CHEMISTRY LETTERS, pp. 99-102, 1978. Published by the Chemical Society of Japan

LIMONOIDS FROM MELIA AZEDARACH LINN. VAR. JAPONICA MAKINO. II.[1] THE NATURAL HYDROXYL PRECURSOR OF SENDANIN

Masamitsu OCHI, Hiyoshizo KOTSUKI, and Hiroaki ISHIDA
Faculty of Science, Kochi University, Asakura, Kochi 780
and
Takashi TOKOROYAMA
Faculty of Science, Osaka City University, Osaka 558

Because sendanin is an artifact which has been isolated from M. azedarach Linn. var. japonica Makino only after the acetylation of crude limonoid fraction, the structure of the natural hydroxyl precursor was studied. The chemical and spectroscopic evidence revealed that it was an epimeric mixture of the hemiacetal 5.

We have recently reported the structure of sendanin (1) ($C_{32}H_{40}O_{12}$) which was isolated as a triacetate after the acetylation of crude limonoid fraction from the bark of M. azedarach Linn. var. japonica Makino.[1] Our continued effort has been directed to the elucidation of the structure of its natural hydroxyl precursor and we wish to present the result herewith.

Solvent partitions and careful silica gel column chromatography of a methanol extract of the bark of M. azedarach Linn. var. japonica Makino gave a mixture of limonoids (Fig. 1, mixture A), from which sendanin (1) was isolated on acetylation. Further separation of mixture A as it is was unsuccessful. Similar treatment of the fruit of this tree afforded the same mixture.

Alkaline hydrolysis of (1) yielded another mixture (Fig. 1, mixture B), which gave a pentaol (2), $C_{26}H_{34}O_9$, mp 246-249°C, $[\alpha]_D^{27}$ -41° (c 0.10, EtOH), as a major component. TLC analysis of mixture A and B indicated that the natural precursor of (1) was a compound of the intermediate polarity between (1) and the completely deacetylated compound, and suggested that the natural product occurred as an acetylated form in some degree. In order to decide the number and positions of the artifically introduced acetate groups in (1), mixture A was subjected to benzoylation (PhCOCl-pyridine) to give the two isomeric monobenzoates (3), $C_{37}H_{42}O_{12}$, mp 238-239°C, $[\alpha]_D^{9}$ +72° (c 0.11, EtOH), and (4), $C_{37}H_{42}O_{12}$, mp 206-208°C, $[\alpha]_D^{26}$ -19° (c 0.33, EtOH). A close structural similarity between (3) and (4) is observed in their IR and ^{1}H NMR (in $CDCl_3$) spectra. These data indicated the presence of two hydroxyl groups [(3): 3600 and 3420 cm^{-1}; (4): 3550 and 3500 cm^{-1}], two acetate groups [(3): 1755 and 1735 cm^{-1}, δ 2.02 and 2.15 (3H each, s); (4): 1740 and 1730 cm^{-1}, δ 2.01 and 2.15 (3H each, s)], and one benzoate group [(3): 1700 cm^{-1}, δ 7.36-8.07 (5H, m, typical for COPh); (4): 1700 cm^{-1} (shoulder), δ 7.36-8.12 (5H, m)] in both compounds.

The location of the benzoate group was deduced from following fact. In the

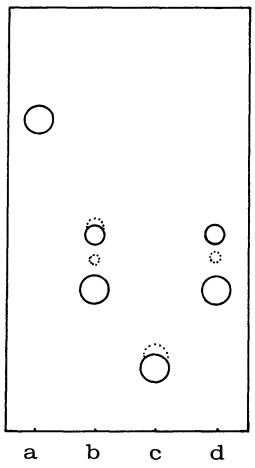
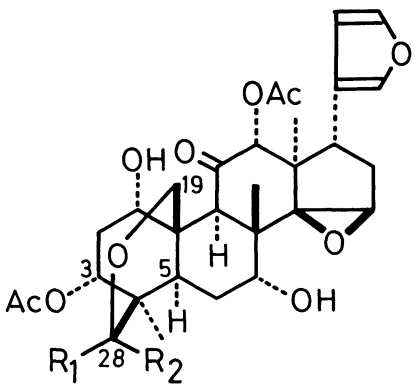
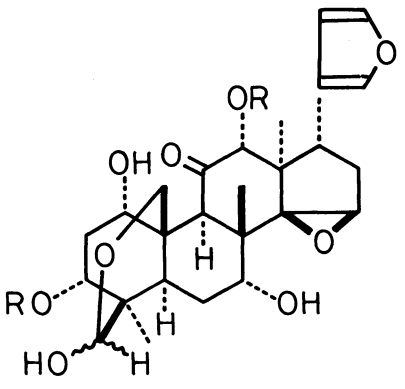


Fig. 1. Thin Layer Chromatogram of
a) Sendanin
b) Mixture A
c) Mixture B
d) Mixture C
Solvent: $CHCl_3$-MeOH (19:1)
Coloring: Ehrlich Reagent

^1H NMR spectra of (3) and (4), the signals due to the C-28 protons appear at a lower field [(3): δ 6.08; (4): δ 6.05] as compared with that of (1) (δ 5.76), the fact indicating the presence of benzoate groups at C-28 in (3) and (4) instead of the acetate group in (1). Consequently, it is concluded that (3) and (4) represent the epimers with respect to C-28.

The stereochemistry of (3) and (4) remains to be assigned and this is done by the examination of ^1H and ^{13}C NMR data. In the ^1H NMR spectra, the signals due to the C-3 protons in (3) and (4) are observed at δ 5.07 and 5.49 respectively, the former value falling in the normal range for the proton attached to an acetoxy-bearing carbon. In (1), where the exo-configuration of the acetoxyl group has been established, the corresponding signal appears at δ 5.25. Taking account of the fact[2] that the alcoholic oxygen[3] disposed in a 1,3-diaxial relationship exerts a marked deshielding effect, the above data suggest that the benzoate groups in (3) and (4) have endo- and exo-configurations respectively. In accordance with this assignment, the signals due to the C-19 methylene protons in (3) appear as an AB quartet (δ 4.38 and 4.46, J_{AB} = 12 Hz), while those in (1) and (4) are singlets (δ 4.31 and 4.42 respectively). The inspection of the model





1 R_1 = OAc, R_2 = H

2 R = H

3 R_1 = H, R_2 = OCOPh

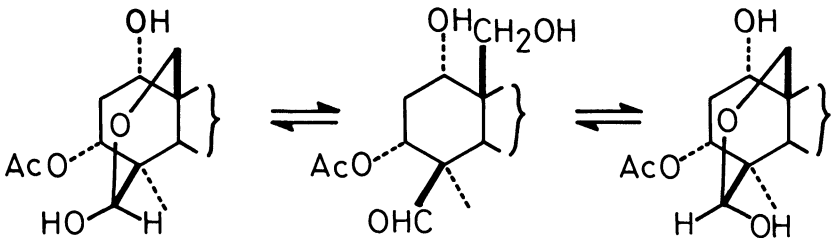
4 R_1 = OCOPh, R_2 = H

5 R = Ac

shows that the C-28 substituent in (3) is in a 1,3-diaxial relationship with the axial hydrogen at C-19, and the magnetic non-equivalence of the protons in this methylene group would be reasonably expected. The ^{13}C NMR spectroscopy provides even more convincing evidence. All of the corresponding ^{13}C resonances of (1) and (4) are observed at very close fields, while among those in (3) only the signals due to the C-3, C-5, and C-19 carbons show the significant shifts from the resonance positions of (4) [$\delta_C(3) - \delta_C(4) = +2.3$, -2.7, and -3.9 respectively]. The shielding of the signals due to the C-5 and C-19 carbons in (3) is excellently explainable by the γ-effect of the axial benzoyloxy group. Such an effect is well established in α-anomers of aldopyranoses, their acetates, and methyl glucosides,[4] the effect across the ether oxygen being usually more prominent [i.e. C-19 in (3)]. The deshielding of the C-3 carbon resonance in (3) relative to that in (4) simply results from the release of the γ-gauche effect which had existed in (4).

The afore-mentioned data suggest that the genuine form of sendanin (1) in the plant would be an equilibrium mixture as shown in Scheme 1. This was confirmed by the selective debenzoylation of (3) and (4). Thus, the treatment of (3) and (4) with oxalic acid[5] yielded an identical mixture (Fig. 1, mixture C), which gave rise to sendanin (1) on acetylation and from which the major component was obtained in a crystalline form (5a), $C_{30}H_{38}O_{11}$, mp 273-276°C, $[\alpha]_D^{27}$ +2.0° (c 0.10, $CHCl_3$). The ^1H NMR spectrum (in C_5D_5N) of (5a) shows the presence of two acetate groups (δ 1.95 and 2.10) and one hemiacetal group (δ 5.28). The appearance of the C-3 proton signal at rather deshielded position (δ 5.90) and the equivalence of the C-19 methylene protons again indicate the exo-configuration of the hemiacetal hydroxyl group.[6]

The absence of the aldehyde proton signal in the ^1H NMR spectra of mixture B and C indicates that the aldehyde form is essentially absent in both mixtures.



5a 5b

Scheme 1

References and Notes

1) M. Ochi, H. Kotsuki, K. Hirotsu, and T. Tokoroyama, Tetrahedron Lett., 1976, 2877.
2) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd Ed., Pergamon, Oxford (1969), p. 81; N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Franscisco (1964), p. 185-190; T. Goto and K. Tori in "Jikken-Kagaku-Koza," Supplement 12, Maruzen, Tokyo (1967), p. 356-360.
3) The deshielding effect of the hydroxyl groups is most prominent and the acylation somewhat diminishes the degree of the paramagnetic shift.
4) N. C. Wilson and J. B. Stothers in E. L. Eliel and N. L. Allinger Ed., "Topics in Stereochemistry," Vol. 8, John Wiley and Sons, New York (1974), p. 63.
5) T. Kubota, T. Matsuura, T. Tsutsui, S. Ueo, H. Irie, A. Numata, T. Fujita, and T. Suzuki, Tetrahedron, 22, 1659 (1966).
6) Naturally the contribution of the solvent effect to this shift should be taken into account. When the spectrum was taken in a mixture of $CDCl_3$ and $(CD_3)_2SO$ (3 : 1), the signals due to the endo isomer (5b) were also observed in a proportion of 1/5 - 1/4, indicating that an equilibrium of the isomers had attained in the presence of trace of the acid in $CDCl_3$. δ (exo, endo): C_4 α-Me (0.78, 0.82), C_8-Me (1.10, 1.15), H_9 (3.82, 3.79), H_{28} (4.80, 4.64), H_{12} (5.00, 5.05), and H_3 (5.21, 4.71).

(Received November 14, 1977)