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STRUCTURES OF PHARBITIC ACIDS C AND D

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The purgative "resin glycosides" such as pharbitin (1) and convolvulin (2) are commonly found in the Convolvulaceae plants and regarded as complex glycolipids in which a number of units of a hydroxyfatty acid glycoside are combined with each other and some of the free hydroxyl groups are esterified with several kinds of organic acids. In spite of the recent advances in the chemistry of glycolipids, particularly of animal origin, the "resin glycosides" have received little attention, the structures have remained unknown, and except for muricatin B ((+)-11-hydroxyhexadecanoic acid 4-O-L-rhamnopyranosyl-L-rhamnopyranoside) (3) even any of their component glycosidic fatty acids has not been characterized in detail.

"Pharbitic acid" (I) (4) which is obtained along with (+)-α-methylbutyric, valeric, tiglic and α-methyl-β-hydroxybutyric acids on alkaline hydrolysis of pharbitin of the seeds of Pharbitis Nil Choisy is only known to consist of ipurolic acid ((+)-3,11-dihydroxytetradecanoic acid) (5), D-glucose and L-rhamnose.

Here we wish to report that I is not a homogeneous compound and its two major constituents, named pharbitic acids C (II) and D (III), are respectively the branched-chain pentaglycoside (IIa) and hexaglycoside (IIIa) of ipurolic acid both having a D-quinovose unit in addition to those of D-glucose and L-rhamnose.

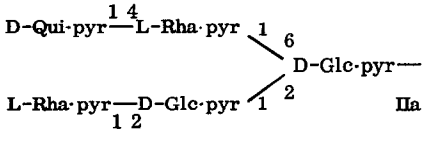
I obtained by the Asahina method (4) showed at least four spots on TLC and two polar and predominant constituents were successfully isolated by means of chromatography of the p-phenyl-phenacylester (PPE) of I on silica gel followed by saponification. The less polar acid II, $C_{44}H_{78}O_{26}\cdot 10\ H_2O$,* M.W. 990 (titration), m.p. 120-129°,* $[\alpha]_D$ -54.1°* (PPE, $C_{58}H_{88}O_{27}\cdot 2\ H_2O$, m.p. 127-130°, $[\alpha]_D$ -54.7°), and the other acid III, $C_{50}H_{88}O_{30}\cdot 2\ H_2O$, M.W. 1250 (titration), m.p. 140-145°, $[\alpha]_D$ -63.2° (PPE, $C_{64}H_{98}O_{31}\cdot 3\ H_2O$, m.p. 135-137°, $[\alpha]_D$ -63.2°), were acid hydrolyzed equally to give D-quinovose as well as ipurolic acid, D-glucose and L-rhamnose, and the molar ratios of methylpentose and glucose were 3:2 in the former and 4:2 in the latter.

Oxidation of I with $Na_2Cr_2O_7$ and subsequent acid hydrolysis yielded 10-hydroxytridecan-2-one and treatment with Ac_2O-AcONa (6) followed by hydrolysis provided 11-hydroxytridec-2-enoic acid. On oxidation with $NaIO_4$ followed by hydrolysis II gave no monosaccharide, while III provided quinovose. The permethyl ether (IV) of II afforded on methanolysis methyl 3-O-methyl-ipurolate and methyl pyranosides of 2,3-di- and 2,3,4-tri-O-methyl-rhamnoses, 3,4-di- and 3,4,6-tri-O-methyl-glucoses and 2,3,4-tri-O-methyl-quinovose. The permethylate (V) of III gave, besides the first five products mentioned above, methyl di-O-methyl-quinovoside instead of the tri-O-methyl ether.

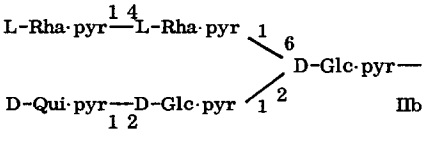
When I (also II and III) was partially hydrolyzed with 80% H·COOH and the products were treated with CH_2N_2, two compounds, $C_{27}H_{50}O_{14}\cdot 1/2\ H_2O$ (VI), m.p. 114-116°, $[\alpha]_D$ -23.6°, and $C_{33}H_{60}O_{18}\cdot H_2O$ (VII), amorphous powder, $[\alpha]_D$ -25.9°, were afforded. VI was hydrolyzed to give methyl ipurolate and glucose, and VII yielded the same two compounds and rhamnose. VI permethylate (VIII) gave on methanolysis methyl pyranosides of 3,4,6-tri- and 2,3,4,6-tetra-O-methyl-glucoses, and VII permethylate (IX) yielded those of 2,3,4-tri-O-methyl-rhamnose and 3,4-di- and 2,3,4,6-tetra-O-methyl-glucoses.

Accordingly the sugar moieties of VI and VII are D-glucopyranosyl-(1-2)-D-glucopyranose and D-glucopyranosyl-(1-2)-[L-rhamnopyranosyl-(1-6)-]-D-glucopyranose, respectively.

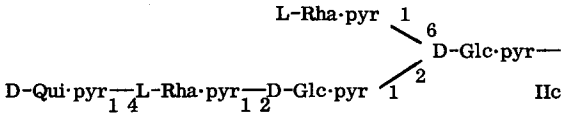
These results indicate that II has a branched-chain pentasaccharide moiety which is linked to 11-OH of ipurolic acid and has one of the following three monosaccharide sequences, and that III has an additional L-rhamnose unit combined with 3-OH of the terminal quinovose of II.



IIa



IIb



IIc

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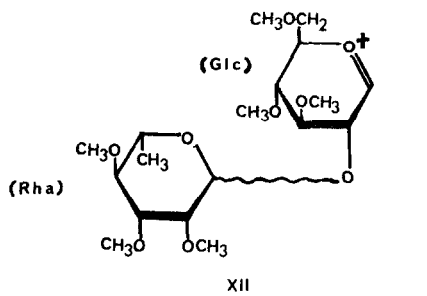
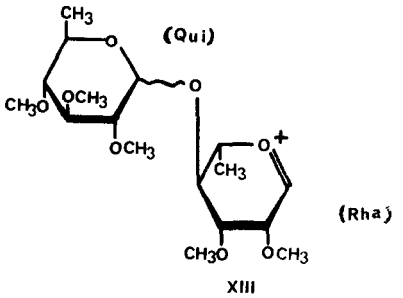
* Analytical data were in good agreement with the molecular formulae indicated. Melting points were determined on a Kofler block and are uncorrected. Rotations were measured in MeOH solutions. NMR spectra were taken at 60 MHz in $CDCl_3$ solutions with TMS as an internal reference and chemical shifts (δ) are given in ppm (s, singlet ; d, doublet).

Acetolysis of II and subsequent deacetylation gave a biose (acetate, $C_{24}H_{34}O_{15} \cdot 1/2\ H_2O$, m.p. 160-161°), and its permethylate (XI) was methanolyzed to give methyl 2,3-di-O-methyl-rhamnoside and 2,3,4-tri-O-methyl-quinovoside. Therefore the sequence IIb is excluded. The mass spectrum of IV showed two diagnostic peaks at m/e 393.215 and 363.203 which are attributable to the fragments XII (393.212) and XIII (363.203) respectively, and their formation can be explained only by the sequence IIa.

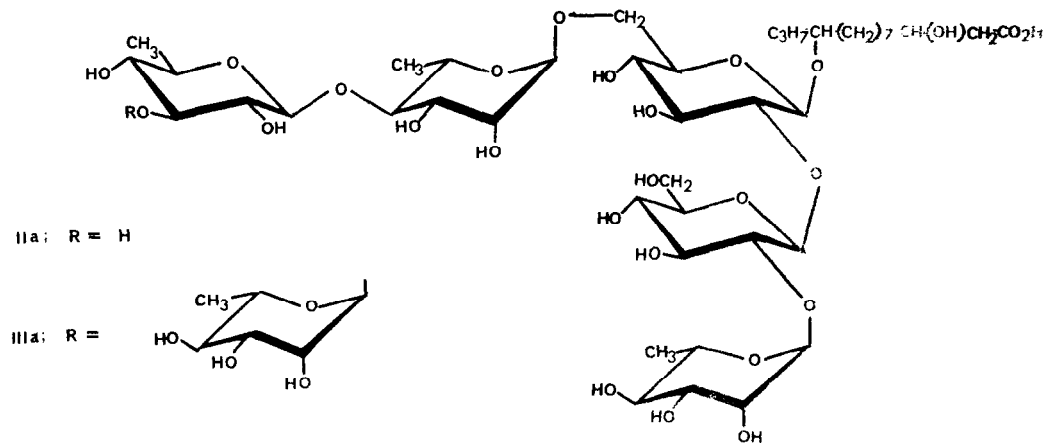
The NMR spectrum* of VIII showed two doublets (δ 4.30, J=7.5 Hz; 4.65, J=7.5 Hz) due to the anomeric protons indicating both D-glucopyranose residues to be β-linked in C1 (Normal) conformation, and that of IX exhibited, besides above two doublets, a singlet at δ4.82 attributable to 1-H of the L-rhamnose unit. In the spectrum of XI the anomeric proton signals appeared at δ 4.75 (s), 4.30 (s) and 4.61 (d, J=7.2 Hz), and the former two are respectively assigned to those of α- and β-L-rhamnose residues by comparing with the



XII



XIII



spectra of synthetic methyl L-rhamnopyranosides and hence the doublet is considered to be due to 1-H of β-D-quinovopyranose unit in C1 (Normal) form. The singlet (δ 5.30) among the five anomeric proton signals (δ 4.16 (d, J=7.2 Hz), 4.83 (s), 5.30 (s), 4.5~4.8 (2H)) of IV is regarded to be that of the terminal L-rhamnose unit. Since the majority of natural L-rhamnopyranosides are thought to have the α-configuration at C-1, two L-rhamnose residues in II are assumed to be α-conjugated and the NMR data suggest their conformations to be 1C (Alternative) form as accepted for methyl α-L-rhamnopyranoside (7).

Consequently the structure of II is depicted as IIa.

The NMR spectrum of V in which another L-rhamnose unit is combined with 3-OH of D-quinovose shows, in addition to the five anomeric proton signals of IV, a new singlet at δ 5.37 which is assigned to the 1-H of the new L-rhamnose residue. When it is assumed also to be α-linked, the above datum indicates it to have 1C (Alternative) conformation, and III is represented by the formula IIIa.

REFERENCES

(1) N. Kromer, Arch. Pharm., 459 (1896).

(2) M. Hoehnel, Arch. Pharm., 647 (1896).

(3) S. N. Khanna and P. C. Gupta, Phytochemistry, 6, 735 (1967).

(4) Y. Asahina and S. Terada, Yakugaku Zasshi, 39, 821 (1919).

(5) Y. Asahina and S. Nakanishi, Yakugaku Zasshi, 45, 515 (1925); T. Kawasaki, ibid., 71, 1065 (1951); T. Kawasaki and H. Okabe, Shoyakugaku Zasshi, 19, 4 (1965).

(6) Y. Asahina and T. Shimizu, Yakugaku Zasshi, 42, 1 (1922).

(7) R. E. Reeves, Advances in Carbohydrate Chemistry, 6, p. 130, ed. C. S. Hudson and S. M. Cantor, Academic Press Inc., New York, N. Y. (1951).