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CHEMISTRY IN THE ANNONACEAE, XXII.[1] 14-HYDROXY-25-DESOXYROLLINICIN FROM THE STEM BARK OF *ANNONA RETICULATA*

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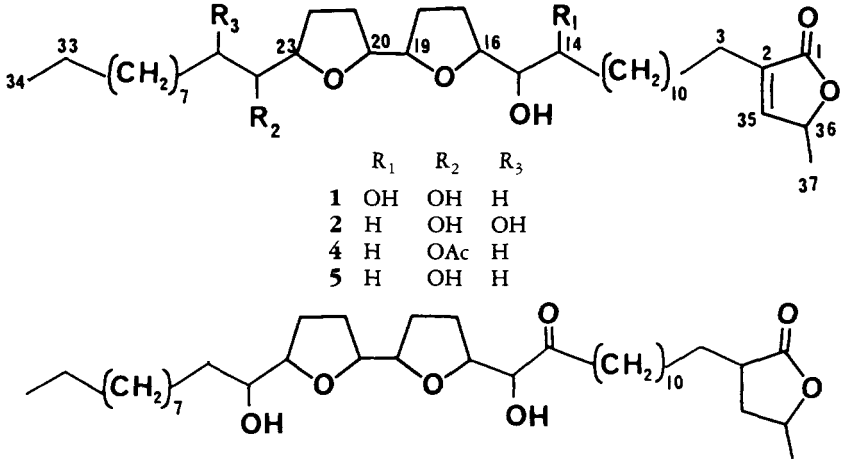
The genus *Annona* L., occurring widely in the neotropics and, to a lesser extent, in Africa (1), is primarily known as a source of alkaloids and diterpenes (2). Previous investigations of the Central American taxon *Annona reticulata* L. have yielded a number of alkaloids (2), but no terpenoid compounds have been reported. As part of our continuing investigation of the chemistry of the Annonaceae, we have reexamined the stem bark of *A. reticulata*, and, in addition to a number of diterpenes and a sesquiterpene, we have isolated a novel C_{37} bis-tetrahydrofuran acetogenin, a type of compound that has previously been reported from two other annonaceous genera, *Uvaria* (3,4) and *Rollinia* (5,6).

The novel acetogenin, which we have identified as **1**, was obtained from a silica gel column after elution of the terpenoid compounds. It was obtained as a waxy solid in a yield of 0.013% and had an optical activity of +15°. The eims failed to show a molecular ion, the highest fragment observed being for *m/z* 604 ($C_{37}H_{64}O_6^+$). However, the off-resonance ^{13}C nmr indicated 63 protons bonded to carbons, and acetylation yielded a triacetate, thereby requiring three hydroxyl moieties and leading to a final proton count of 66. This suggested that in the mass spectrum, **1** was undergoing facile loss of H_2O, thus requiring an empirical formula of $C_{37}H_{66}O_7$, identical to that recorded previously for rollinicin (**2**) (5) and rollinone (**3**) (6).



	R_1	R_2	R_3
1	OH	OH	H
2	H	OH	OH
4	H	OAc	H
5	H	OH	H

3

The mass spectral fragmentation of **1** revealed ions that could be assigned on the basis of fission between C-5/C-6, C-14/C-15, C-15/C-16, C-19/C-20, and C-23/C-24. A comparison of the data obtained (see Experimental section) with fragmentation patterns previously recorded for **2** (5) and **3** (6) revealed that **1** gave ions showing identical oxygenation levels to **3**, but C-5/C-6 fission gave *m/z*

[1]For Part XXI, see J.T. Etse and P.G. Waterman, *Phytochemistry*, (in press).

139 (normal furanone terminal group) rather than the *m/z* 141 (dihydrofuranone moiety) of the latter. By contrast for fission through C-15/C-16, C-19/C-20, and C-23/C-24, **2** gave ions with different oxygenation levels to those obtained from **1**, indicating the occurrence of different oxygenation patterns in the two compounds. Thus, on the basis of ms and ^{1}H- and ^{13}C-nmr spectroscopy, **1** must have the same oxygenation pattern as **3** but clearly possesses three secondary hydroxy groups and the α,β-unsaturated lactone moiety as found in **2** and in uvaricin (**4**) (3) and desacetyluvaricin (**5**) (4). From the above data, the new compound must be assigned structure **1**. The chirality of the asymmetric centers in **1** have not been established.

The finding of an acetogenin in *Annona* is not surprising, considering their previous isolation from *Rollinia*. These two genera are placed close to one another in the classifications of both Fries (1) and Hutchinson (7).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected. Uv spectra were measured in EtOH and ir spectra as KCl discs. ^{1}H-nmr spectra were run at 250 MHz and ^{13}C-nmr spectra at 90.56 MHz, in $CDCl_3$ using TMS as internal standard. High resolution eims were obtained on an AEI MS902 double focusing instrument by direct probe insert at elevated temperatures and at 70 eV.

PLANT MATERIAL.—Stem bark of *A. reticulata* was collected from the Santa Rosa National Park, Guanacaste Province, Costa Rica, and a voucher specimen has been preserved at the Herbarium of the Missouri Botanic Gardens, St. Louis, Missouri, as part of a general collection of plants from the Park (8).

ISOLATION OF 14-HYDROXY-25-DESOXY ROLLINICIN.—Ground stem bark (400 g) was macerated with ammoniacal MeOH for 5 days, the extract then being filtered and evaporated to dryness. The resulting solid (100 g) was refluxed with EtOAc and the extract subjected to column chromatography over silica gel 60. Elution of the column with petroleum ether (bp 40-60°) containing increasing amounts of EtOAc yielded sesqui- and diterpenes.[2] Continued elution with EtOAc alone gave crude **1** (55 mg) which was further purified by centrifugal preparative tlc (silica gel G; solvent, toluene-EtOAc-HOAc, 5:4:1) to give **1** (44 mg).

14-Hydroxy-25-desoxyrollinicin (**1**).—Waxy solid from $CHCl_3$, mp 68-70°, $[\alpha]^{25}+15°$ (c. 0.06, MeOH); uv max 218, 245 sh, 285, 293 sh, 332 nmr; ir max 3400, 3080, 2900, 1740, 1715, 1640, 1060 cm^{-1}; ^{1}H nmr δ 0.87 (t, J=6.5 Hz, 3H, 34-CH_3), 1.20-1.30 (br. s, 34H), 1.44 (d, J=7 Hz, 3H, 37-CH_3), 1.36-1.58 (m, 4H, 4-, 25-CH_2), 1.80-2.00 (m, 8H, 17-, 18-, 21-, 22-CH_2), 2.43 (m, 2H, 3-CH_2), 3.40 (m, 2H, 14-, 24-H), 3.80-3.97 (m, 5H, 15-, 16-, 19-, 20-, 23-H), 5.06 (dq, 1H, J=7, 1.5 Hz, 36-H), 7.19 (d, J=1.5 Hz, 1H, 35-H) ppm; ^{13}C nmr 13.9 q (C-34), 18.9 q (C-37), 22.5 t (C-33), 24.4-32.4 21 x t (C-4-C-12, C-17, C-18, C-21, C-22, C-26-C-32), 33.6 t (C-25), 37.3 t (C-13), 69.8 d (C-15), 71.3, 74.0 2 x d (C-14, C-24), 77.8 d (C-36), 82.0, 82.3, 82.7, 83.1 4 x d (C-16, C-19, C-20, C-23), 131.1 s (C-2), 151.6 d (C-35), 174.4 s (C-1) ppm; eims (*m/z*, rel. int.) 604.4635 (M^+-H_2O, 0.5%) (calcd. for $C_{37}H_{64}O_6$, 604.4703); the following significant fragments are listed according to the bond fission leading to their formation and then under (a) if arising from that part of **1** right of the fission bond (i.e., toward C-1) in structure **1** and (b) if from the left of the fission bond (i.e., toward C-34). All fragments listed were confirmed by high resolution measurements. Fission between C-5 and C-6, (a) 139 ($C_8H_{11}O_2^+$, 26%), 125 (139-CH_2, 6%), 111 (125-CH_2, 1%), 97 (111-CH_2, 1%), 83 (111-CO, 11%), 69 (97-CO, 62%) fission between C-14 and C-15, (a) 282 ($C_{19}H_{30}O_3^+$, 2%), (b) 341 ($C_{20}H_{37}O_4^+$, 0.5%). fission between C-15 and C-16, (a) 311 ($C_{18}H_{31}O_4^+$, 100%), 293 (311-H_2O, 5%), 275 (293-H_2O, 1%), 247 (275-CO, 1%), (b) 309 ($C_{19}H_{33}O_3^+$, 0.5%), fission between C-19 and C-20, (a) 381 ($C_{22}H_{37}O_5^+$, 17%), 363 (381-H_2O), 42%), 345 (363-H_2O, 14%), 317 (345-CO, 3%), (b) 241 ($C_{15}H_{29}O_2^+$, 11%), 223 (241-H_2O, 3%), fission between C-23 and C-24, (a) 451 ($C_{26}H_{43}O_6^+$, 5%), 433 (451-H_2O, 5%), 415 (433-H_2, 5%), (b) 169 ($C_{11}H_{21}O^+$, 1%), fission between C-27 and C-28, (b) 95 ($C_7H_{11}^+$, 21%), other fragments, 141 ($C_8H_{13}O_2^+$, 9%, bistetrahydrofuran system), 71 ($C_4H_7O^+$, 33%, tetrahydrofuran system).

14-Hydroxy-25-desoxyrollinicin triacetate.—Compound **1** (13 mg) was treated with Ac_2O-pyridine (8 ml) at room temperature for 12 h. Normal workup of the reaction mixture gave the triacetate (10 mg) as an oil; ir max 2940, 2850,

[2]P.G. Waterman and J.T. Etse, unpublished results.

1760, 1720 cm^{-1}; ^1H nmr δ 0.87 (t, 3H, 34-CH_3), 1.20-1.30 (br. s, 34H), 1.40 (d, 3H, 37-CH_3), 1.55-1.60 (m, 4H, 25-, 4-CH_2), 1.80-2.00 (m, 8H, 17-, 18-, 21-, 22-CH_2), 2.03, 2.05, 2.08 (3 x s, 3 x 3H, 3 x OAc), 2.51-2.57 (m, 2H, 3-CH_2), 3.80-4.10 (m, 4H, 16-, 19-, 20-, 23-H), 4.82-5.10 (m, 3H, 14-, 15-, 24-H), 5.03 (dq, 1H, 36-H), 7.19 (d, 1H, 35-H) ppm.

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