

FURTHER STUDIES ON THE BIANTHRAQUINONES  
OF PENICILLIUM ISLANDICUM SOPP

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By the earlier works (1,2,3), the following anthraquinones have been isolated from several strains of Penicillium islandicum Sopp:

Monomeric anthraquinones---- chrysophanol (I), islandicin (II), emodin (III) and catenarin (IV) ; dimeric anthraquinones ---- iridoskyrin (VI), skyrin (VII), oxyskyrin (VII, CH<sub>2</sub>OH instead of one CH<sub>3</sub>), skyrinol (VII, CH<sub>2</sub>OH instead of CH<sub>3</sub>), and dicatenarin (VIII).

Some partially hydrogenated anthraquinone derivatives, such as flavoskyrin, rubroskyrin and luteoskyrin, have also been obtained, and in addition to them a nitrogen containing polyene type pigment, erythroskyrin, has been isolated from that mould.(1,2,4)

Further investigation employing improved methods has made us possible to isolate some other new homologous colouring matters from P. islandicum Sopp, E-strain cultivated stationarily on Czapek-Dox medium. The acetone extracts of the mycelia were separated into two parts by the solubilities in boiling benzene. The benzene-soluble fraction was chromatographed on silica gel impregnated with 0.5 N oxalic acid using benzene-hexane (1:1) mixture as the developing solvent. The fraction which is sparingly soluble in boiling benzene was separated into the anthraquinone- and non-anthraquinone fractions by the chromatography on activated carbon column with acetone as the solvent.

Only the aromatic anthraquinones were adsorbed on carbon from which the pigments were recovered by the extraction with 1 N NaOH. Then the chromatography on silicic acid was repeated several times to get a complete separation.

Some of the pigments can only be separated by the chromatography after acetylation.

The non-anthraquinone pigments were not adsorbed on carbon, and the eluted portion was chromatographed on silicic acid or silica gel impregnated with 0.5 N oxalic acid using benzene-acetone (9:1) as the solvent.

In addition to the known bianthraquinones of P. islandicum, we have obtained 7 new compounds of this series: Dianhydrorugulosin\* (V), roseoskyrin(IX)\*\* , auroskyrin (X), rhodoislandin A (XI), rhodoislandin B (XII), punicoskyrin (XIII) and aurantioskyrin (XIV)\*\*. All these compounds gave no melting points below 300°, but they can be identified by the distinct colouring spots on the thin layer chromatogram developed on silica gel (impregnated with 0.5 N oxalic acid) using the following solvent systems: a) Benzene-hexane (1:1) for V, VI and IX ; b) benzene-acetone (20:1) for X, XI, XII and XIII; c) benzene-acetone (4:1) for VII, VIII and XIV.

The structures of the new pigments were established by the reductive cleavage with alkaline sodium dithionite and by the NMR spectral analysis of the acetates. The results of reductive cleavage of the bianthraquinones were shown as follows:

Dianhydrorugulosin (V)	————→	chrysophanol (I)
Roseoskyrin (IX)	————→	chrysophanol (I) + islandicin (II)
Auroskyrin (X)	————→	chrysophanol (I) + emodin (III)
Rhodoislandin A (XI)	————→	chrysophanol (I) + catenarin (IV)
Rhodoislandin B (XII)	————→	emodin (III) + islandicin (II)
Punicoskyrin (XIII)	————→	islandicin (II) + catenarin (IV)
Aurantioskyrin (XIV)	————→	emodin (III) + catenarin (IV)

Rhodoislandin A and B acetates were inseparable on chromatography.

Accordingly, the yields of monomers on reductive cleavage of the acetates mixture were determined quantitatively by the ultraviolet spectral method.

A dimer would form by the cleavage two monomers in almost the same yield.\*\*

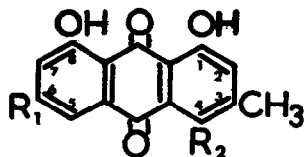
The experimental results showed that chrysophanol and catenarin were afforded in almost the equal amounts, while emodin and islandicin were given in the same grade of yield, about 5 times more than the former couple of monomers. Rhodoislandin A is formulated by the combination of chrysophanol

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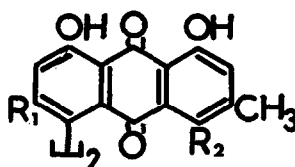
(-)Dianhydrorugulosin has already been known, as it was prepared from (+)rugulosin, a pigment of P. rugulosum, P. brunneum etc., by dehydration reaction.

\*\* Roseoskyrin and aurantioskyrin were prepared also from dianhydrorugulosin and skyrin, respectively, by the oxidation with peracids.

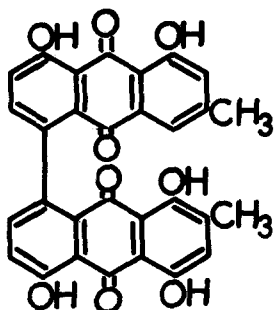
\*\*\* Under the same experimental condition of reductive cleavage, auroskyrin (X) and punicoskyrin (XIII) gave the corresponding monomeric components in the same proportion of 1 : 1, respectively.



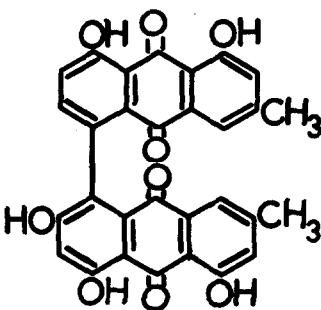
- R<sub>1</sub>=R<sub>2</sub>=H, chrysophanol (I)  
 R<sub>1</sub>=H, R<sub>2</sub>=OH, islandicin (II)  
 R<sub>1</sub>=OH, R<sub>2</sub>=H, emodin (III)  
 R<sub>1</sub>=R<sub>2</sub>=OH, catenarin (IV)



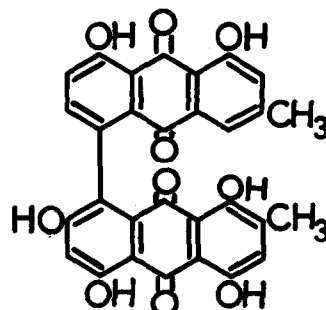
- R<sub>1</sub>=R<sub>2</sub>=H, dianhydrorugulosin (V)  
 R<sub>1</sub>=H, R<sub>2</sub>=OH, iridoskyrin (VI)  
 R<sub>1</sub>=OH, R<sub>2</sub>=H, skyrin (VII)  
 R<sub>1</sub>=R<sub>2</sub>=OH, dicatenarin (VIII)



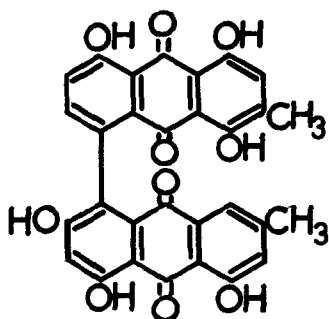
Roseoskyrin (IX)



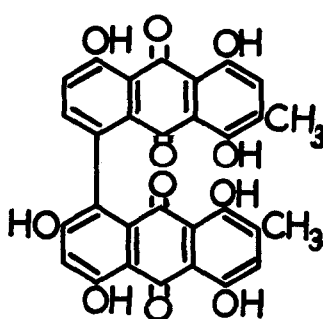
Auroskyrin (X)



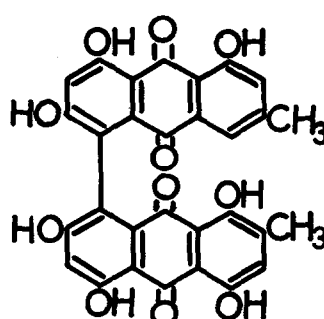
Rhodoislandin A (XI)



Rhodoislandin B (XII)



Punicoskyrin (XIII)



Aurantioskyrin (XIV)

and catenarin, and rhodoislandin B is represented as a dimeric compound consisting of emodin and islandicin. The NMR spectral signals of the aromatic protons of the peracetates of pigments were shown in Table I.

TABLE I  
Aromatic Proton Signals in NMR Spectra of Peracetates of Anthraquinone  
Pigments of Penicillium islandicum ( $\tau$  in  $\text{CDCl}_3$ )

Position of arom. proton	5	6	6'	7	7'	2	2'	4	4'
Peracetate of									
Chrysophanol	1.80	2.27		2.63		2.80		2.02	
Islandicin	1.95	2.32		2.68		2.76			
Emodin	1.99			2.80		2.77		2.06	
Catenarin	2.13			2.83		2.77			
Dianhydrorugulosin		2.58	2.58	2.58	2.58	2.84	2.84	2.34	2.34
Iridoskyrin		2.60	2.60	2.60	2.60	2.80	2.80		
Skyrin				2.62	2.62	2.85	2.85	2.31	2.31
Oxyskyrin				2.60	2.60	2.83	2.62	2.31	2.31
Dicatenarin				2.62	2.62	2.80	2.80		
Roseoskyrin		2.58	2.58	2.58	2.58	2.82	2.82	2.30	
Punicoskyrin		2.68		2.63	2.69	2.77	2.77		
Auroskyrin		2.60		2.60	2.70	2.80	2.80	2.30	2.30
Aurantioskyrin				2.59	2.64	2.84	2.84	2.28	

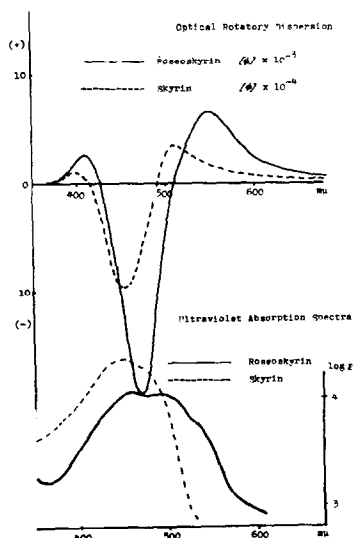
The protons of  $\text{C}_{(6,6')}$  of V, VI, IX, X and XIII, and those of  $\text{C}_{(4,4')}$  of V, VII, IX, X, XIII and XIV are shifted to up-field by the effect of ring current in the other half of the molecules.

The NMR proton signals of acetyl and aromatic methyl groupings were shown in Table II. The proton signals of acetate attached to  $\text{C}_{(6,6')}$  or  $\text{C}_{(4,4')}$  of VI, VIII, IX, X, XIII and XIV are shifted to up-field by the effect of ring current of the other half of the molecules. The methyl signals at  $\text{C}_{(3,3')}$  of VI, VIII, IX, XIII and XIV show up-field shift by the effect of the introduction of acetyl group to the neighbouring hydroxyls.

All the dimeric anthraquinones of P. islandicum exhibit optical activities which are accounted for the restricted rotation about C-C linkage connecting the monomeric halves. The optical rotatory dispersion (ORD) and the circular dichroism (CD) curves of these compounds show the same feature of the Cotton effects suggesting the same stereochemistry of the restricted rotation about C-C linkage.

TABLE II  
Acetyl and Methyl Proton Signals in NMR Spectra of Peracetates of  
Anthraquinone Pigments of Penicillium islandicum ( $\tau$  in  $\text{CDCl}_3$ )

Position	OC(=O)CH <sub>3</sub>								CH <sub>3</sub>	
	6	6'	8	8'	1	1'	4	4'	3	3'
Peracetate of										
Chrysophanol			7.55		7.55				7.50	
Islandicin			7.58		7.58		7.51		7.70	
Emodin	7.62		7.54		7.54				7.47	
Catenarin	7.63		7.55		7.55		7.49		7.64	
Dianhydrorugulosin			7.48	7.48	7.50	7.50			7.59	7.59
Iridoskyrin			7.53	7.53	7.55	7.55	8.14	8.14	7.78	7.78
Skyrin	8.07	8.07	7.50	7.50	7.53	7.53			7.58	7.58
Dicatenarin	8.04	8.04	7.54	7.54	7.54	7.54	8.04	8.04	7.78	7.78
Oxyskyrin	8.09	8.09	7.51	7.51	7.51	7.51			7.59	7.59
									CH <sub>2</sub> OAc	
									4.88	
									7.88	
Roseoskyrin			7.51	7.51	7.51	7.51		8.11	7.58	7.79
Punicoskyrin	8.01		7.54	7.54	7.54	7.54	8.12	8.08	7.77	7.77
Auroskyrin	8.15		7.50	7.50	7.50	7.50			7.58	7.58
Aurantioskyrin	8.07	8.06	7.52	7.52	7.52	7.52		8.10	7.61	7.81



A prefix (+) is attached hereafter to all the bianthraquinones of P. islandicum which show (+) Cotton effect at the highest wave length region of the ORD curve. A stereospecificity of the biological oxidative coupling has been suggested in the biogenesis of these mould bianthraquinones which are occurring by all the possible combinations of the monomeric anthraquinones isolated so far from P. islandicum.

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