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DESACETYLUVARICIN FROM *UVARIA ACCUMINATA*, CONFIGURATION OF UVARICIN AT C-36

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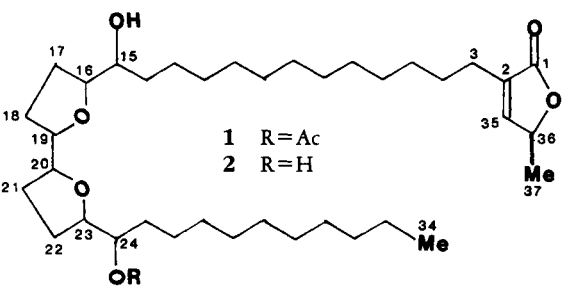
DISCUSSION

As part of our continuing search for plants containing tumor inhibitory constituents, we isolated and determined the constitution of the antitumor agent uvaricin (**1**) (1). We now report that it is accompanied in this extract by a free diol (**2**), which we term desacetyluvaricin, and that we have determined the C(36) configuration of these substances to be *S*.



From the chromatography fractions just after those containing uvaricin (**1**) (1), we isolated a colorless crystalline substance with mp 63-65°, whose ir spectrum showed all characteristic group absorption bands displayed by **1** except the acetate carbonyl band. Its ^{1}H-nmr spectrum was similar to that of uvaricin (**1**), but it lacked the acetate methyl singlet at 2.05 and had *two* broad singlets for OH protons (at 2.34 and 2.63) rather than one (at 2.47). That this substance was desacetyluvaricin (**2**) was supported by finding all of the peaks for protons attached to carbons 1-18 and 26-37 within 0.01 ppm of where they were reported for **1**; HC(24) shifted from 4.94 in **1** to the 3.8-4.0 envelope [where HC(16), HC(19), HC(20), and HC(23) also absorbed] in **2**, and HC(25) shifted from 1.55 to 1.28. Confirmation came from the ^{13}C-nmr spectrum of **2**, which had peaks within 0.1 ppm of those of **1** for C(1)-C(18) and C(26)-C(37), but lacked the acetyl peaks and showed C(19) and C(20) shifted from 82.0 and 81.6 to 82.2 and 82.4, C(23) from 80.7 to 82.9, C(24) from 75.5 to 71.6, and C(25) from 31.3 to 32.6. Since **2** has a peak at 77.3 but none at 75.5, it is now possible to assign the former peak in the spectrum of **1** to C(36) (which should absorb at the same place in both compounds) and the latter to C(24).

The mass spectrum of desacetyluvaricin (**2**), which essentially follows the fragmentation pattern outlined for uvaricin (**1**) (1), provided further support, showing a base peak at *m/z* 295, an extremely small molecular ion peak at *m/z* 606, and peaks at *m/z* 588, 570, and 552 corresponding to losses of one, two, and three molecules of H_2O. The fragments that lack the C-23 side-chain occur with the same masses, and those

that retain the C-23 side-chain are shifted to lower mass numbers by 42, as required by the substitution of a hydroxyl for an OAc group at C-24 in **2**.

To determine the absolute configuration of **1** and **2** at C(36), we ozonized uvaricin (**1**) with an oxidative workup in basic solution. The acidic fraction (15 mg), which contained lactic acid and a long-chain acid, was derivatized and subjected to glc on a column with a chiral stationary phase that had been shown to cleanly resolve the derivatives of (*R*)- and (*S*)-lactic acids (2). A peak was obtained coinciding with that of the derivative of (*S*)-lactic acid, indicating **1** (and by analogy **2**) to have the *S* configuration at C(36).

The configurations at the chiral centers in the middle of the chain are not known, but the large difference in the chemical shifts of HC(15) and HC(24) in the ^{1}H-nmr spectrum of **2** rules out the possibilities in which the C(15), C(16), and C(19) configurations are the same as those of C(24), C(23), and C(20), respectively (pseudo-twofold axis), or mirror them (pseudo-mirror plane).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Instrumental procedures were the same as in previous work by Jolad *et al.* (3).

ISOLATION OF DESACETYLUVARICIN (**2**).—Desacetyluvaricin (**2**), which had a lower Rf (0.28) than uvaricin (**1**; 0.68) [CH_2Cl_2-EtOAc (3:2), silica gel], was isolated from the EM SiO_2-60 column chromatography fractions following uvaricin (**1**) in the isolation procedure outlined by Jolad *et al.* (1). Purification by preparative tlc [CH_2Cl_2-EtOAc (3:2)] followed by crystallization from Et_2O-isopropyl ether (1:1 v/v) gave desacetyluvaricin (**2**) as tiny needles: mp 63° $[\alpha]^{25}D$ +9.3° (c 1.41, MeOH). Its ir [($CHCl_3$) 1755 cm^{-1}], ^{1}H-nmr, ^{13}C-nmr, and mass spectra were in accord with structure **2** (see text). Desacetyluvaricin (**2**) was not submitted for antitumor activity since it was obtained in very small amount.

Anal. calcd for $C_{37}H_{66}O_6$: C, 73.26; H, 10.89. Found: C, 72.79; H, 10.94.

OZONOLYSIS OF UVARICIN (**1**).—Uvaricin (**1**, 20 mg) was ozonized by bubbling a mixture of O_3 and O_2 through a solution in 8 ml EtOAc at 78° until a blue color was observed (20 sec). This solution was added to a stirred solution containing 4 ml 30% H_2O_2 and 4 ml 10% NaOH. After stirring overnight, washing with Et_2O, acidifying, extracting with Et_2O, and evaporating, the residue was derivatized with $CF_3CH_2N{=}C{=}O$ and run through a glc column with a stationary phase of XE-60-L-valine-(*S*)-phenylethylamide. A peak corresponding in position and shape to the (*S*)-lactic acid derivative was obtained (chromatography and co-chromatography).

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