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THE STRUCTURES OF SALICORTIN AND TREMULACIN

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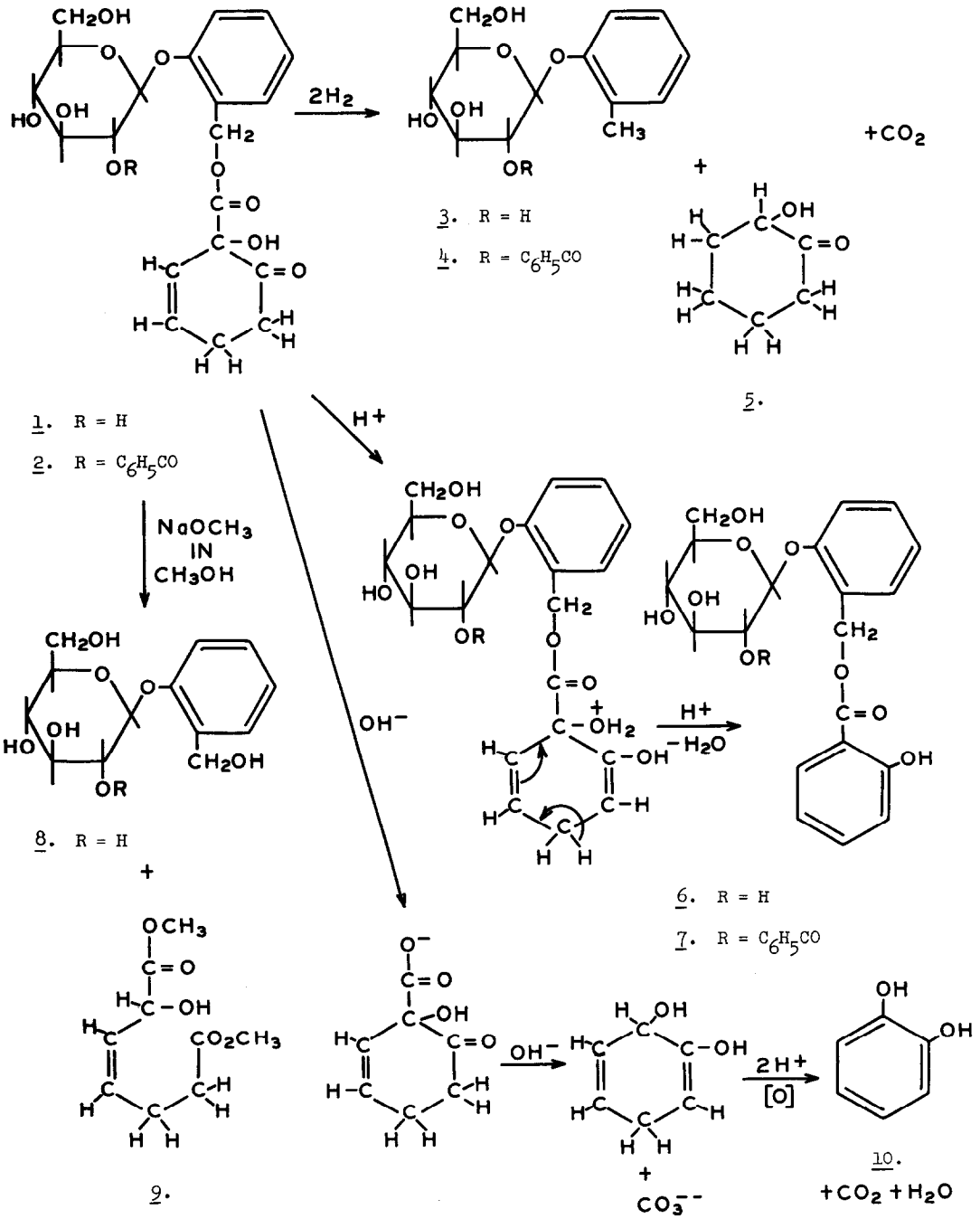
In 1964 Thieme[1] isolated a new glucoside, salicortin, from the bark of Salix purpurea, and in a subsequent paper[2], demonstrated by means of paper chromatography that salicortin was an important component of all the Populus and Salix species barks he had investigated. Thieme submitted salicortin to treatment with acid to obtain ω-salicyloylsalicin and to cleavage with sodium methylate followed by alkaline saponification to give an aliphatic hydroxy acid. These results, together with his finding that salicortin was not hydrolyzed by emulsin, led Thieme to conclude that salicortin is a derivative of ω-salicyloylsalicin in which the primary hydroxyl of the glucose moiety and the hydroxyl of the salicyloyl moiety are bound by an unidentified aliphatic hydroxy acid.

In our continuing studies on the barks and leaves of the family Salicaceae, we have isolated salicortin in quantity from the barks and leaves of a number of P. and S. species[3-6] and confirmed Thieme's earlier conclusion[7] that this labile glucoside is probably the precursor of much of the salicin found in these materials. The possible structure suggested by Thieme became suspect when salicortin was submitted to treatment with dilute alkali at room temperature. After a short while, acidification yielded salicin (8), carbon dioxide, and an oil which on further alkaline hydrolysis, yielded pyrocatechol (10). No trace of salicylic acid could be found, and thus, salicortin could not be a derivative of salicyloylsalicin. Nevertheless, treatment of salicortin with acid converted it to ω-salicyloylsalicin (6) in high yield. The present communication reports the structure determination of salicortin, m.p. 135-137°, and that of the related glucoside, tremulacin, m.p. 122-123°, originally isolated from P. tremula bark by Thieme and Richter[8], and which we isolated from P. tremuloides bark[6].


2H2
+CO2
3. R = H
4. R = C6H5CO
5.
1. R = H
2. R = C6H5CO
H+
NaOCH3 IN CH3OH
OH−
8. R = H
+
6. R = H
7. R = C6H5CO
H+ −H2O
2H+ [O]
9.
10.
+CO2 +H2O

The structure 1 can be assigned to salicortin on the basis of the noted alkaline and acid hydrolyses experiments and the following experimental evidence.

Catalytic hydrogenolysis of salicortin at room temperature and atmospheric pressure resulted in the absorption of two moles of hydrogen and the production of o-cresol-β-D-glucoside (3), adipoin (5), and carbon dioxide. The carbon dioxide liberation from this and the alkaline hydrolysis experiment suggested a carbonate or a β-ketoacid, but the i.r. spectrum indicated two carbonyl groups, thus eliminating the carbonate possibility.

Treatment of salicortin with sodium methylate in methanol yielded 8 and dimethyl 2-hydroxy-3-heptenedioate (9) ($C_9H_{14}O_5$) identified by mass, i.r., and n.m.r. spectra. Mass spectrum gives M^+, m/e 202 and a prominent peak at m/e 143 corresponding with the stable carbonium ion $CH_3OCOCH_2CH_2CH{=}CHCH^+(OH)$ formed by the loss of $-CO-OCH_3$ from the molecular ion. The n.m.r. spectrum in $CDCl_3$ with TMS as the internal standard showed the following signals: 7.5τ (multiplet, 4H, methylenes), 6.2τ (singlet, 3H methyl) and 6.3τ (singlet, 3H methyl), 5τ (doublet, 1H, -CHOH), and 4.2 to 4.6τ (multiplet, 2H, vinyl). The latter multiplet in the vinyl region is simplified by irradiating the methylene region at 7.47τ to yield a typical AB system influenced by the adjacent C-H from the -CHOH. The i.r. spectrum confirmed structure 9.

The n.m.r. spectrum of salicortin in D6 acetone with TMS as internal standard indicated 24 protons in agreement with the analysis for $C_{20}H_{24}O_{10}$. The assignments of these protons were made as follows: 4H in the aromatic region downfield between 2.6τ and 3.0τ are the protons of the salicyl alcohol moiety; 2 vinyl protons between 3.8τ and 4.2τ appear as a typical AB pair of doublets with distant coupling; 2 benzyl protons are a distinct AB pair of doublets at 4.6τ and 4.7τ; the single proton appearing as a doublet at 4.9τ with a J = 7.4 is the anomeric proton of glucose, consistent with the β form of the glucoside; the single alicyclic hydroxyl proton appears as a broad triplet at 5.2τ; the 2 C6 glucose protons are the strong singlet at 6.1τ; the other 4 glucose C-H protons have a strong singlet at 6.5τ; the 4 glucose hydroxyl protons are the strong singlet at 7.05τ; and 4 methylene protons appear as a complicated multiplet between 7.2τ and 7.5τ. The 5 hydroxyl protons were not present in an n.m.r. spectrum made in D_2O. Irradiation of the methylene region at 7.47τ caused decoupling in the vinyl region to yield a simple AB doublet and no change in the aromatic region, the benzyl

proton responses, nor the anomeric proton response. Therefore, it appears that the original two vinyl protons are coupled only with methylene protons since the response due to the CHOH in the spectrum of 9 is missing in the spectrum of salicortin, and the alicyclic ring of salicortin must contain the arrangement $-CH=CHCH_2CH_2-$.

The structure 1 accounts for all chemical reactions of salicortin as noted in the figure. The possible alternative structure in which the methylene groups and vinyl group in the alicyclic ring of 1 are interchanged was dismissed because such a conjugation of double bond and carbonyl should exhibit strong u.v. absorption at 227 nm. However, subtraction of the u.v. molecular absorption spectrum of 3 from that of salicortin indicated no such conjugation.

In their communication on tremulacin, Thieme and Richter[8] noted that treatment with dilute acid yielded salicyloyltremuloidin (7). This result suggested a structure analogous to that of 1, and analysis agreed with that of a monobenzoate of 1, $C_{27}H_{28}O_{11}$. Hydrogenolysis yielded carbon dioxide, adipoin, and 2-O-benzoyl-o-cresol-β-D-glucoside (4), m.p. 190-193°, identified by analysis and mass spectrum of its acetate, m.p. 138-140°, $C_{26}H_{28}O_{10}$. Thus, the structure of tremulacin must be 2.

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