

venously in the cat initially increased the response of tibialis to single maximal shocks applied to the motor nerve, and this response was followed by a small prolongation of the contraction, together with a widespread fibrillation of the musculature for 20–30 sec. not unlike that resulting from the injection of anticholinesterases. Intra-arterial injection of the C₉ derivative in a dose of 20 μgm. into the cat's tibialis itself produced a twitch before block ensued. The curare-like action was not antagonized by prostigmine in doses adequate to antagonize the effect of *d*-tubocurarine chloride, either in the cat's tibialis or in the rabbit's head-drop test.

Comparison of potency with *d*-tubocurarine chloride was complicated by the remarkable finding that while *d*-tubocurarine chloride is unaltered in potency when given after these *bis*-quaternary salts, the converse is not true; thus, following the injection of two-thirds head-drop dose, approximately twice as much of the C₁₀ derivative was required to produce head-drop as was normally needed.

The results reported represent preliminary findings on a series of simple compounds, some of which have a potency which exceeds that of *d*-tubocurarine chloride. They serve to demonstrate, however, the importance of pharmacological testing of possible substitutes for *d*-tubocurarine chloride on more than one test object, and to suggest that before clinical application can be considered it is desirable to find some satisfactory antagonist to their effects.

We are much indebted to Dr. H. King, who synthesized the first compound tested, and to Dr. F. C. MacIntosh for their encouragement and advice.

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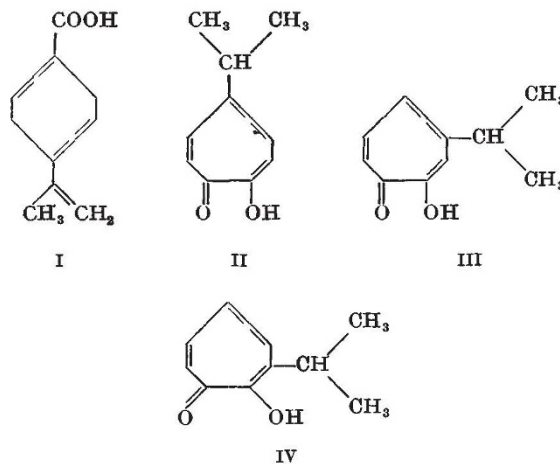
¹ Brown, G. L., *J. Physiol.*, **92**, 23 P (1938).

Antibiotic Substances from the Heart Wood of *Thuja plicata* Don.

THE heart-wood of western red cedar (*Thuja plicata* Don.), which possesses a low specific gravity and is very resistant towards decay, has been examined by Anderson and Sherrard¹. The steam distillate of this wood furnished an acid, C₁₀H₁₂O₂, termed dehydroperillie acid, showing low toxicity, and a very toxic 'phenol', m.p. 82°, of the same composition. For dehydroperillie acid they suggest the formula (I), but the structure of the compound of m.p. 82° was not elucidated.

In a private communication Anderson describes the separation of the 'phenolic' fraction of the steam distillate into the above compound, m.p. 82°, and an oil, also C₁₀H₁₂O₂, which he has kindly given us the opportunity to examine. It had meanwhile partly crystallized and afforded a compound, C₁₀H₁₂O₂, m.p. 52–52.5°, the investigation of which will be described jointly with Dr. Anderson.

From *Thuja plicata*, grown in Sweden, we have isolated dehydroperillie acid, the compound, m.p. 82°, and a less acidic isomeride, m.p. 34°, but none of the isomeride, m.p. 52–52.5°. The ultra-violet absorption spectrum of dehydroperillie acid shows maxima at 220 and 280 mμ. This behaviour suggests a structure with a more extended conjugated system than that in (I).



The ultra-violet absorption spectra of the three isomerides, melting points 82°, 52–52.5° and 34° respectively in alcoholic solution, are very similar, with maxima at 230–240 mμ and broad absorptions between 320 and 370 mμ. These isomerides absorb four moles of hydrogen on catalytic hydrogenation. The compound, m.p. 82°, thereby yields a diol, C₁₀H₂₀O₂, m.p. 87–88°, and as a by-product an oil, probably a diastereoisomeride or a mixture of such. The two other isomerides only give oily hydrogenation products. The diol, m.p. 87–88°, is easily cleaved by periodic acid to a dialdehyde, C₁₀H₁₈O₂, characterized as its *bis*-2 : 4-dinitrophenylhydrazone, m.p. 194–195°. Oxidation with potassium permanganate yields a dicarboxylic acid, C₁₀H₁₈O₄, m.p. 65.5–66.5°. The barium salt of this acid on dry distillation afforded 1-isopropylcyclohexanone-(4), identified as the 2 : 4-dinitrophenylhydrazone, m.p. 118–119°, and semicarbazone, m.p. 188–189°; both melting points were undepressed on admixture with authentic specimens. Hence the dicarboxylic acid, m.p. 65.5–66.5°, must be γ -isopropylpimelic acid. Consequently, the compound, m.p. 82°, most probably possesses the structure (II). This conclusion is supported by the fact that oxidation of the compound, m.p. 82°, with chromic acid furnished isobutyric acid (*p*-bromophenacyl ester, m.p. 76–77°; mixed m.p. 76–77°).

The absorption spectra and other evidence make it probable that the compounds, m.p. 52–52.5° and m.p. 34°, are represented by the formulae (III) and (IV) respectively.

The compound, m.p. 82°, is termed γ -thujaplicin because the isopropyl group occupies the γ -position in the cycloheptatrieneolone. If our views on the structure of the compounds, m.p. 52–52.5°, and m.p. 34°, are confirmed, these should be termed β - and α -thujaplicin respectively. The structure proposed for γ -thujaplicin recalls the constitution of the azulenes, stipitatic acid according to Dewar², and purpurogallin according to Prof. R. D. Haworth, and to Dr. J. A. Barltrop (private communications).

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¹ Anderson and Sherrard, *J. Amer. Chem. Soc.*, **55**, 3813 (1933).

² Dewar, *Nature*, **155**, 50 (1945).