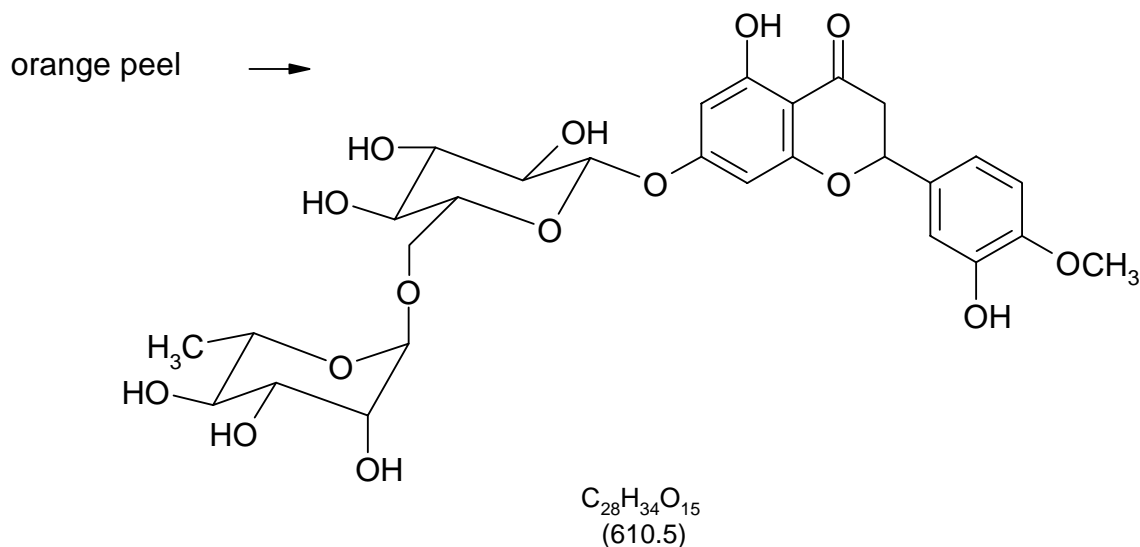


## 1023 Isolation of hesperidine from orange peel



### Classification

#### Reaction types and substance classes

isolation of natural products

natural product

#### Work methods

extracting with Soxhlet extractor, stirring with magnetic stir bar, heating under reflux, filtering, evaporating with rotary evaporator, recrystallizing, heating with oil bath

### Instruction (batch scale 20 g)

#### Equipment

250 mL round bottom flask, reflux condenser, 100 mL Soxhlet extractor, extraction sleeve, glass wool, suction flask, Buechner funnel, heatable magnetic stirrer, magnetic stir bar, desiccator, oil bath

#### Substances

orange peel	20 g
6% acetic acid	about 60 mL
petroleum ether (bp 40-60 °C)	150 mL
methanol (bp 65 °C)	150 mL
DMSO (bp 189 °C)	about 20 mL
isopropanol (bp 82.4 °C)	about 10 mL

**Reaction**

150 mL petroleum ether (40 – 60°C) are filled in a 250 mL round bottom flask with magnetic stir bar. 20g dried and powdered orange peel are placed in the extraction sleeve of a Soxhlet extractor and covered with a little glass wool. A reflux condenser is put on the Soxhlet extraction unit, then the reaction mixture is stirred and heated for 4 hours under strong reflux. The petroleum ether extract is discarded (see waste management). In order to remove the adherent petroleum ether, the content of the extraction sleeve is laid out in an extensive crystallisation dish.

Afterwards the substance is placed again in an extraction sleeve and, like before, but with 150 mL methanol, extracted unless the solvent leaving the extraction sleeve is colourless (1 to 2 hours).

**Work up**

The extract is evaporated at the rotary evaporator until syrup consistency is reached. The residue is mixed with 50 mL of 6% acetic acid, the precipitated solid is the crude hesperidine. It is sucked off with a Buechner funnel, washed with 6% acetic acid and dried 60 °C until it is constant in weight.

Crude yield: 780 mg; mp 236-238 °C

For recrystallization, a 5% solution of the crude product in dimethyl sulfoxide is produced under stirring and heating to 60–80 °C. Afterwards the same amount of water is added slowly whilst stirring. When cooling to room temperature the hesperidine precipitates. It is sucked off, first washed with little warm water and then with *iso*-propanol and dried in the desiccator until it is constant in weight.

Yield: 450 mg; mp 262 °C, colourless crystals

**Comments**

Because of extraction with petroleum ether first etheric oils are extracted from the orange peel.

**Waste management****Recycling**

From the first extract the petroleum ether is evaporated, collected and redistilled.

The evaporated methanol is collected and redistilled.

**Waste disposal**

Waste	Disposal
residue from the petroleum ether extract	dissolve in a small amount of acetone, then: organic solvents, halogen free
acidic filtrate	solvent water mixtures, halogen free
filtrate from DMSO, water, <i>iso</i> -propanol	solvent water mixtures, halogen free
extraction sleeve with content	solid waste, free from mercury

**Time**

8-9 hours, from it minimum 4 hours heating under reflux, without drying period

**Break**

Before extracting with methanol

Before recrystallizing

**Degree of difficulty**

Easy

**Analytcs****Reaction control with TLC**

TLC-Conditions:

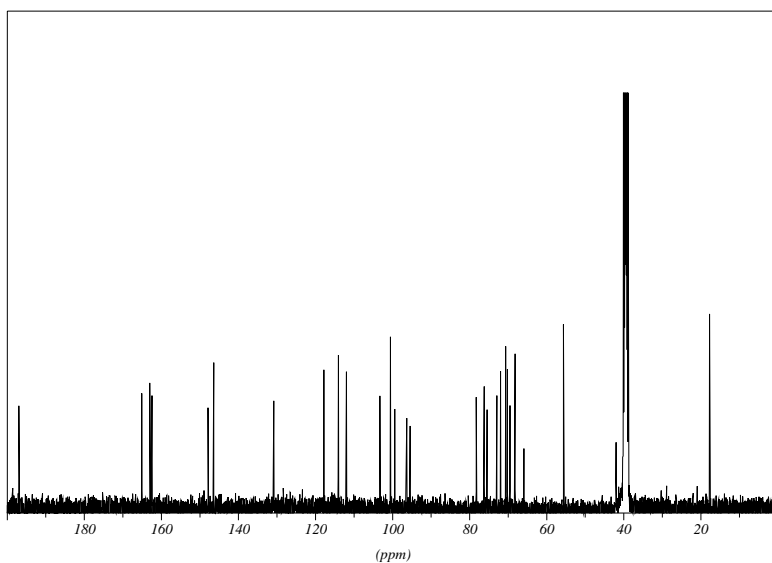
adsorbant: Macherey and Nagel Polygram SilG/UV foils, 0.2 mm

inlet: *n*-butanol : acetic acid : water = 4 : 1 : 5

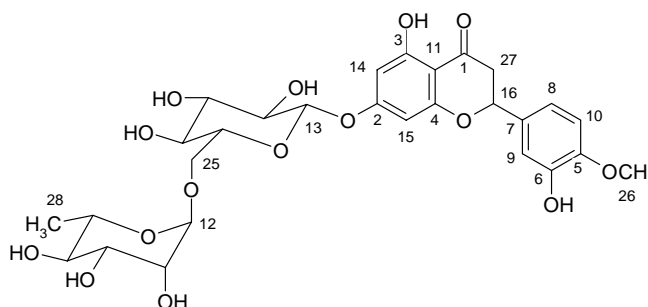
R<sub>f</sub> (hesperidine) 0.6

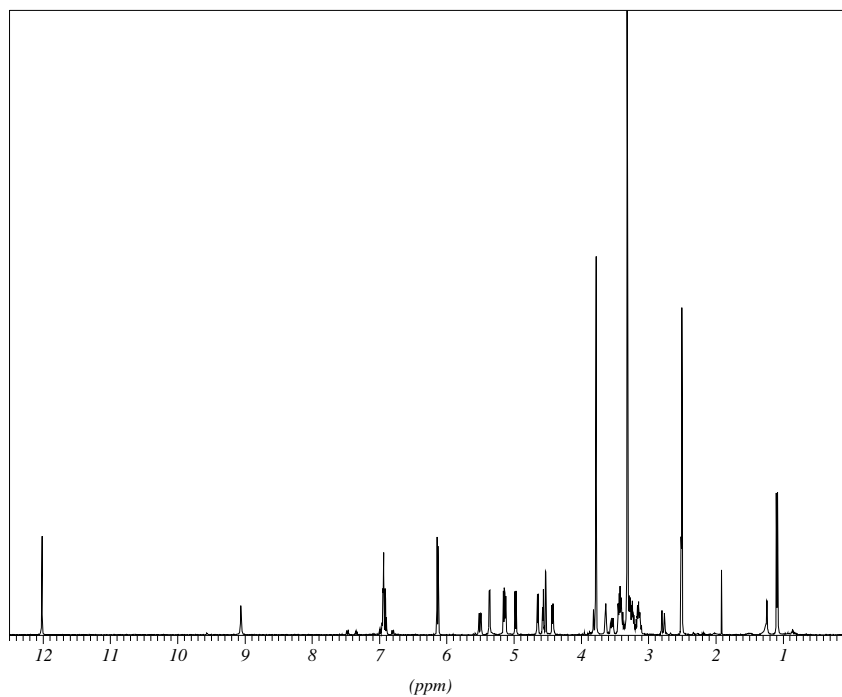
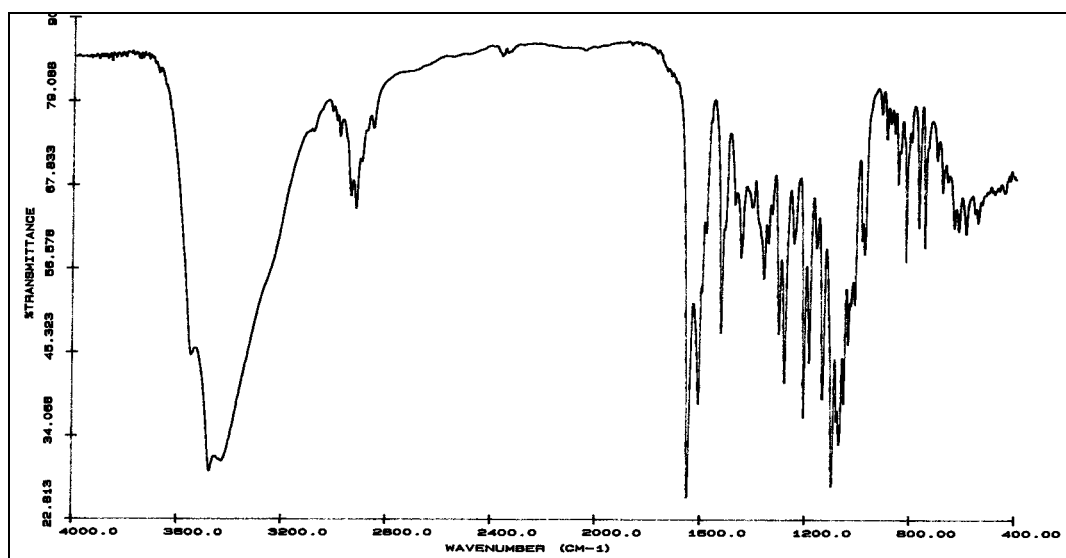
**UV spectrum (methanol)**

$\lambda_{\max}$ (nm)	log $\epsilon$
204	5.34
284	5.71
328	6.42
222	5.58
228	5.60
352	6.68

**$^{13}\text{C}$  NMR spectrum of hesperidine (400 MHz, DMSO- $\text{D}_6$ )**

$\delta$ (ppm)	Assignment
196.92	C-1
165.06	C-2
162.93	C-3
162.42	C-4
147.87	C-5
146.41	C-6
130.86	C-7
117.83	C-8
114.09	C-9
112.00	C-10
103.23	C-11
100.53	C-12
99.37	C-13
96.31	C-14
95.47	C-15
78.29	C-16
76.21	
75.45	
72.91	
71.99	
70.62	
70.20	
69.51	
68.23	
65.97	C-25
55.62	C-26
41.96	C-27
17.73	C-28
40.1-38.8	solvent



**$^1\text{H}$  NMR spectrum of hesperidine (400 MHz, DMSO- $\text{D}_6$ )****IR spectrum of hesperidine (KBr)**

( $\text{cm}^{-1}$ )	Assignment
3500	O-H-valence
3080-3010	C-H-valence, arene
2980-2865	C-H-valence, alkane
2850	C-H-valence, alkane ( $\text{OCH}_3$ )
1650	C=O-valence