,3,3-TRIMETHYL-2-OXOCYCLOHEXYL)-3,4-DIACETOXY-5-ISOPROPYL-BENZOATE [**2**].—Crystallized from *n*-hexane/EtOAc, mp 132.3°; ir ($CHCl_3$) 3020, 2960, 2860, 1770, 1760, 1720, 1685, 1465, 1430, 1400, 1365, 1310, 1240, 1190, 1170, 1160, 1075, 1025, 940, 865 cm$^{-1}$; uv λ max (EtOH) nm 285; $^1$H-nmr (Table 1); $^{13}$C nmr (Table 2); ms *m/z* (rel. int.) 432 ($M^+$, 2.1), 404 (4.5), 401 (1.4), 390 (5.9), 373 (2), 361 (59.8), 360 (7.8), 348 (11), 330 (42.6), 320 (37.6), 315 (18.9), 303 (15.6), 301 (10), 287 (20.4), 274 (90.2), 264 (39.8), 259 (28), 249 (31.8), 237 (33.7), 232 (33.4), 221 (36.8), 220 (7.9), 217 (34.8), 199 (38.8), 189 (26.6), 175 (15.4), 161 (13.2). Anal calcd. for $C_{24}H_{32}O_7$: MW, 432.2148. Found: MW, 432.2149 (hrms).

X-RAY DATA.[1]—$C_{24}H_{32}O_7$, (MW=432.521) Crystallizes in the orthorhombic space group $P2_12_12_1$, with a=37.681 (2), b=15.279 (1), and c=8.2167 (4), Z=8, Dc=1.2174 g/cm$^3$, F(000)=1864. Cell parameters were determined by least-squares from θ values, measured from 22 strong reflexions with CuKα radiation (λ=1.5418 Å) on a four-circle diffractometer (Phillips 1100).

A colorless needle-shape crystal of size 0.15×0.20×0.08 mm was used to collect the data on a four-circle diffractometer Phillips PW 1100 with graphite monochromated CuKα radiation. The intensities of two standard reflections were measured every 90 reflections and showed no decay in intensity with time. Of 4011 unique reflections measured to a maximum θ=65°, 2343 reflexions with $I>2\sigma(I)$ were considered observed and used for the structure analysis. The data were corrected for Lorentz and polarization factors and put on an absolute scale with a Wilson plot. The number of variables is 559, the degrees of freedom 1784 and the ratio of freedom 4.19. The absorption correction was neglected (μ=6.921 cm$^{-1}$).

The structure was solved by direct methods (MULTAN) (9), a successive Fourier syntheses. Scattering factors for neutral atoms were taken from The International Tables for X-Ray Crystallography (10). The refinement was performed by least-squares analysis using anisotropic thermal coefficients for non-H atoms and isotropic fixed contribution for H-atoms.

A weighting scheme was chosen to obtain flat dependence of $<\Delta^2F>$ vs. <Fo> and $<\sin\theta/\lambda>$.

SALVICANARIC ACID ACETATE METHYL ESTER [**1**].—A light yellow oil $[\alpha]^{25}D$ −72.0 (*c* 0.072, $CHCl_3$); ir ($CHCl_3$) 3750, 2950, 2930, 2860, 1760, 1715, 1615, 1575, 1450, 1430, 1410, 1360, 1280, 1240, 1190, 1175, 1160, 1080, 1070, 1035, 1012, 975, 950, 920, 895 cm$^{-1}$; $^1$H nmr (Table 1); ms *m/z* (rel. int.) 390 ($M^+$, 20.3), 372 (0.5), 348 (66.7), 330 (5.4), 320 (25.7), 319 (11.8), 315 (11.5), 277 (17.4), 274 (13.5), 264 (17.3), 249 (30.4), 237 (26.4), 236 (24.6), 232 (24.1), 221 (21.6), 219 (19.4), 217 (22.3). *Anal* calcd. for $C_{22}H_{30}O_6$: MW, 390.2051. Found: MW, 390.2061 (hrms).

SALVICANARIC ACID METHYL ESTER [**3**].—Compound **1** was treated with KOH-MeOH at room temperature for 15 min, yielding **3** as a colorless gum; ir ($CHCl_3$) 3550, 2950, 2930, 2860, 1725, 1710, 1620, 1580, 1500, 1475, 1460, 1430, 1420, 1370, 1355, 1325, 1240, 1090, 1070, 1040, 1010, 972, 945, 915, 890 cm$^{-1}$; $^1$H nmr (Table 1); $^{13}$C nmr (Table 2); ms *m/z* (rel. int.) 348 ($M^+$, 80.5), 330 (13), 320 (25.4), 315 (16.2), 288 (8.7), 277 (36.1), 274 (36.1), 264 (35), 259 (22.1), 249 (80.4), 236 (61),

[1]Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK.

group of very intense peaks between 235-205, 203-189, and 175-115, 91 (29.2), 69 (34.5), 55 (54.2), 43 (52.1), 41 (100), 32 (87.7). *Anal* calcd. for $C_{20}H_{28}O_5$: MW, 348.1919. Found: MW, 348.1903 (hrms).

REACTION OF **2** WITH KO-*t*-BU/DMSO AND SUBSEQUENT ACETYLATION.—Compound **2** was treated with a solution of KO-*t*-Bu in DMSO and refluxed for 5 h under $N_2$ atmosphere. A product with spectral data identical to those of **3** was obtained in abundance. This product was then acetylated with $Ac_2O$-pyridine (25°, 12 h) yielding a substance with the same spectroscopic properties and optical activity as **1**.

SALVICANARIC ACID [**4**].—Obtained as a colorless foam; ir ($CHCl_3$) 3550, 2950, 2930, 2860, 1680, 1620, 1580, 1455, 1415, 1355, 1315, 1265, 1230, 1085, 995, 920, 890 $cm^{-1}$; $^1H$ nmr (Table 1); $^{13}C$ nmr (Table 2); ms *m/z* (rel. int.) 334 ($M^+$, 31.4), 316 (13), 306 (8.6), 301 (10.9), 263 (18.2), 260 (13.2), 245 (12.4), 235 (33.4), 232 (11.4), 223 (30.7), 222 (31.4), 219 (39.4), 217 (31.2), 205 (13), 149 (22), 91 (13.1), 83 (10.3), 77 (10.9), 69 (20), 57 (100), 55 (33), 41 (80), 39 (20), 29 (43), 27 (29). *Anal.* calcd. for $C_{19}H_{26}O_5$: MW, 334.1780. Found: MW, 334.1780 (hrms).

SALVICANARIC ACID ACETYLATION PRODUCTS [**5a**,**5b**].—Compounds **5a** plus **5b** were obtained by treatment of **4** with $Ac_2O$-pyridine (25°, 24h), yielding a colorless gum. The mixture of **5a** and **5b** epimers was not separable by gc. $|\alpha|^{25}D$ +46.76 (*c* 0.3, $CHCl_3$); ir ($CHCl_3$) 3590, 3020, 2960, 2930, 2870, 1770, 1715, 1609, 1460, 1420, 1365, 1310, 1295, 1192, 1170, 1155, 1010, 970 $cm^{-1}$; $^1H$ nmr at 50°, **5a** (200 MHz, $CDCl_3$) δ 0.70 (3H, s), 1.21, 1.26 (each 3H, d), 1.3 (3H, s), 1.5 (3H, s), 2.29, 2.30 (each 3H, s), 2.9 (1H, h), 3.23 (1H, s broad), and 8.1 (1H, s); **5b** (200 MHz, $CDCl_3$) 1.15, 1.26, 1.38 (each 3H, s), 1.21, 1.26 (each 3H, d), 2.27, 2.29 (each 3H, s), 2.8 (1H, m), 3.29 (1H, s broad), and 8.1 (1H, s); $^{13}C$ nmr ($CDCl_3$) δ 18.2, 19.0, 20.5, 20.9, 22.9, 25.2, 25.4, 25.7, 25.9, 27.8, 31.9, 34.4, 36.2, 37.9, 39.7, 41.7, 43.6, 45.7, 77.4, 105.6, 107.2, 124.7, 124.9, 127.0, 127.3, 138.7, 141.0, 141.4, 145.5, 145.7, 163.9, 167.7; ms *m/z* (rel. int.) 418 ($M^+$, 3.6), 400 (1.6), 376 (2.4), 358 (15.4), 347 (4), 334 (7.9), 316 (54.6), 303 (10.5), 289 (11.7), 279 (10.8), 261 (26.6), 260 (11.4), 247 (15.6), 234 (53.4), 232 (14), 231 (9.4), 219 (44.1), 217 (11.8), 203 (8.6), 167 (11.2), 149 (74), 113 (16.7). *Anal* calcd. for $C_{23}H_{30}O_7$: MW, 418.1976. Found: MW, 418.1961 (hrms).

REACTION OF [**5a**,**5b**] WITH $CH_2N_2$.—The mixture **5a** plus **5b** was dissolved in $Et_2O$ and treated with $CH_2N_2$ for 24 h, yielding a product with identical spectroscopic properties with **2**.

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