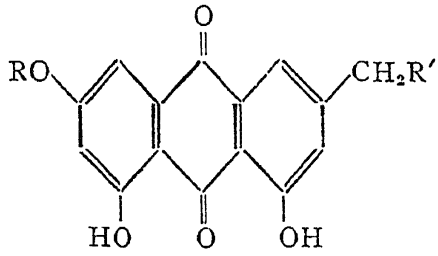
CHEMICAL INVESTIGATION OF INDIAN LICHENS*

Part XX. A New Synthesis of Teloschistin

BY S. NEELAKANTAN, T. R. SESHADRI, F.A.SC.
AND SANKARA SUBRAMANIAN
(Department of Chemistry, Delhi University, Delhi, and Department of Pharmacy, Andhra University, Waltair)

TELOSCHISTIN was first isolated by Seshadri and Subramanian[1] from the Indian lichen *Teloschistes flavicans* Norm., and its constitution was established as 4: 5-dihydroxy-7-methoxy-2-hydroxymethyl anthraquinone (I).[1, 2] In connection with the study of ω-hydroxy emodin (II), isolated from the mould *Penicillium cyclopium* Westling, Anslow *et al.*,[3] effected a partial methylation of it and the product was found to be identical with teloschistin.[2]



I, R = CH_3; R′ = OH

II, R = H; R′ = OH

III, R = CH_3; R′ = H

As an alternative method of synthesis, physcion (III) has now been used as the intermediate. The occurrence of physcion (III) and teloschistin (I) together in *T. flavicans* would indicate close biogenetic relationship. Physcion diacetate is converted into the corresponding ω-bromo derivative using N-bromo succinimide in carbon tetrachloride solution in the presence of benzoyl peroxide. This method has recently been used extensively by Seshadri and co-workers[4–7] for the synthesis of 2-hydroxymethyl chromones, -isoflavones, chromeno-chromones and 4-hydroxymethyl coumarins. Recently, Venkataraman *et al.*[8, 9] have also reported the use of this reagent for the conversion of rubiadin (1 : 3-dihydroxy-2-methyl anthraquinone) to the corresponding ω-hydroxy derivative, lucidin. In 2-methyl anthraquinones, the methyl group is reactive because of conjugation with the carbonyl group and hence is easily brominated with N-bromo succinimide. To avoid nuclear bromination, physcion (III) is converted into its diacetate (IV) which is subsequently brominated. The intermediate bromo derivative (V) is treated with silver acetate and acetic anhydride when teloschistin triacetate (VI) is obtained in satisfactory yield. Subsequent hydrolysis of the acetate with methanolic sulphuric acid gives teloschistin (I).

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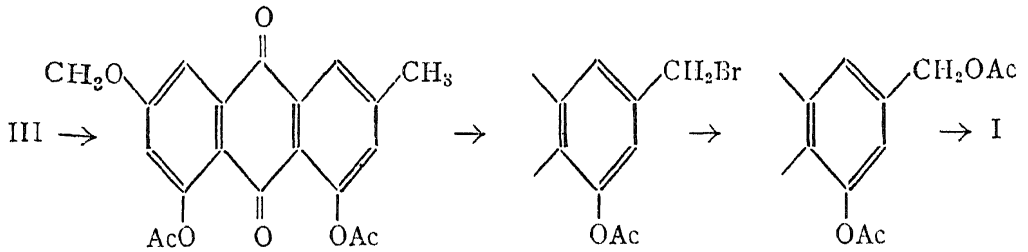

IV V VI

The synthetic sample melts at 245–47° whereas natural teloschistin[1] was reported to melt at 229–30°. It was possible that the natural sample was slightly impure and hence had a lower melting point since it is known that, in anthraquinone derivatives, traces of impurities depress the melting points of the compounds considerably. Hence, natural teloschistin has been acetylated and subsequently deacetylated. It is found that the resulting purified sample melts at 244–6° and does not depress the m.p. of the synthetic sample. However, the possibility of two melting points of teloschistin (m.p. 229–30° and 245–47°) being due to dimorphism is not ruled out.

As a derivative of teloschistin, Seshadri and Subramanian[1] reported the preparation of teloschistin dimethyl ether using the dimethyl sulphate-acetone-potassium carbonate method. It is now found that methylation of teloschistin dimethyl ether with excess of methyl iodide and silver oxide in dry benzene solution, according to the method of Raistrick and Ziffer,[10] gives a trimethyl ether (m.p. 186–87°) and the melting point of this substance is the same as that of O-tetramethyl citreorosein, prepared by Posternak and Jacob[11] from citreorosein. Posternak[12] as well as Hind[13] claimed to have obtained the same substance by completely methylating 2-hydroxymethyl-4-methoxy-5: 7-dihydroxy anthraquinone (= roseopurpurin = carviolin) using dimethyl sulphate and aqueous alkali in acetone solution. But this method fails to give teloschistin trimethyl ether from teloschistin but yields only teloschistin 4: 5-dimethyl ether. A similar failure was also reported by Raistrick and Ziffer[10] who attempted the complete methylation of nalgiovensin (4: 5-dihydroxy-7-methoxy-2-hydroxypropyl anthraquinone) by this method.

Experimental Procedure

Synthesis of teloschistin

(i) *Bromination of physcion diacetate.*—To a solution of physcion diacetate[1] (m.p. 186–87°; 0·2 g.) in dry carbon tetrachloride (100 c.c.) were added freshly crystallised and dried N-bromo succinimide (0·15 g.) and benzoyl peroxide (0·02 g.) and the mixture refluxed on a water-bath for 24 hrs. The solution was then cooled in ice but no solid separated and hence the solvent was distilled off when a sticky yellow residue was left behind.

It was first washed with cold water twice and then with boiling water to remove the succinimide and unreacted NBS. The insoluble sticky solid was dried in a vacuum desiccator and directly used for the next stage. It gave a positive test for the presence of bromine.

(ii) *Conversion of the bromo derivative into the corresponding acetate.*—The above crude bromo compound (0·15 g.) was dissolved in acetic anhydride (5 c.c.) and silver acetate (0·5 g.) added. The mixture, after being refluxed in an oil-bath (150–60°) for 6 hrs., was poured into ice-water (200 c.c.) and stirred. The brownish yellow solid was filtered, washed with water and dried. It was boiled with benzene (4×50 c.c.), filtered to remove the silver bromide and the filtrate evaporated when a yellow solid was left behind which crystallised from ethyl acetate as lemon-yellow broad rectangular plates, m.p. 192–93°, identical with teloschistin triacetate. Yield, 0·1 g. It did not give any colour with alcoholic ferric chloride and did not answer the test for bromine.

(iii) *Hydrolysis to teloschistin.*—The above acetate (0·1 g.) was refluxed with a mixture of methyl alcohol (50 c.c.) and concentrated sulphuric acid (1·5 c.c.) on a water-bath for 45 mts. 2-Hydroxymethyl-4: 5-dihydroxy-7-methoxy anthraquinone crystallised from benzene as orange rectangular plates melting at 245–47°. Yield, 0·05 g. It was insoluble in aqueous sodium carbonate but dissolved in aqueous sodium hydroxide and potassium hydroxide giving a pink red solution. It gave a reddish brown colour with alcoholic ferric chloride (Found: C, 64·4; H, 3·8. $C_{16}H_{12}O_6$ requires: C, 64·0; H, 4·0 per cent.).

Hydrolysis of triacetate of natural teloschistin

Teloschistin triacetate[1] (m.p. 193°; 0·25 g.) was hydrolysed with a mixture of methyl alcohol (100 c.c.) and concentrated sulphuric acid (3 c.c.) as in the above case. The product crystallised from benzene as orange plates melting at 244–46°. Mixed melting point with the above synthetic sample was undepressed, and with the lower melting sample of teloschistin had a range (228-45°).

Teloschistin trimethyl ether

To a solution of teloschistin dimethyl ether[1] (0·25 g.) in dry benzene (75 c.c.) were added methyl iodide (20 c.c.) and dry silver oxide (3 g.). After refluxing the mixture for 2 hrs., more of methyl iodide (10 c.c.) and silver oxide (2 g.) (1 g. each time at the end of the first and second hour) were added. The refluxing was continued for 8 hrs. more and the mixture filtered off and the residue washed repeatedly with boiling benzene. The benzene solution

was concentrated to a small volume (about 10 c.c.) under reduced pressure. A yellow crystalline solid (0·2 g.) separated which was filtered off and crystallised from ethyl acetate when it was obtained as lemon-yellow needles, m.p. 185–86° (Found: C, 66·4; H, 5·4; OCH_3, 34·6. $C_{15}H_6O_2$ $(OCH_3)_4$ requires: C, 66·7; H, 5·2; OCH_3, 36·2 per cent.). Hind[13] reported a melting point of 186° for carviolin trimethyl ether and Posternak[12] reported a melting point of 187° for tetramethyl citreorosein (trimethyl roseopurpurin).

Teloschistin tribenzoate

Teloschistin (0·2 g.) was benzoylated using benzoyl chloride (1·5 c.c.) and pyridine (2 c.c.) and heating for 1 hr. on a boiling water-bath. The benzoate was worked up as usual and crystallised from ethyl acetate when it was obtained as yellow needles. m.p. 230–31°. Yield, 0·2 g. It was insoluble in cold aqueous sodium hydroxide (2%) and did not give any ferric chloride colour (Found: C, 72·1; H, 4·1; $C_{37}H_{24}O_9$ requires: C, 72·5; H, 3·8 per cent.).

Summary

Teloschistin has been prepared from physcion, the essential stage being the ω-bromo compound obtained by the use of N-bromo-succinimide. The higher m.p. of 244–46° is now recorded both for the synthetic and for the natural sample purified through the acetate. Complete methylation of teloschistin requires the use of methyl iodide and silver oxide at the final stage.

References

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