The Properties of Some Arjunolic Acid Derivatives

By Shin-ichi SASAKI, Hung Cheh CHIANG, Kazuo HABAGUCHI
Hong-Yen HSÜ and Koji NAKANISHI

Department of Chemistry, Tohoku University, Katahira-cho, Sendai

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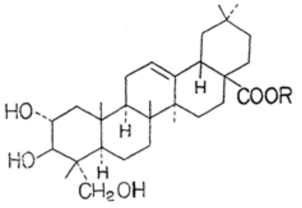
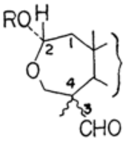
In connection with our investigations of South-East Asian plants,[1] the roots of *Psidium guaijava L.* ("banjiro" or "banzakuro") from Taiwan were studied because of the reputed cancerostatic activity of this Chinese herb. Since the ether extract was an intractable mixture, it was first methylated; the ester was then chromatographed and recrystallized. This ester eventually turned out to be methyl arjunolate,[2] the methyl ester of arjunolic acid (1).[3,4] Preliminary chemical and spectroscopic studies carried out prior to its identification, however, disclosed a few points worthy of comment; these points will be reported below.

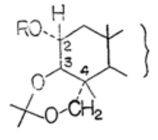
Although the product obtained by the periodate oxidation of the ester 2 was analyzsed in the correct manner for a dialdehyde, it afforded only a mono-2, 4-dinitrophenylhydrazone, and its NMR spectrum showed only one aldehydic proton as a singlet (9.09 p. p. m.). Furthermore, the one-proton quartet (*J* 9.5 and 5 c. p. s.) that newly appeared at 5.12 p. p. m. in the oxidation product was shifted to 6.01 p. p. m. (*J* 9.1 and 5) in its acetate, a behavior which is characteristic of hemiacetals.[5] As has been mentioned above, the aldehyde proton signal is a singlet; therefore, the aldehyde group must be attached to a tertiary carbon atom. It follows that the structures of the oxidation product and its acetate should be 3 and 4 respectively, and that they are derived by means of hemiacetal formation between the primary hydroxyl group and the 2-aldehyde group. The C_2–H in Structures 3 and 4 is represented as β-axial in view of its 9.5- and 5-c. p. s. coupling constants.

The ester 2 afforded an acetonide 5 when reacted with acetone and cupric sulfate; the acetonide is formed between the 3-OH and 4-CH_2OH, as is evidenced by the appearance of a one-proton multiplet due to C_2-H at 5.5 p. p. m. in the NMR spectrum of the acetonide acetate 6.



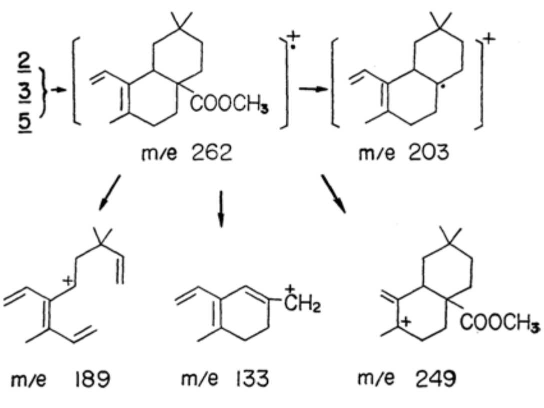


1 R=H 2 R=Me 3 R=H 4 R=Ac } (C_{20} as COOMe)



5 R=H 6 R=Ac } (C_{20} as COOMe)

The mass spectra of methyl arjunolate 2, the hemiacetal 3, and the acetonide 5 are very similar in the high mass range in that they are characterized by peaks at *m/e* 262, 249, 203, 189 and 133, all derived from a retro-Diels-Alder-type cleavage of the β-amyrin skeleton.[6]



Experimental

The mass spectra were measured with a Hitachi RMU-6D model; ionizing energy: 70 eV.; ionizing chamber heater: 250°C; evaporation temperature: 200°C.

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1) Cf. K. Nakanishi, S. Sasaki, A. K. Kiang, J. Goh, H. Kakisawa, M. Ohashi, M. Goto, J. Watanabe, H. Yokotani, C. Matsumura and M. Togashi, *Chem. Pharm. Bull.* **13**, 882 (1965).

2) We are grateful to Professor R. E. Corbett, University of Otago, New Zealand, and Professor E. Ritchie, Department of Organic Chemistry, University of Sydney, Australia, for gifts of arjunolic acid derivatives.

3) F. E. King, T. J. King and J. M. Ross, *J. Chem. Soc.*, **1954**, 3995.

4) F. E. King, T. J. King and J. D. White, ibid., **1958** 2830.

5) For example: P. de Mayo, R. E. Williams and E. Y. Spencer, *Can. J. Chem.*, **43**, 1357 (1965).

6) H. Budzikiewicz, J. M. Wilson and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3688 (1963),

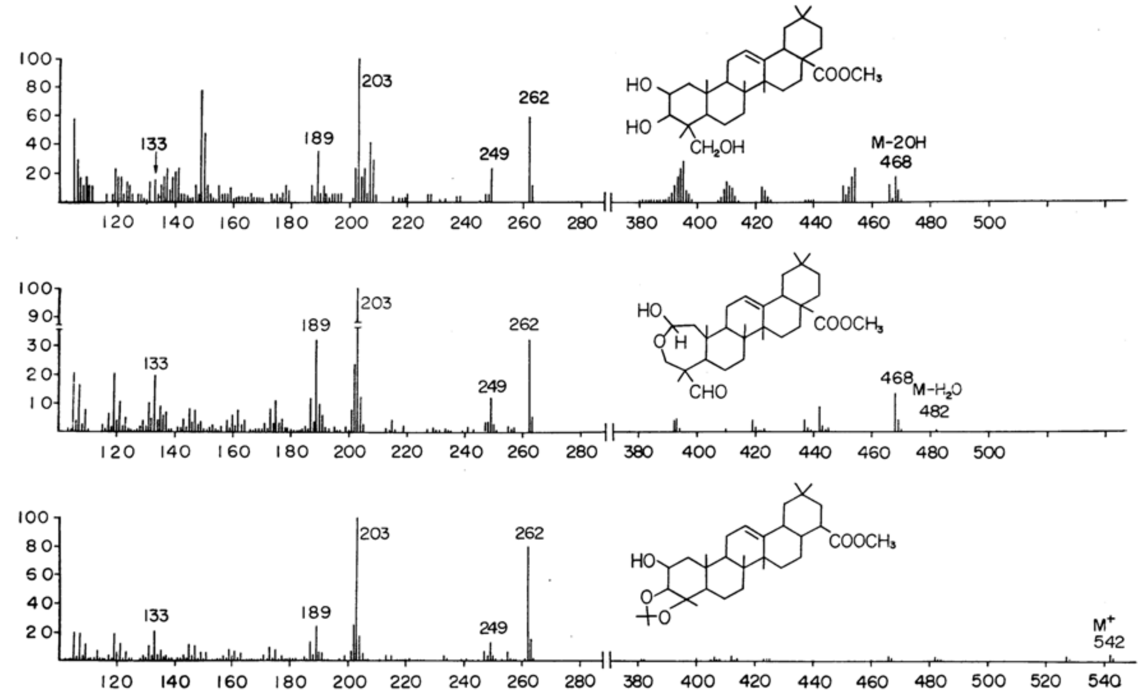

Fig. 1. Mass spectra of arjunolic acid derivatives.

The Extraction of Arjunolic Acid.—The roots (10 kg.) of pulverized *Psidium guaijava L.* were extracted continuously with ethanol to give 300 g. of a brown powder. After the powder had been extracted with petroleum ether, the residue was extracted with ether; when the ether extract was evaporated, 25 g. of a crude pale yellow residue was obtained. This was dissolved in methanol and treated with diazomethane; the solution was then passed through a column of silicic acid (1250 g., 100 mesh, Mallinckrodt) and eluted with chloroform to yield 2.5 g. of crude crystals. Several recrystallizations from acetone gave 2.0 g. of pure methyl arjunolate as white needles; m. p. 240—242°C, $[\alpha]_D$ 60.75° (c 1.0%, $CHCl_3$). ν_{max}^{KBr} 3425, 1730, 1460, 1385, 1365, 1040 cm^{-1}.

Found: C, 74.08; H, 10.01. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03%.
The compound was identified as methyl arjunolate by a mixed melting point test and by a comparison of its IR spectrum with that of an authentic specimen.[2)]

The Periodate Oxidation of Methyl Arjunolate.—A solution of 100 mg. of the ester 2 in 20 ml. of ethanol was treated with 100 mg. of sodium periodate dissolved in 2 ml. of water; the mixture was then left in the dark for 24 hr. The crystalline precipitate was filtered and recrystallized several times from ethanol to give 60 mg. of needles; m. p. 200—201°C, $[\alpha]_D$ 191.8° (c 1.0% $CHCl_3$), ν_{max}^{KBr} 3530, 2720 1725 cm^{-1}.

Found: C, 74.50; H, 9.61. Calcd. for $C_{31}H_{48}O_5$; C, 74.36; H, 9.66%.

2, 4-*Dinitrophenylhydrazone;* m. p. 194—196°C.

Found: C, 65.54; H, 7.95; N, 8.08. Calcd. for $C_{37}H_{52}O_6N_4$: C, 65.59; H, 7.70; N, 8.23%.

The Acetate 4 (prepared by the treatment of 3 with acetic anhydride-pyridine): m. p. 197—198°C.

Found: C, 73.79; H, 9.31. Calcd. for $C_{33}H_{50}O_6$: C, 73.03; H, 9.31%.

The Acetonide 5.—The methyl ester 2 (200 mg.), dissolved in 40 ml. of anhydrous acetone, was treated with 1.8 g. of anhydrous cupric sulfate and the mixture was then stirred for 24 hr. at room temperature. The mixture was filtered, the filtrate was dried in vacuo, and the residual solid was dissolved in chloroform and chromatographed through silicic acid (100 mesh, Mallinckrodt) to yield the acetonide 5. The crude compound was recrystallized from ethanol and then from acetone to give 120 mg. of needles, m. p. 152—153.5°C.

Found: C, 74.45; H, 9.30. Calcd. for $C_{34}H_{54}O_5$: C, 75.23; H, 10.03%.

The Acetate 6: m. p. 197—200°C.

Found: C, 74.18; H, 9.77. Calcd. for $C_{36}H_{56}O_6$: C, 73.93; H, 9.65%.

We are grateful to the Toyo Rayon Company for the grant which enabled us to purchase the RMU-6D mass spectrometer.