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STRUCTURE OF THALICTOSIDE

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Summary: Thalictoside (I), a novel glycoside containing a nitro group, has been isolated from *Thalictrum aquilegifolium* and the structure has been established by chemical transformations, spectral analysis and synthesis.

Thalictrum aquilegifolium (*Karamatsuso* in Japanese, Ranunculaceae) is known as a poisonous plant to domestic animals. In course of our research for poisonous substances of this plant, we have isolated a novel glycoside containing a nitro group, named thalictoside (I). In this paper we wish to describe the isolation, structure and synthesis of thalictoside.

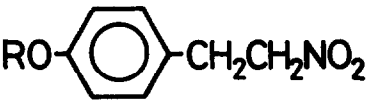
The methanolic extract of dried whole parts (including roots) of *Thalictrum aquilegifolium* was extracted with 5% acetic acid. This aqueous acetic acid solution was extracted with ethyl acetate and precipitates were filtered off from the concentrated ethyl acetate extract. The filtrates were chromatographed on silica gel and eluted with benzene-ethyl acetate (1:10) to give colorless crystals of thalictoside (I) (in ca. 0.01%): mp 102-103°, $C_{14}H_{19}NO_8$, $[\alpha]_D^{25}$ -48.8° (c=1.1, MeOH), IR (KBr, cm^{-1}): 3350 (OH), 1610 (aromatic ring), 1550, 1380 (NO_2), UV (H_2O, nm): 270 (ε 1063), 218 (ε 7532) (NO_2).

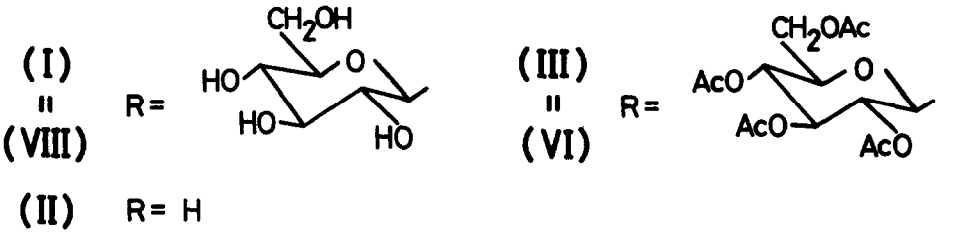
Acetylation of I with acetic anhydride in pyridine afforded a tetraacetate (III): mp 167-168°, $C_{22}H_{27}NO_{12}$, $[\alpha]_D^{21}$ -2.6° (c=1.3, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, δ) of III revealed the presence of a *para* substituted benzene ring [7.14, 6.94 (each 2H, d, J=8.0Hz)] and $-CH_2CH_2-$ [4.58, 3.28 (each 2H, t, J=7.0Hz)].

Acid hydrolysis of I with MeOH-10% HCl (2:1) yielded D-(+)-glucose [identified by GLC (as its Me_3Si derivative) and ORD] and an aglycone (II) as a pale yellow oil which gave a red purple color with 2% aqueous ferric chloride. High resolution mass spectroscopy of II indicated a molecular formula of $C_8H_9NO_3$ (m/e 167.0576) and furthermore, IR [($CHCl_3$, cm^{-1}), 1550 and 1380] spectrum suggested the presence of a nitro group.

^{1}H-NMR (C_5D_5N, δ) spectrum of I exhibited a signal of one anomeric proton [5.45 (1H, d, J=7.0Hz)] which indicated the presence of β-glucopyranoside linkage. These data led to the structure of thalictoside as I.

Thalictoside (I) was synthesized as follows. *p*-Hydroxybenzaldehyde was condensed with nitromethane to yield nitrostylene (IV)[1] in acetic acid in the presence of ammonium acetate. The reduction product of IV with sodium borohydride (3 mols) in ethanol was identified with II by IR, MS and ^{1}H-NMR spectra.





(II) R= H

This phenolic aglycone (II) was condensed with 2,3,4,6-tetra-O-acetyl-α-D-glucosyl bromide (V)[2] in toluene in the presence of cadmium carbonate.[3] Two isomeric products, VI [sugar protons in ^{1}H-NMR ($CDCl_3$, δ): 5.34-4.96 (4H, m, H-1,2,3,4), 4.20 (2H, m, H-6,6'), 3.90(1H, br-m, H-5)] and VII [mp 111-112°, sugar protons in ^{1}H-NMR ($CDCl_3$, δ): 5.68(1H, d, J=3.0Hz, H-1), 5.66(1H, t, J=9.0Hz, H-3) 5.24-4.90 (2H, m, H-2,4), 4.24-3.92 (2H, m, H-5,6), $[\alpha]_D^{21}$ +147.2° (c=1.4, $CHCl_3$)] were separated by preparative TLC on silica gel. These isomers (VI for β- and VII for α-anomers) were clearly distinguished by ^{1}H-NMR data on sugar moieties. Furthermore, VI was identified with III by IR, ^{1}H-NMR, specific rotation and mixed melting point determination.

Treatment of both VI and VII with 5% KOH in methanol gave VIII and IX [α-anomer, mp 90-91°, anomeric proton in ^{1}H-NMR (C_5D_5N, δ): 5.88 (1H, d, J=3.0Hz)] respectively. The former glycoside (VIII) was identified with the naturally occuring glycoside (I) by IR, ^{1}H-NMR, specific rotation and mixed melting point determination.

Thalictoside is the rare natural product which is a new addition to the small number of naturally occuring aliphatic nitro compounds (e.g. miserotoxin,[4] endecaphyllins[5]).

On the test of toxity performed by injection of I into the abdominal cavities of mice, toxity we had expected was not observed.

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