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

II.* The Constitution of γ-Thujaplicin

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In a series of investigations relating to coniferous resin components and heart wood constituents we have hitherto only been concerned with trees belonging to the family *Pinaceæ*. Apart from ordinary terpenes and resin acids the resins and heart woods of these trees generally contain components of a phenolic nature.

Some of these, *e. g.* the pinosylvin of the heart wood of *Pinus silvestris* appear to be characteristic constituents of a whole genus. Other pines, however, in addition to pinosylvin contain a characteristic pattern of other heart wood constituents including flavones, flavanones, pinitol and arabinose [1]. Ultimately it appears to be possible to construct a chemical taxonomy for the genus *Pinus* on the basis of these findings. This should support and amplify that based on purely botanical evidence.

The amount or distribution of a component, *e. g.* a heart wood constituent, may sometimes differ widely from one individual to another probably through racial causes.

Some of these extraneous components occur in several genera of the *Pinaceæ* family either as such or in a structurally slightly modified state. Examples are conidendrin in *Picea*, *Tsuga* (and in the *Podocarpaceæ* family in *Podocarpus*), pinoresinol in *Picea* and *Pinus* and the closely related lariciresinol in *Larix*. This and other evidence indicate phylogenetic relations within the group.

Other large groups of conifers include the families *Taxodiaceæ* and *Cupressaceæ*. Their chemistry has been less closely investigated. However, there

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appears to be a marked difference between *Pinaceæ* and these families, although there are a few examples of common constituents. Redwood (*Sequoia sempervirens* Endl., *Taxodiaceæ*), *e. g.* contains in its heart wood pinitol, and *Chamæcyparis obtusa* Sieb. et Zucc. (*Cupressaceæ*) among other heart wood constituents hinokinin, a lignan closely related to the matairesinol of *Podocarpus spicatus*, conidendrin, pino- and lariciresinol.

On the whole, in the *Cupressaceæ* there appear to be less phenolic extraneous constituents, the majority being related to terpenes and sometimes possessing unusual structures. Examples are dehydrogeranic acid [2] (*Callitropsis araucarioides* Compt.), rhodinic acid [3] (*Chamæcyparis obtusa* Sieb. et Zucc., *Thujopsis dolabrata* Sieb. et Zucc.), citronellic acid [4] (*Callitris glauca* R. Br.), »dehydroperillic acid» [5] (*Thuja plicata* D. Don) and shonanic acid [6] (*Libocedrus formosana* Florin). When phenols are present they usually exhibit close relations to the terpene group *e. g.* carvacrol and hydrothymoquinone [7] (*Callitris quadrivalvis* Vent.). Hence, also from a chemical point of view these families appear to be separated from the *Pinaceæ*.

The present series of investigations deals with the elucidation of the unusual structure of some components of the heart wood of western red cedar (*Thuja plicata* D. Don, *Cupressaceæ*) which were previously unknown or regarded as being phenols.

Thuja plicata grows abundantly in the north western part of America between Alaska and California. It has been introduced frequently into Europe and in Sweden there is a plantation at Böda, island Öland in the Baltic.

Western red cedar possesses a very light non-resinous wood which, nevertheless, is very resistant to decay and is extensively used as timber. When in contact with unprotected iron the wood develops a black stain and the metal corrodes.

In 1907 Blasdale [8] isolated from the heart wood of *Thuja plicata* a compound $C_{10}H_{12}O_2$ m.p. 80°. In 1933 Anderson and Sherrard [5] described the isolation of an acid termed »dehydroperillic acid» m. p. 88° having the same elementary composition. In addition these authors reported the isolation of a »phenolic» isomeride m. p. 82° which was highly toxic towards *Fomes annosus*.

Anderson and Sherrard recovered their substances by steam distillation of the wood. In the course of their investigations they also obtained a liquid material possessing the composition $C_{10}H_{12}O_2$ (unpublished observations). Dr. Anderson has been kind enough to provide us with this product, which in the meantime had partly crystallised. From this material a new isomeride m. p. 52—52.5° was easily obtained. From reasons which will become obvious we term this compound *β-thujaplicin* and the elucidation of its structure will be the object of a joint communication with dr. Anderson (Part IV).

The present authors have extracted the heart wood of Swedish *Thuja plicata* with ether. It was found that in this way an almost negligible amount of the above mentioned compounds could be isolated. When the wood was extracted with acetone, however, a dark coloured material was obtained which was partly soluble in ether. The ether insoluble portion resembled Brauns' »native lignin» and was partly dissolved by hot bisulphite cooking acid.

This material or part of it apparently forms ether insoluble membranes in the wood within which the ether soluble constituents are deposited exactly as the pinosylvin of pines and conidendrin of the spruce [9].

»Dehydroperillic acid» was removed from the ether solution by sodium hydrogen carbonate. Less acidic components were extracted with sodium hydroxide. Acidification of the latter followed by steam distillation afforded an oil which was dissolved in alkali. Through a fortunate observation by one of us (J. G.) it was found that only part of the material was easily precipitated by carbon dioxide, forming an oil which readily crystallised in the ice chest.

This substance melts at 34° and constitutes still another isomeride $C_{10}H_{12}O_2$. It has been termed *α-thujaplicin* for reasons given in Part III. Prolonged treatment with carbon dioxide resulted in the precipitation of a more acidic fraction which crystallised directly proving to be identical with Anderson and Sherrards »phenol» m. p. 82° and for which we suggest the term *γ-thujaplicin.*

Thus, no less than four isomerides $C_{10}H_{12}O_2$ have been isolated from *Thuja plicata;* from American trees »dehydroperillic acid», γ- and β-thujaplicin but no α-thujaplicin; from Swedish grown trees »dehydroperillic acid», α- and γ-thujaplicin but no β-thujaplicin.

All the thujaplicins are stable compounds and no transformation of *e. g.* α-thujaplicin into β-thujaplicin has been observed. It remains to be investigated whether this difference between American and Swedish grown trees is due to racial causes.

α-, β- and γ-thujaplicin exhibit one and the same green ferric reaction. With copper acetate green copper salts are obtained which are readily soluble in chloroform. This is a characteristic and sensitive test for the presence of thujaplicins.

Their U. V. absorption spectra (Fig. 1) are very similar but differ greatly from that of »dehydroperillic acid». Hence the thujaplicins are evidently structurally closely related.

On catalytic hydrogenation γ-thujaplicin absorbs four molecules of hydrogen yielding a crystalline product $C_{10}H_{20}O_2$ (II) together with an oil which probably is a mixture of stereoisomeric octahydro-γ-thujaplicins.

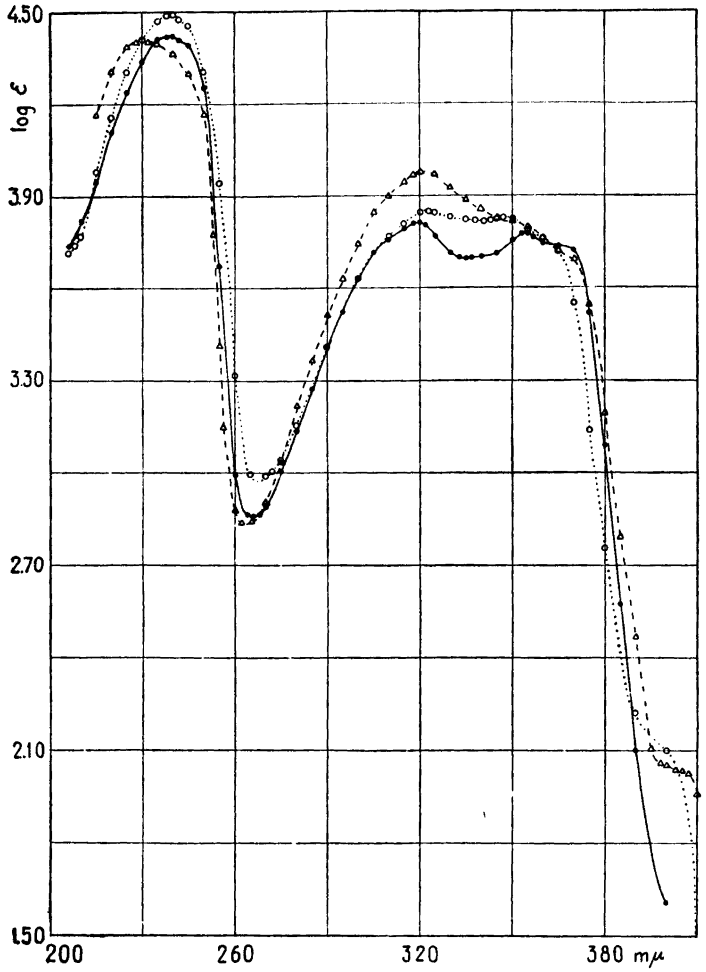


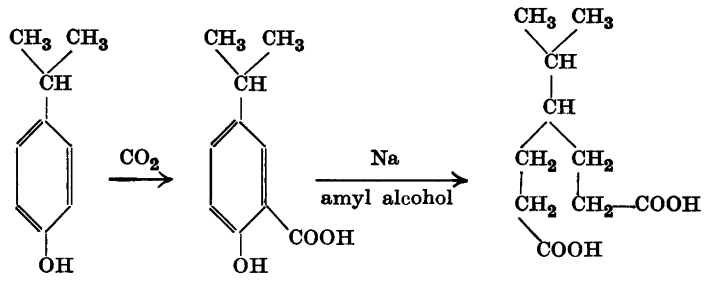
Fig. 1. Ultraviolet absorption curves: ●—● *α-thujaplicin,* ○···○ *β-thujaplicin and* △--△ *γ-thujaplicin in alcohol.*

On oxidation with periodate the compound $C_{10}H_{20}O_2$ affords a dialdehyde containing all ten carbon atoms of the original substance (III). The dialdehyde was characterised as its crystalline 2,4-dinitrophenylhydrazone. When oxidised with potassium permanganate both the crystalline and the liquid hydrogenation products of γ-thujaplicin yielded a dicarboxylic acid $C_{10}H_{18}O_4$ m. p. 65.5—66.5° (IV). These reactions characterise the hydrogenation products as being cyclic 1,2-diols.

Careful oxidation of γ-thujaplicin with chromic acid resulted in the formation of *iso*butyric acid, indicating the presence of an *iso*propyl group. Estimation of methyl attached to carbon yielded 0.49 moles of acetic acid. This is a normal yield from compounds containing *iso*propyl groups and excludes the presence of additional C-methyl groups.

On dry distillation of the barium salt of the dicarboxylic acid m. p. 65.5—66.5° an oil was obtained showing ketonic properties (V). This oil yielded a 2,4-dinitrophenylhydrazone and a semicarbazone which proved to be identical with the corresponding derivatives of 4-*iso*propyl*cyclo*hexanone. Furthermore, the oil, on oxidation with nitric acid, afforded β-*iso*propyladipic acid m. p. 76—77° (VI) identical with an authentic specimen.

It follows that the acid m. p. 65.5—66.5° must be γ-*iso*propylpimelic acid (IV). This acid which previously has not been described was prepared from *p*-*iso*propylphenol according to the following route:

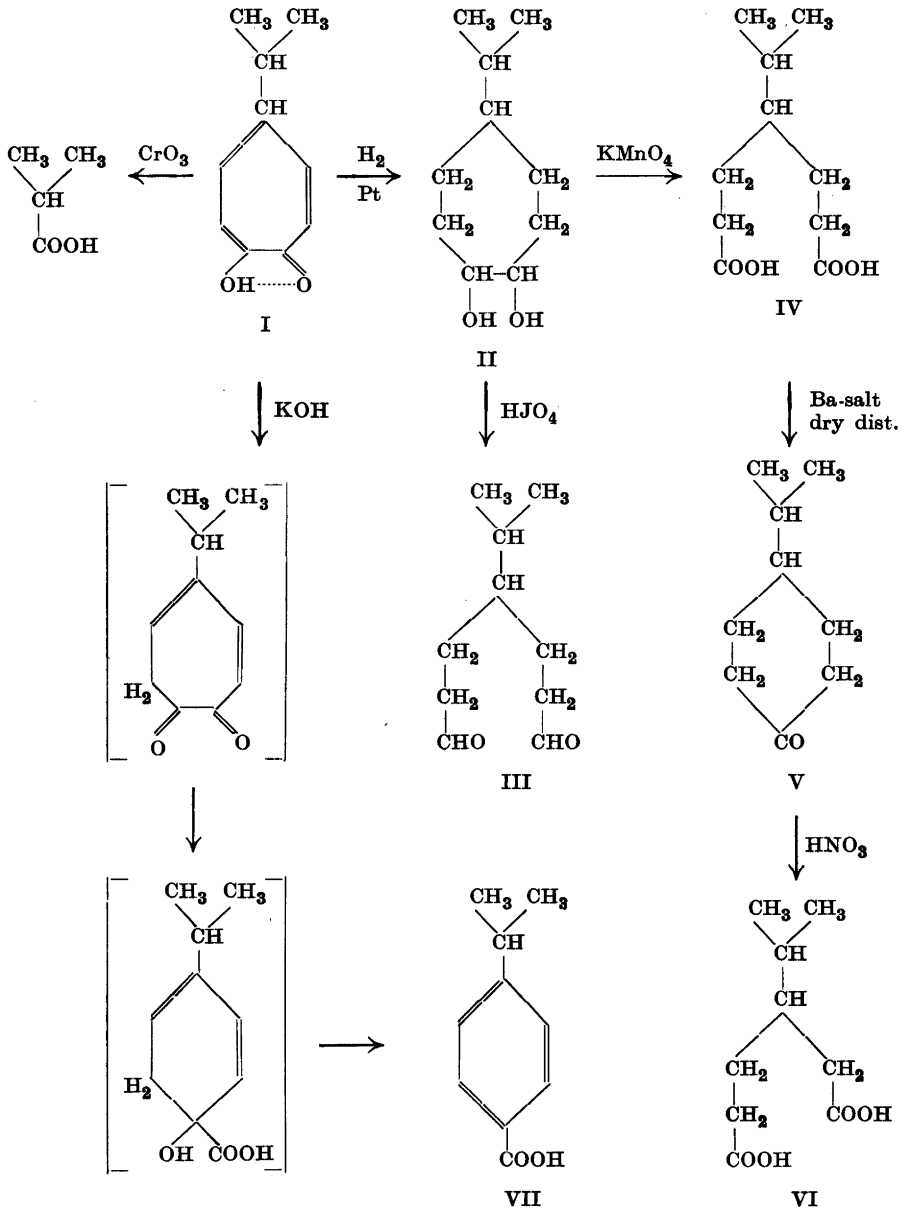


IV.

With diazomethan γ-thujaplicin yields an oily methyl derivative. It does not give any colour reaction with ferric chloride and therefore is obviously an O—CH_3 derivative. γ-Thujaplicin does not react with carbonyl reagents but reacts with bromine with formation of hydrogen bromide and a crystalline bromo derivative. It couples with diazotised amines giving red products. These reactions and the general stability of the compound recall the »aromatic nature» of benzene and its derivatives.

When heated with very strong alkali γ-thujaplicin is transformed into cuminic acid (*p*-*iso*propylbenzoic acid) (VII).

All these experimental results are readily explained on the basis of formula I for γ-thujaplicin and they are summarised in the following scheme:



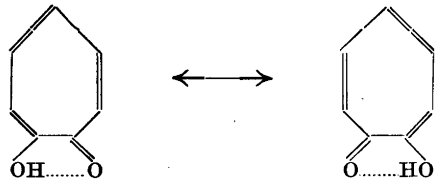
The name γ-thujaplicin refers to the fact that the *iso*propyl group occupies the γ-position relative to the oxygen atoms in the cycloheptatrien system. It is worth noting that γ-thujaplicin does not obey the isoprene rule although its close relation to the terpenes appears unmistakeable.

The formula I is in complete harmony with the properties of γ-thujaplicin. Since the structures of α- and β-thujaplicin are closely related to γ-thujaplicin (compare the two following papers) the discussion following below does also apply to them.

The acidic nature of the thujaplicins is to be expected by analogy with the carboxylic acid group, the hydroxy quinones and β-diketones. O = C — OH *viz.* O = C — C = C — OH. In the thujaplicins there are three double bonds interposed between the carbonyl group and the hydroxyl group. The acidity is due to the resonance:

$$(O{=}C{-}C{=}C{-}C{=}C{-}C{=}C{-}\overset{-}{O})\overset{+}{H} \longleftrightarrow \overset{-}{(O}{-}C{=}C{-}C{=}C{-}C{=}C{-}C{=}O)\overset{+}{H}$$

and this also explains the unreactive nature of the carbonyl group and the yellow colour of alkaline solutions of the thujaplicins. The formation of metal complexes soluble in chloroform probably arises through chelation. As a matter of fact the hydrogen atom of the hydroxyl group may be regarded as being shared between both oxygen atoms (hydrogen bond resonance VIII



VIII IX

—IX) although there appears to be some objection to this arising from the somewhat too long O—O-distance which can be calculated and which would not permit an ordinary hydrogen bond [10]. This is not a point of major structural concern but the peculiar properties of this novel structure merit further physico-chemical investigation.

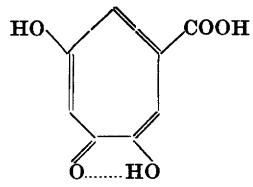
From the heart wood of the Japanese »hinoki» (*Chamaecyparis obtusa* Sieb. et Zucc.) *l*-rhodinic acid and a liquid compound $C_{10}H_{12}O_2$ termed »hinokitiol» have been isolated [3]. With ferric acetate a red crystalline complex was obtained which could be sublimed in a high vacuum (»hinokitin»). Several other metal complexes have been described [3, 11]. Hinokitiol was thought at first to be a cyclic β-diketone containing a five membered ring. Later the compound has obviously been regarded as containing a seven membered ring. In the *Chemical Abstracts* of 1947 a paper by Hiroshi Iinuma on »Coordination compounds of hinokitiol, *o*-diketone with seven membered ring» has been abstracted [11]. We have been unable, however, to find any article substantiating this statement.

Hinokitiol appears to be closely related to the thujaplicins. As it appears not to have been obtained in crystalline form it may perhaps be a mixture of different thujaplicins.

The unusual *cyclo*heptatrien ring structure of the thujaplicins appears not to be unique in the vegetable kingdom. It resembles, of course, the azulenes and could be regarded as an azulene in which the five membered ring has been removed by oxidation.

Some years ago Birkinshaw, Chambers and Raistrick [12] described a metabolite of the mould *Penicillium stipitatum* called stipitatic acid.

Dewar [13] interpreted their experimental results and advanced the formula X for this acid:

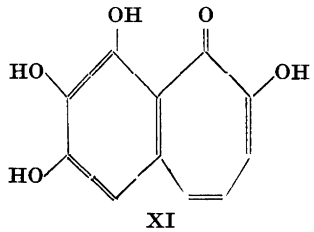


X

It exhibits a red ferric reaction and is converted into 5-hydroxy*iso*phthalic acid on heating with alkali.

Dewar [14] also suggested that colchicine might possess a similar *cyclo*heptatrienolone (»tropolone») structure and this idea has recently been confirmed by Arnstein, Tarbell, Huang and Scott [15]. With dilute acid colchicine is cleaved into methyl alcohol and colchiceine which is a true *cyclo*heptatrienolone. The latter compound shows a green ferric colour indistinguishable from that of the thujaplicins. It also gives a green copper complex soluble in chloroform. E. Rennerfelt has been kind enough to test the toxicity of colchiceine and its O-methyl derivative, colchicine, to fungi and reports that colchiceine is highly toxic whilst colchicine only possesses a low toxicity.

Quite recently Barltrop and Nicholson [16] advanced a new formula for purpurogallin (XI) the well known dehydrogenation product of pyrogallol, a glucoside of which is said to be a constituent of different galls (dryophantin) [17, 18].



XI

The tetramethyl ether of this compound on oxidation with permanganate, affords 3,4,5-trimethoxyphthalic acid, not formed, however, from the trimethyl ether which consequently must contain methoxyl groups distributed in both nuclei *.

When warmed with 2 *N* hydrochloric acid purpurogallin tetramethyl ether affords purpurogallin trimethyl ether identical with that obtained on methylation of purpurogallin with diazomethane. Thus the methoxyl group adjacent to the carbonyl group of the seven membered ring is not hydrolysed but one of the methoxyls of the benzene ring, probably the neighbouring one.

Similar to stipitatic acid purpurogallin [19] readily undergoes a benzilic acid change with formation of a six membered ring when subjected to the action of strong alkali.

All thujaplicins are highly toxic towards a great variety of wood destroying fungi and are obviously responsible for the great durability of the wood. A comprehensive study of this mycological aspect will be published elsewhere by Docent Rennerfelt, Statens Skogsforskningsinstitut, Stockholm. Thujaplicin appears to be a fungicidic substance rather than a fungistatic. When spores of *Pullularia pullulans* were treated with a 0.02 % solution of γ-thujaplicin all were alive after one hour. After three hours treatment 11 % were alive and after 6 and 24 hours all spores were killed. Quite recently the antibiotic character of the crude aqueous extract of the heart wood of *Thuja plicata* has been emphasized by Southam [20].

The toxicity of β-thujaplicin (compare part IV) to fish has been studied. *Lebistes reticulatus* died in a 0.02 % solution within 10 minutes and within 3 hours in a 0.002 % solution of this substance.

It appears to be more toxic than pinosylvin (Erdtman [9] 1939).

EXPERIMENTAL

Extraction of the wood

Batches of about 2 kg of finely powdered heart wood of *Thuja plicata* were extracted for 48 hours with acetone in a continuous extractor. From the combined extracts of several such batches the acetone was distilled off on a water bath. The remaining thick,

* This agrees with earlier unpublished results by one of us (H. E.) in University College, London, 1929. It was found that the trimethyl ether did not yield O-trimethylgallic acid as would be expected from the old Willstätter-Heiss formula. On oxidation with permanganate in the presence of magnesium sulphate a brown red crystalline compound (m. p. 163—165°) of hydroxyquinone character was obtained from the manganese sludge. From the tetramethyl ether 3,4,5-trimethoxyphthalic acid was obtained, isolated as the corresponding phthalimid and identified with an authentic specimen. On this occasion XI and alternatives with different distribution of the ionisable hydrogen atoms was discussed.

almost black oil was poured into a large volume of ether when a sticky resinous precipitate was formed. The ether was decanted and the precipitate washed thoroughly with ether. The combined ethereal solutions were extracted with a saturated solution of sodium hydrogen carbonate in order to remove »dehydroperillic acid». This was followed by extractions with 2 *N* sodium hydroxide solution. The very dark alkaline solution was acidified with sulphuric acid and extracted with ether. The ether was distilled off and the residue distilled with steam, until the distillate no longer showed any green colour in the ferric test. The distillate was saturated with sodium chloride and extracted with ether. The ether was extracted first with sodium hydrogen carbonate solution then with 2 *N* sodium hydroxide. The alkaline solution was agitated with a mechanical stirrer and carbon dioxide passed in. At pH ~ 9 an oil began to separate. The introduction of carbon dioxide was continued to pH ~ 8. The precipitated red oil was extracted with ether (Extract A). Carbon dioxide was passed again when a further precipitate appeared. When the solution had been saturated with carbon dioxide the precipitate was filtered and the solution extracted with ether (Extract B). The slightly brown crystalline precipitate consists of γ-thujaplicin.

Extract A was evaporated to dryness and the oily residue kept in a refrigerator overnight when it partly crystallised. The crystals were α-thujaplicin.

On evaporation extract B yielded an oil from which a small amount of γ-thujaplicin slowly crystallised. The combined mother liquors of extract A and B were dissolved in ether, the ethereal solution extracted with sodium hydroxide and the stepwise precipitation of α- and γ-thujaplicin with carbon dioxide repeated. In this way further amounts of α- and γ-thujaplicin were obtained. The yield varies considerably ranging from about 0.05 per cent down to almost nothing.

The γ-thujaplicin was distilled in a high vacuum and recrystallised from light petroleum. It formed long colourless needles, m. p. 82°.

$C_{10}H_{12}O_2$(164.1)	Calc.	C 73.13	H 7.37	$-CCH_3$ 9.15
	Found	» 72.97	» 7.37	» 4.0

With ferric chloride the alcoholic solution gives a green colour. By shaking its chloroform solution with a cupric acetate solution the chloroform is coloured intensely green. Evaporation of the chloroform gives a green crystalline copper complex m. p. 259—260°, easily soluble in the common organic solvents except light petroleum.

Oxidation of γ-thujaplicin

γ-Thujaplicin (0.2 g) was dissolved in dilute sulphuric acid (1 : 1, 20 ml). Sodium bichromate (1.5 g) dissolved in a small amount of water was then added in small portions. By external cooling the temperature was kept below 20°. After standing overnight the solution was distilled with steam. In the distillate the acid was determined by titration with standard alkali. This showed the presence of 0.53 millimoles of volatile acid (44 % of theoretical amount). The acid was converted to its p-bromophenacyl ester in the usual manner. After recrystallisation from dilute methanol it had m. p. 76—77°, undepressed in admixture with authentic *iso*butyric acid p-bromophenacyl ester.

Catalytic hydrogenation of γ-thujaplicin

γ-Thujaplicin (2.5 g) was dissolved in absolute ethanol and hydrogenated with Adams' platinum oxide catalyst. 1400 ml of hydrogen were consumed (calculated for 4 moles: 1360 ml). The catalyst was removed by filtration and the alcohol evaporated in a vacuum. On cooling the remaining oil partly crystallised. The crystals (1.3 g) were recrystallised from ligroin, m. p. 87—88°.

$C_{10}H_{20}O_2$ (172.2)	Calc.	C 69.69	H 11.73
	Found	» 69.60	» 11.85

A solution of this glycol, octahydro-γ-thujaplicin, in water consumes 1 mole of periodic acid. On addition of 2,4-dinitrophenylhydrazine dissolved in 2 *N* hydrochloric acid to the solution of the oxidised glycol a yellow precipitate was slowly formed. This was recrystallised from ethyl acetate, m. p. 194—195°.

$C_{22}H_{26}O_8N_8$ (530.3)	Calc.	N 21.14
	Found	» 21.24

Oxidation of octahydro-γ-thujaplicin

Octahydro-γ-thujaplicin (0.95 g) was suspended in 100 ml of water containing a small amount of sodium carbonate and 1.8 g potassium permanganate was then added in small portions at room temperature. When the permanganate colour had disappeared, dilute sulphuric acid was added and the manganese dioxide dissolved with sulphur dioxide. The solution was extracted with ether, the ethereal solution extracted with sodium hydrogen carbonate, the acid liberated by sulphuric acid and recovered with ether. After evaporation of the ether, the remaining oil (0.8 g) soon crystallised. On recrystallisation from a mixture of ether and light petroleum it had m. p. 51—52.5°, but after a few days the melting point increased to 65.5—66.5°. Subsequently only the higher melting point was observed.

$C_{10}H_{18}O_4$ (202.2)	Calc.	C 59.35	H 9.00
	Found	» 59.43	» 8.95

The oily portion of the hydrogenated γ-thujaplicin (0.47 g) on oxidation in a similar manner gave 0.4 g of the same acid.

4-*Iso*propyl*cyclo*hexanone

The above acid was converted into its barium salt. Dry distillation of this afforded an oil with a menthone-like smell. The oil was divided into two parts and these treated with 2,4-dinitrophenylhydrazine and semicarbazide respectively. After recrystallisation from methanol the 2,4-dinitrophenylhydrazone was obtained as orange red needles m. p. 118—119°.

$C_{15}H_{20}O_4N_4$ (320.2)	Calc.	N 17.50
	Found	» 17.62

The semicarbazone was recrystallised from dilute alcohol, m. p. 188—189°.

$C_{10}H_{19}ON_3$ (197.2)	Calc.	N 21.30
	Found	» 21.01

Neither substance showed any depression of melting point when mixed with the corresponding derivative of synthetic 4-*iso*propyl*cyclo*hexanone prepared according to Vavon and Callier [21] from *p-iso*propylphenol.

Oxidation of 4-*iso*propyl*cyclo*hexanone to *β-iso*propyladipic acid

The crude 4-*iso*propyl*cyclo*hexanone (0.05 g) was treated with conc. nitric acid. When the evolution of nitric oxides had ceased and the oil had disappeared the solution was neutralised and then made acid to congo red. After extraction with ether and evaporation of the ethereal extract an oil remained which partly crystallised. The crystals were dried on a porous plate and recrystallised from ether—light petroleum. A few milligrams of a substance m. p. 77—78° were obtained. The melting point was not depressed in admixture with an authentic sample of *β-iso*propyladipic acid, m. p. 78—80°.

Rearrangement of γ-thujaplicin to cuminic acid

γ-Thujaplicin (0.1 g) was added to potassium hydroxide (1 g) and a few drops of water and the mixture heated to about 230° in a nickel crucible. After 30 min. at this temperature the top layer was almost black. The melt was dissolved in water, a small amount of unchanged γ-thujaplicin precipitated with carbon dioxide and dilute sulphuric acid added. A precipitate (0.01 g) was formed. This was sublimed and recrystallised from dilute acetic acid, m. p. 115—116°, undepressed by an authentic sample of cuminic acid, m. p. 116—117°.

Synthesis of γ-*iso*propylpimelic acid

2,2-Di-(*p*-hydroxyphenyl)-propane (20 g) was mixed with about 1 g of a 15 % palladium charcoal catalyst and distilled very slowly (2—3 hours). The distillate was fractionated through a short column to remove phenol. When the temperature had reached 220° the distillation was interrupted and the residue distilled in a vacuum from an ordinary Claisen flask, b. p. 109—110°/10 mm. The distillate (5 g) immediately solidified and had m. p. 61°. The yield obtained by this process, which does not require any high pressure apparatus, is quite comparable with that reported by Cook, Philip and Somerville [22].

The 4-*iso*propylphenol was converted into 2-hydroxy-5-*iso*propylbenzoic acid as described by Paternò and Mazzara [23].

This acid (0.55 g) was dissolved in amyl alcohol (50 ml) and to the boiling solution was added small pieces of sodium (3 g). After the sodium had dissolved the amyl alcohol was removed by steam distillation. The residue was acidified and extracted with ether. The ether was evaporated and the remaining oil distilled with steam. The water solution

containing the nonvolatile acid was evaporated on a water bath. An oil which readily crystallised was obtained. After recrystallisation from ether—light petroleum the melting point was 65—66°.

$C_{10}H_{18}O_4$ (202.2)	Calc.	C 59.30	H 9.00
	Found	» 59.26	» 8.95

When mixed with the acid m. p. 65.5—66.5° obtained by oxidation of octahydro-γ-thujaplicin no depression of the melting point was observed.

Hydrolysis of O-tetramethyl purpurogallin

O-tetramethyl purpurogallin (0.1 g) was heated on a water bath with 2 *N* hydrochloric acid (10 ml). The substance melted and long yellow needles soon appeared. When all the oil had disappeared the crystals were recovered and recrystallised from alcohol, m. p. 174—176°, undepressed in admixture with an authentic sample of the trimethyl ether of purpurogallin obtained by methylation of purpurogallin with diazomethane.

SUMMARY

From the heart wood of western red cedar (*Thuja plicata* D. Don.) grown in Sweden, »dehydroperillic acid», $C_{10}H_{12}O_2$, together with two isomeric, crystalline compounds which have been termed α- and γ-thujaplicin have been isolated. In addition to »dehydroperillic acid» Anderson and Sherrard in 1932 working with American grown wood have isolated a compound which is identical with γ-thujaplicin. One of the liquid fractions obtained by them had crystallised in the meantime and from this material we isolated another isomeride $C_{10}H_{12}O_2$ which has been termed β-thujaplicin.

The structure of γ-thujaplicin, which is highly toxic to a great variety of fungi and to fish, has been elucidated. It contains a seven membered ring and is 1-*iso*propyl*cyclo*heptatrien-(1,3,6)-ol-(4)-one-(5), or on the basis of Dewar's suggestion to term this particular *cyclo*heptatrienolone system tropolone, γ-*iso*propyltropolone.

We wish to express our sincere thanks to Dr. A. B. Anderson, Portland, Oregon for providing us with products isolated by him from American *Thuja plicata*. Generous grants from *Statens Tekniska Forskningsråd* are also gratefully acknowledged.

The analyses were carried out by W. Kirsten, Upsala.

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