THE "PHENOLS" OF AUSTRALIAN ESSENTIAL OILS.

(A). "CALLITROL".

Constitution and preparation of isomers.

(B). "TASMANOL".

D.E.White.

[redacted]/3/43

(A). "CALLITROL".

Constitution and Preparation of Isomers.

The "Callitris" genus is the typical native pine of Australia, occurring as it does over the whole continent. In New South Wales the predominant species is Callitris glauca, which grows in the valleys and on the plains, while Callitris calcarata is restricted to the hilly areas. Seven other species also occur but are not nearly so widespread. Several more species occur in West Australia and Tasmania, while Callitris intratropica is the predominant type in Northern Australia.

Although systematic work, founded on the morphological characters was undertaken by the early botanists, the genus was much more fully investigated by R.T.Baker and H.G.Smith, who in their work "A Research on the Pines of Australia" (Sydney, 1910) published details of the histology, physiology, phylogeny, embryology and chemistry of the genus.

In the chemical section they investigated the oils obtained by steam distillation of the leaves and of the wood. In the leaf-oils they found pinene, dextro and laevo limomene, dextro borneol and bornyl acetate, geraniol and geranyl acetate. These were generally present, but varied in amount in the different species in such a manner that the species could be identified by the oil yielded by the leaves.

From the wood of Callitris glauca, cut into shavings, Baker and Smith obtained a yield of 0.82% of steam volatile oil, on distillation for 8-9 hours. The material so obtained was squeezed through cloth, by which means the solid was retained. This on recrystallisation from alcohol melted at 91°C. and was recognised as the sesquiterpene alcohol "Guaiol", being identical with that obtained from guaiac wood oil.

The liquid material was dark coloured and of specific gravity 0.9854 at 16°C. The rotation could not be determined as light would not pass through the tube. The saponification number is given as 106.6 and the acid number 68.8. On distillation three fractions were obtained :-

1.	B.P. 248-255°C.	60%	
2.	B.P. 255-265°C.	21%	Bright blue
3.	B.P. 266-296°C.	10%	Deep indigo-blue.

Fraction (1) was redistilled, boiling at 250-252°C. This was but little coloured and had a specivic gravity of 0.9266 at 15°C. and a refractive index of 1.4926 at the same temperature. This was stated to consist mainly of a sesquiterpene, although far from pure.

To separate the constituents of the oil, it was treated with boiling alcoholic potassium hydroxide, water added in quantity and after the separated oil had crystallised it was removed. The solution was then evaporated to remove alcohol, filtered, and acidified.

The alkali soluble oil was then removed and washed thoroughly with water. This material was acid to litmus but on washing ~~this~~ with sodium carbonate solution an oil remained which was but little coloured, was thick and somewhat viscous and according to Baker and Smith, evidently a phenol.

This substance was more readily obtained by agitating the original crude oil with 10% aqueous soda. The pasty, insoluble material was removed and the alkaline solution diluted largely with water and extracted with ether. The "phenol" obtained in this manner was identical with that obtained after saponification.

Its reactions were :-

1. With ferric chloride	No colouration
2. With bromine in alcohol	Purple colour on evaporating the alcohol
3. With bromine in acetic acid	Red colour changing to purple and indigo-blue. Destroyed by water.
4. With sulphuric acid in acetic acid	Red colour changing to deep purple.
5. With sulphuric and nitric acids in acetic acid	Colour changes from red to purple but more rapidly.

Baker and Smith also suggested that this "phenol", if it should prove new, should be called "callitrol".

Further investigation by the Council for Scientific and Industrial Research (Journal 2, 178) showed that the alkali soluble extract from the timber of Callitris glauca was the material responsible for the well known resistance of that timber to fungus and termite attack. It was therefore highly desirable that the constitution of the material should be investigated and so this was undertaken, with the added object of studying the types of substances which act as termite deterrents.

Logs for the investigation were procured through the kindness of the Department of Agriculture, the timber used being that of Callitris glauca. The wood was cut into shavings and steam distilled, as described in the experimental part, and a good yield of oil obtained. The alkali soluble portion of this oil, on careful purification -- "callitrol" -- was completely soluble in aqueous solutions of sodium carbonate and bicarbonate and when submitted to the abovementioned tests gave negative results in each case. The crude oil gave the characteristic test described by Baker and Smith :-

> A drop of the oil on a watch glass is dissolved in acetic acid and bromine vapour passed over it. A purple colour forms, soon becoming a rich purple.

This, however, was found to be due, not to the main constituent of the alkali soluble oil but to a substance contained in a small fraction (11%) of higher boiling point.

"Callitrol" was readily methylated with dimethyl sulphate and sodium hydroxide in the cold but the methyl derivative, on refluxing with 15% potassium hydroxide in aqueous solution, was easily hydrolysed, the original "callitrol" being recovered.

This seemed to indicate that "callitrol" was not a phenol, and this was supported by analyses for carbon and hydrogen, in conjunction with molecular weight determinations made on the methyl derivative in benzene at the freezing point. These indicated a formula $C_{10}H_{18}O_2$ for "callitrol" and $C_{11}H_{20}O_2$ for the methyl derivative. The molecular weight of the "callitrol" in benzene could not be accepted, as high values were obtained which increased with the concentration, thus indicating that the substance was associated in solution.

As unsaturation had been observed in "callitrol" it was titrated with bromine in chloroform at 0°C. It was found that one molecule of "Callitrol" absorbed 2.7 atoms of bromine while 0.6 molecule~~s~~ of hydrobromic acid ~~were~~ was set free. This shows that there is probably one double bond in the molecule, while one atom of hydrogen is being substituted by bromine.

Reduction with hydrogen in the presence of finely divided platinum confirmed these results, a colourless oil "dihydrocallitrol" being readily obtained. This substance was fully saturated and thus indicated an open chain structure. On treatment with sulphur in the usual way for dehydrogenation the original substance was recovered in small yield, no other dehydrogenation product being obtainable.

It was now apparent that "callitrol" must be either an enolisable ketone, a lactone or an acid. However, no ketone properties could be detected with phenyl hydrazine, no phenyl urethane could be prepared and anhydrous formic acid was without action on "dihydrocallitrol". Also, the possibility of it being a lactone was ruled out by the analyses quoted previously, the methyl derivative containing merely a CH_2 group more than "callitrol". Moreover, "callitrol" and "dihydrocallitrol" were both found to be soluble in sodium bicarbonate and calcium hydroxide solutions, although partially precipitated on the addition of a large amount of water, the substance then being capable of extraction with ether. Thus it seemed practically certain that "callitrol" was a very weak acid.

Treatment with methyl alcohol and hydrochloric acid gas resulted in the addition of HCl at the double bond as well as methylation, while the p-nitrobenzyl ester although readily prepared could not be crystallised.

However, a crystalline silver salt was obtained on the addition of silver nitrate solution to a neutral solution of the sodium or ammonium salt. Also, on treatment of the acid chloride, obtained by the action of thionyl chloride on "callitrol", with a solution of aniline in ether a solid anilide was obtained. This proved beyond doubt that "callitrol" was an open chain unsaturated acid.

The amide and p-toluidide were obtained in a similar manner, together with the amide and anilide of "dihydrocallitrol". The latter was also obtained from the anhydride, made by treating "dihydrocallitrol" with acetyl chloride at 120-180° C.

By comparison of the properties of these derivatives of "dihydrocallitrol" with those of the known acids $C_{10}H_{20}O_2$ it appeared certain that it was identical with dihydro-citronellic acid, the amide and anilide having similar melting points to those described, while the refractive indices of the acids were also in agreement.

In the case of the unreduced, citronellic acid, the only derivative described in the literature is the amide and although the melting point of this and the amide of "callitrol" agreed, as well as the refractive indices of the acids, this was not considered sufficient identification. It was , therefore, desirable to obtain some citronellic acid for comparison and as neither l-citronellal nor the laevo acid ("callitrol" being laevo rotatory) were available the dextro acid was prepared from d-citronellal by the method described by Semmler (Ber. deutch. chem. Ges., 26, 2255) . This method was much preferable to Semmler's earlier method (Ber. 24, 208).

The acid obtained in this way was then converted into the acid chloride with thionyl chloride, and this on treatment with andline and p-toluidine in ether gave the anilide and p-toluidide respectively.

These were found to have melting points identical with the corresponding derivatives of "callitrol". Mixtures of the anilides ~~of the anilides~~ etc.,of the dextro and laevo acids, however,showed a depression of melting point,but this is quite normal when no true racemate is formed.

Finally,distillation of the calcium salt of "callitrol" with calcium formate gave a small yield of an aldehyde,which on conversion into the corresponding atophan had a melting point identical with that obtained from d-citronellal.

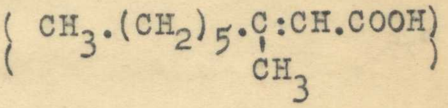
Thus we see that the main constituent of the alkali soluble oil from the wood of Callitris glauca is not a phenol,but laevo citronellic acid.

Experiments carried outby Mr. Dadswell of the Council for Scientific and Industrial Research,on carefully purified specimens,showed that while laevo citronellic acid is completely toxic to the wood destroying fungus Fomes annosus at a concentration of 0.016%,the dextro acid is slightly less toxic, while laevo dihydro-citronellic acid shows a similar toxicity to the unreduced acid.

In order that the effect of different configurations on the toxicity and anti-termitic properties might be studied,the preparation of a series of decenoic acids was commenced.

Two acids have already been obtained, the straight chain nonene (2) 1-carboxyllic acid ($C_6H_{13}.CH:CH.CH_2.COOH$) being obtained by the distillation of n-hexyl paraconic acid (Schneegans , Annalen der Chemie, 227, 87). In the preparation of the latter, however, it was found that freshly prepared sodium succinate was essential for success.

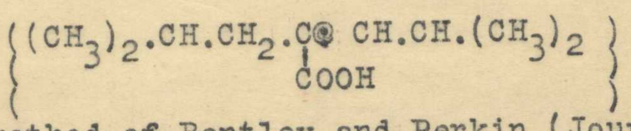
2 methyl octene (1) carboxyllic acid



$(CH_3.(CH_2)_5.\underset{CH_3}{C}:CH.COOH)$

was prepared by hydrolysis of the ester with 20% aqueous potassium hydroxide. The latter had been prepared by Bouveault and Blanc (Bull.Soc.Chim., 1904, 1208) by the condensation of methyl hexyl ketone and ethyl bromacetate in a Reformatsky reaction, followed by dehydration of the product. It was found, however, that the Reformatsky reaction was best performed in benzene solution with a little ethyl acetate as catalyst -- the above authors do not state the conditions used-- while in the dehydration potassium bisulphate gave superior results to the ~~original~~ method described, ~~with~~ (zinc chloride in acetic acid solution.)

The preparation of a third acid, 2:6 dimethyl heptene (3) 4-carboxyllic acid



$((CH_3)_2.CH.CH_2.\underset{COOH}{C}@\ CH.CH.(CH_3)_2)$

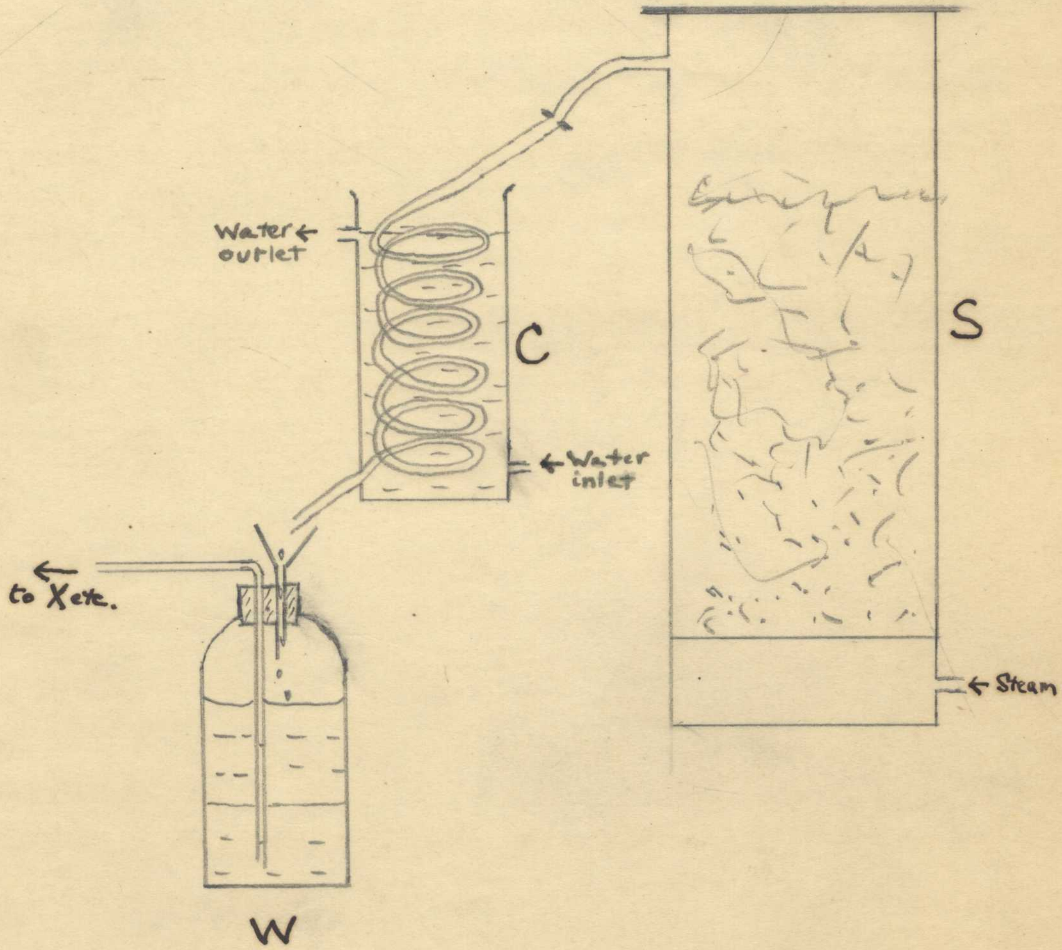
was commenced, but the method of Bentley and Perkin (Journal of the Chemical Society, 73, 67) was found to be unsatisfactory, as the yield of ethyl di-isobutyl-malonate obtainable was so very poor.

Freylon (Annales de Chimie,ser.8,20,60) had also obtained a good yield from this reaction,but Marshall(Journal of Chemical Society,1930,2754) experienced difficulty in the analogous reaction with isopropyl bromide. As he had overcome this by using cyanacetic ester,it was decided to try this method here. In this case,however,it was found that only one isobutyl group could be readily introduced,the main product of further treatment with sodium or potassium ~~hydroxide~~ ethoxide and isobutyl bromide being isobutyl cyanacetic acid. Freylon (Annales de Chimie,ser.8,19,562) obtained ethyl di-isobutyl cyanacetate by treatment of ethyl cyanacetate with one molecule of isobutyl bromide but Hessler (Journal of the American Chemical Society,38,912) obtained a mixture,consisting mainly of the mono substituted ester,under the same conditions.

It is hoped that these difficulties may yet be overcome,and the work is being continued with that end in view.

EXPERIMENTAL.

In the distillation of the oil from the wood of Callitris glauca, the apparatus shown in the diagram was found to be most [illegible] suitable :-



The wood, after the bark had been removed, was cut into shavings and placed in the still S and when the lid had been securely attached, steam from the boiler was passed in. The vapour issuing from the still was condensed in the condenser C and the liquid was allowed to flow into a bottle W containing water and a top layer of about 500 ccs of benzene. On flowing through this the oil was extracted, while the water sank to the bottom, from whence it was syphoned into a similar bottle X, where it was treated similarly, and thence to a third and fourth (Y and Z). The water issuing from the bottle Z was allowed to flow away, the outflow being controlled by a clip, so that the levels in all the bottles remained practically constant. This process allowed a fourfold extraction -- this being all that was found necessary -- and had the added merit of being continuous and practically automatic in operation.

Following are the results of a typical distillation of 33.95 kilograms of Callitris glauca timber cut into shavings :-

Steam Distillation.

First Day	5 hours	210 gm.
Second "	6 "	95 "
Third "	5 "	34 "
		339 gm.

This oil was not completely free from benzene, the latter having only been removed on the water bath.

Alkali Extraction.

This was carried out by allowing the oil to stand for some hours in contact with 5% aqueous sodium hydroxide. Ether was then added and the two layers separated. THe ethereal layer was then extracted several more times with 5% sodium hydroxide and then the alkaline extracts were combined, washed with ether and then acidified, after which the alkali soluble oil was extracted with ether.

Soluble : 118 gm 54%
Insoluble : 101 gm 46%
219 gm.

Distillation.

The alkali soluble portion (118 gm) was distilled under reduced pressure and the following fractions collected :-

1.	B.P. -121° C. at 0.7 mm.	6 gm	5%
2.	B.P. 118-120° C. at 0.55 mm.	82 gm	70%
3.	B.P. 120-135° C. at 0.55 mm.	5 gm	4%
4.	Residue	20 gm.	18%.

Re-distillation of Fraction (2).

2.(a). B.P. -114 at 0.4 mm.	2 gm
2.(b). B.P. 116-7 at 0.5 mm	27 gm
2.(c). B.P. 116.5-8 at 0.5 mm.	50 gm
Residue	8.5 gm.

Fraction 2(c) was again redistilled, when it was found to have the following properties:-

B.P. 117-9° C. at 0.6 mm.

Refractive Index at 24°C. : 1.4563

Specific Gravity at 25°C. : 0.9274
(compared to water at 25°C)

Optical Rotation at 24°C. in 5 cm. tube : -2.81°
(Sodium light)

i.e. Specific Rotation : -6.60°

Completely soluble in sodium carbonate and bicarbonate and calcium hydroxide solutions.

Analyses.

0.0822 gm gave 0.2121 gm CO_2 and 0.0763 gm H_2O
0.1406 gm " 0.3605 gm " " 0.1286 gm "

i.e. C : 70.4 ,69.93 %
H :: 10.3 ,10.16 %

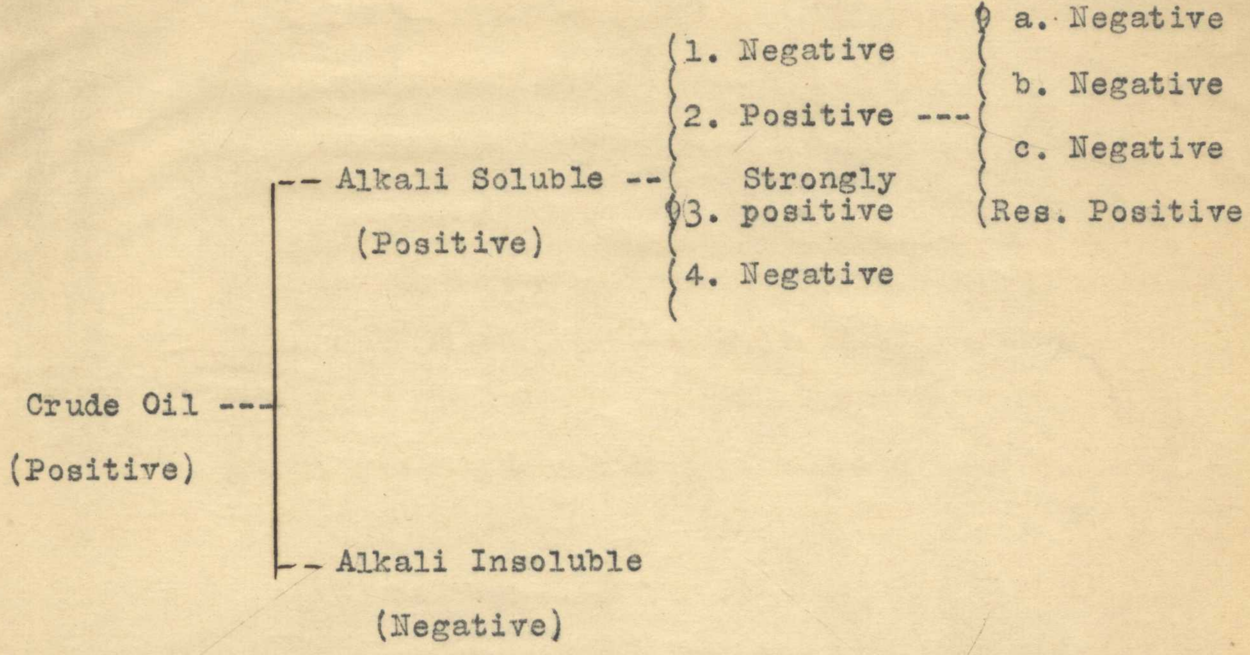
Calculated for $C_{10}H_{18}O_2$: C : 70.58%
H : 10.58%.

Molecular Weight.

In	1. 286%	benzene	solution	M.W. : 292.1
"	1.924 %	"	"	M.W. : 302.6
"	2.390 %	"	"	M.W. : 317.2

Action of Bromine Vapour.

The following results were obtained when the oil obtained from the steam distillation of the wood of Callitris glauca was submitted to the "characteristic" test for "callitrol" described by Baker and Smith and mentioned previously (p.4) :-



This table shows conclusively that the substance responsible for this colour reaction is contained exclusively in the small fraction boiling at a higher temperature than the main bulk, and totalling only 11% of the alkali soluble oil. Even then it is certain that this fraction is by no means pure so that the amount of the substance causing the colour must be very small.

Methylation of "Callitrol".

"Callitrol" (7 gm) was dissolved in 20% aqueous sodium hydroxide (50 ccs) and treated with dimethyl sulphate (20 ccs). The resulting insoluble oil was extracted with ether, the extract washed with sodium hydroxide solution, and then with water, dried, the ether removed and the product distilled.

Yield: 6 gm.   B.P. 85-7° C. at 1.1 mm.

Hydrolysis.

The methyl derivative was refluxed with 15 % aqueous potassium hydroxide (6 gm with 100 ccs) for 1hour. The oil was then completely dissolved and after cooling and washing with ether the alkaline solution was acidified with dilute HCl and extracted with ether. The ethereal extract was washed with water, dried and after removal of the ether, distilled.

Yield : 3 gm.

B.P. 120-1° C. at 0.8 mm. (This is in very good agreement with that of the original "callitrol").

Analyses of Methyl Derivative.

0.1065 gm gave 0.2792 gm CO_2 and 0.1005 gm H_2O
0.0766 gm " 0.2005 gm " " 0.0753 gm "

i.e. C : 71.5 , 71.4 %
H : 10.49, 10.94 %

Calculated for $C_{11}H_{20}O_2$: C : 71.7%
H : 10.9%.

Molecular Weight.

The following values were obtained :-

176.4
170.8
182.8

$C_{11}H_{20}O_2$ requires ~~172~~. 184.

Bromine in Chloroform.

As "callitrol" had been observed to be unsaturated it was decided to titrate it with bromine in chloroform in an attempt to ascertain the number of double bonds present in the molecule. The bromine solution (0.03932 gm bromine per cc.) was run into a solution of the "callitrol" in chloroform cooled to $0^oC.$,until the colour of the bromine just persisted.

The chloroform solution was then shaken with water and the hydrobromic acid solution so obtained titrated with standard sodium hydroxide solution.

1. 0.2290 gm "callitrol" absorbed 7.5 ccs bromine solution and gave 0.06537 gm HBr

2. 0.3537 gm "callitrol" absorbed 11.3 ccs bromine solution and gave 0.0998 gm HBr.

Thus one molecule absorbed 2.7 atoms of bromine and 0.6 mols. of HBr were liberated.

From this it appears that there is one double bond in the molecule, but one atom of hydrogen is also being substituted with bromine.

Reduction of "Callitrol".

"Callitrol" was reduced, catalytically, in several solvents with the following results :-

1. In Glacial Acetic Acid.

"Callitrol" (5 gm) was dissolved in glacial acetic acid(50cc) and platinic oxide (0.35 gm) added. The mixture was then shaken with hydrogen, when the oxide was very quickly reduced, the absorption of hydrogen being complete in 2½ hours, when 835 ccs had been absorbed. The platinum was then removed by filtration and the acetic acid distilled from the water bath at 25 mm. The product was then distilled.

Yield : 4 gm.

B.P. 113-5° C. at 0.55 mm.

Refractive Index : 1.4365 (at 24° C.)

Optical Rotation : -2.0° (at 23.5° C. in a 5 cm. tube).

Completely soluble in sodium carbonate and bicarbonate solutions

2. In Absolute Alcohol.

"Callitrol" (25 gm) was dissolved in absolute ethyl alcohol (120 ccs) and platinic oxide (1 gm) added. The mixture was then shaken with hydrogen till absorption was complete.

Hydrogen absorbed : 4030 ccs i.e. one molecule.

The platinum was then removed by filtration and the alcohol evaporated. The product was then distilled.

Yield : 20 gm

B.P. 114-6° C. at 0.62 mm.

Difficulty was experienced in this experiment in obtaining all the platinum in a filtrable state, the tendency being for it to remain colloidal.

3. In Ethyl Acetate.

"Callitrol" (15 gm) was dissolved in ethyl acetate(75 ccs) and platinic oxide(1.0 gm) added. The mixture was then shaken in an atmosphere of hydrogen until absorption was complete (2560 ccs absorbed). The platinum was then removed by filtration and the ethyl acetate evaporated.The product was then distilled.

Yield : 13.5 gm

B.P. 114-5° C. at 0.7 mm.

Refractive Index : 1.4370 at 23° C.

Optical Rotation : -1.91° at 22° C. in a 5 cm. tube.

This was the most satisfactory of the methods of reduction tried,the platinum coagulating easily when the reaction was complete and the solvent being easily removed on the water bath.

Treatment of "Dihydrocallitrol" with Sulphur.

"Dihydrocallitrol" (10 gm) and pure sulphur (20 gm) were heated together in a Perkin flask in a metal bath to 250-280° C until there was no further evolution of H_2S. (28 hours). The loss in weight in this time was 15 gm. The product was distilled from the Perkin flask at 0.85 mm with the bath at 150-180° C. and then redistilled.

Yield : 1.7 gm

B.P. 108-111° C. at 0.5 mm.

This substance was soluble in sodium carbonate,did not crystallise in a freezing mixture and contained no sulphur. Later it was shown by preparation of the anilide that it was identical with "dihydrocallitrol".

Analyses of "Dihydrocallitrol".

0.1120 gm gave 0.2862 gm CO_2 and 0.1153 gm H_2O

0.1051 gm " 0.2702 gm " " 0.1108 gm "

i.e. C : 69.8 , 70.3 %

H : 11.43 , 11.72 %

Calculated for $C_{10}H_{20}O_2$: C : 69.8 %

H : 11.62 %.

"Dihydrocallitrol" and Formic Acid.

"Dihydrocallitrol"(5 gm) was added to formic acid (12 ccs; S.G. 1.22) and the solution refluxed for 45 minutes. On cooling and adding water the liquid separated into two layers. Ether was then added and the extract washed very rapidly with 5% sodium carbonate solution. After washing with water, drying, and removal of the ether, the product was distilled.

Yield : 1.2 gm

B.P. 103-8° C. at 0.6 mm.

This product was found to be soluble in sodium carbonate and was later proved to be identical with "dihydrocallitrol" by the preparation of the anilide (M.P. 90°C) which did not depress the melting point of the anilide of "dihydrocallitrol". A further 3.5 gm was also recovered from the sodium carbonate washings.

"Callitrol" and Phenyl Isocyanate.

Formic acid having failed to reveal the presence of a hydroxyl group in"dihydrocallitrol" this reaction was tried in order to confirm thosw results.

"Callitrol" (0.5 gm) and phenyl isocyanate (0.5 gm) were heated together on the water bath for 15 minutes when a crystalline solid had begun to separate. On standing overnight this precipitation was complete. This product was filtered.

Yield : 0.5 gm.

M.P. 237° C.

This was diphenyl urea,as shown by the melting point ,which was identical when mixed with an authentic specimen,and was produced by the addition of the elements of water to phenyl isocyanate.

Thus "callitrol" appears not to contain an alcoholic or phenolic hydroxyl group as it will not give a phenyl urethane and its reduction product is unaffected by formic acid.

"Callitrol" and Phenyl Hydrazine

"Callitrol" (0.5 gm) and phenyl hydrazine (0.5 gm) were heated together on the water bath for 3 hours. No reaction could be detected and the " callitrol" was recovered on extraction with alkali.

Phenyl Hydrazine and Methyl Derivative.

Phenyl hydrazine (1 gm) and the methyl derivative of "callitrol" (1 gm) were heated together on the water bath for 4 hours. No reaction took place.

Action of Methyl Alcohol and HCl.

"Callitrol" (5 gm) was dissolved in methyl alcohol (21 gm) and dry HCl gas (1.5 gm) passed into the solution while cooling in ice. The solution was then refluxed for 30 minutes, when it had darkened somewhat. The methyl alcohol was then distilled and the product dissolved in ether and washed with 10% sodium hydroxide solution and then with water. The extract was then dried and the ether evaporated and the product distilled.

Yield : 3. 7 gm

B.P. 85-8° C. at 0.4 mm.

Analysis.

0.1038 gm gave 0.2364 gm CO_2 and 0.0896 gm H_2O

~~[illegible]~~

0.1037 gm gave 0.2366 gm CO_2 and 0.0905 gm H_2O

i.e. C : 62.2 , 62.3 %

H : 9.52 , 9.67 %

Calculated for $C_{11}H_{21}O_2Cl$: C : 64.8 %

H : 9.95 %.

Action of p-Nitrobenzyl Chloride.

As it now appeared certain that "callitrol" was an acid it was decided to attempt to prepare the p-nitrobenzyl ester.

"Callitrol" (5 gm) was dissolved in absolute alcohol (50 ccs) and p-nitrobenzyl chloride (3.4 gm) and potassium carbonate (dry, powdered; 1.5 gm) added.

The whole was then heated under reflux on the water bath. The p-nitrobenzyl chloride dissolved rapidly and crystals of potassium chloride could be observed separating. After 5 hours refluxing the solid was filtered and the alcohol evaporated on the water bath and the residue distilled.

Fraction 1 : B.P. 110-1° C at 0.8 mm p-nitrobenzyl chloride

Fraction 2 : B.P.115-7° C. at 0.9 mm " and"callitrol"

Fraction 3 : B.P.190-3° C. at 0.7 mm Ester.

Yield : 2.5 gm.

There appeared to be some decomposition taking place during the distillation of the highest fraction.

The ester could not be made to crystallise.

Silver Salt.

"Callitrol" (2 gm) was dissolved almost completely in sodium carbonate solution. Excess silver nitrate solution was then added and the precipitated silver salt filtered and washed free from silver nitrate. It was then recrystallised from boiling water,in which it was slightly soluble. Addition of a little silver nitrate solution was necessary for the complete separation of the salt in recrystallisation.

Yield : 0.5 gm (From 2 litres of water.).

As the salt decomposed on exposure to the light it was dried in a vacuum dessicator in the dark.

Analysis.

0. 1443 gm silver salt gave 0.0561 gm silver

0. 1398 gm 2 " " 0.0541 gm "

i.e. Equivalent weight : 277.49 , 278.77

i.e. Equivalent weight of "callitrol" : 170.61 , 171.89

Calculated for $C_{10}H_{18}O_2$: 170

Preparation of Anilide.

"Callitrol" (1 gm) was treated with thionyl chloride (1.5 ccs) with warming on the water bath. The excess thionyl chloride was then removed on the water bath at 25 mm and the residue treated with aniline (1.5 ccs in 10 ccs ether). Heat was evolved and the reaction was completed by warming on the water bath. The ethereal solution of the product was the washed with dilute HCl and then with water, the extract dried and the ether removed on the water bath. The residue crystallised on cooling and was recrystallised from petroleum ether (60-80)
Yield : 0.7 gm M.P. 73-4° C.
On recrystallisation further from petroleum ether :-
M.P. 76° C. (Constant).
This substance crystallised in long white prisms (needles). It was soluble in acetone , ethyl acetate, benzene, chloroform, ether and methyl and ethyl alcohols. It could be recrystallised from petroleum ether and aqueous methyl alcohol. It was practically insoluble in water.

Analysis of Anilide.

5.100 mgm gave 0.252 ccs nitrogen at 27°C and 758 mm

4.816 mgm gave 0.238 ccs nitrogen at 27°C and 758 mm

i.e. N : 5.652 , 5.654 %

Calculated for $C_{16}H_{25}ON$, N : 5.71 %

Preparation of Amide.

"Callitrol" (1 gm) was allowed to react with thionyl chloride (2 ccs) during 5 minutes, after which the excess thionyl chloride was removed on the water bath at 25 mm. Ammonia (S.G. 0.880; 10 ccs) was then added and the brownish coloured product filtered and washed. It was then recrystallised from petroleum ether (60-80) when it was obtained in colourless leaflets.

Yield : 0.2 gm (pure).

M.P. 84-5° C. (Constant).

Preparation of p-toluidide.

To a solution of the acid chloride, prepared as above, in ether (5 ccs), excess of a solution of p-toluidine in ether was added. Water was then added to dissolve the [illegible] p-toluidine hydrochloride, and after the ethereal solution had been washed thoroughly with dilute HCl and then with water and dried, the ether was evaporated. The product then crystallised on treatment with petroleum ether and was recrystallised from aqueous methyl alcohol.

Yield : 0.4 gm M.P. 93-4° C. (Constant).

Analysis of p-toluidide.

5.476 mgm gave 0.255 ccs of nitrogen at 29°C and 758 mm

5.628 mgm gave 0.234 ccs of nitrogen at 29°C and 758 mm

i.e. N : 5.290 , 5.288 %

Calculated for $C_{17}H_{25}ON$, N : 5.41 %.

Anilide of "Dihydrocallitrol".

"Dihydrocallitrol" (1 gm) was converted into the acid chloride by treatment with thionyl chloride (2 ccs) warming to the temperature of the water bath during 5 minutes. The excess thionyl chloride was then removed on the water bath at 25 mm. The acid chloride, dissolved in ether (5 ccs) was then treated with an excess of a solution of aniline in ether. The ethereal solution was then washed with water, to remove aniline hydrochloride, dilute HCl, to remove excess aniline, and finally with water again. After drying, the ether was evaporated and the product crystallised. It was recrystallised from aqueous methyl alcohol.

Yield : 0.4 gm

M.P. 90-1° C. (Constant).

Analysis.

4.63 mgm gave 0.228 ccs nitrogen at 27°C and 758 mm

5.122 mgm gave 0.253 ccs nitrogen at $28^{\overset{8}{\circ}}$ C and 758 mm

N : 5.632 , 5.63 %

Calculated for $C_{16}H_{25}ON$, N : 5.67 %.

Amide of "Dihydrocallitrol".

The acid chloride, prepared as described above, was treated with ammonia (S.G. 0.880 ; 10 ccs) and the product filtered. It was recrystallised from petroleum ether.

Yield : 0.3 gm

M.P. 108-9°(Constant).

Analysis.

4.872 mgm gave 0.345 ccs at 27° C and 758.5 mm

4.328 mgm gave 0.307 ccs at 27° C and 758.5 mm

Nitrogen : 8.106 , 8.12 %

Calculated for $C_{10}H_{21}ON$, N : 8.18 %.

Anilide from Anhydride.

The anhydride of "dihydrocallitrol" was prepared by heating 5 gm in a small flask under reflux to 120°C. Acetyl chloride (2.5 gm) was then dropped in slowly, the temperature being allowed to rise during 30 minutes to 180°C. The product was then distilled:-

1. B.P. -100°C at 1.0 mm Acetic anhydride
2. B.P. 110-154°C at 0.9 mm
3. B.P. 154-156°C at 0. 9mm Anhydride. 2.5 gm

The anhydride was insoluble in 2% aqueous sodium carbonate solution, even on long standing.

The anhydride (1 gm) and aniline (2 gm) were warmed together on the water bath for 5 minutes, cooled and washed with dilute HCl, when the product solidified.

M.P. 91-2° C. (Constant). Unaffected by admixture with anilide from acid chloride.

Preparation of Aldehyde.

"Callitrol" (17 gm), quicklime (2.8 gm) and calcium formate (6.5 gm) were mixed with a little ethyl alcohol and the mixture evaporated on the water bath until it became a solid mass. This was finely powdered and mixed with an equal weight of purified sand and distilled from a copper retort.

Yield : 8 gm.

This was dried and redistilled :-

1. B.P? -100° C at 27 mm
2. B.P. 103-108° C at 27 mm 1 gm

Fraction 2 was taken up in ether, washed with sodium carbonate and redistilled.

The semicarbazone and 2:4 dinitro phenylhydrazone could not be obtained crystalline, but the atophan was obtained by the action of B-naphthylamine and pyruvic acid in alcohol.

The product crystallised on cooling. M.P. 239° C.

Recrystallised from ethyl alcohol M.P. 249° C.

The atophan obtained similarly from d-citronellal and recrystallised from alcohol melted at 249°C.

Preparation of d-Citronellic Acid. (Semmler, Ber. 24, 208).

Silver oxide was first prepared by the addition of a solution of barium hydroxide (44 gm) to a solution of silver nitrate (57 gm). After filtering and washing free from alkali, the silver oxide was dissolved in the minimum amount of 5% ammonia (2 litres) and 50 gms of citronellal added. The mixture was then stirred vigorously for 4 hours and allowed to stand overnight. The mixture was then strongly acidified with phosphoric acid and steam distilled, the distillate being extracted with ether.

Yield : 6 gm.

This yield was rather unsatisfactory, considering the cost of the process and so Semmler's later and more indirect method was tried.

1. **Citronellal oxime.** (Semmler , Ber. 26, 2255).

Citronellal (154 gm) was dissolved in methylated spirit (200 ccs) and a solution of hydroxylamine hydrochloride in water (70 gm in 100 ccs) added. A solution of sodium hydroxide in water (40 gm in 100 ccs) was then added with stirring and warming on the water bath for 30 minutes. On cooling and adding more water (300 ccs) the product was extracted with ether, the extract dried, the ether removed and the product distilled :-

1. B.P. 100-143° C at 22 mm --- Mainly citronellal
2. B.P. 143-148° C at 22 mm --- Oxime.

Yield : 71 gm.

2. Nitrile.

d-Citronellal oxime (70 gm) and acetic anhydride (140 gm) were refluxed in an oil bath at 160° C for 2 hours and the product distilled:-

1. B.P. -100°C at 23 mm --Acetic anhydride
2. B.P. 115-20°C at 23 mm --Nitrile.

Yield : 41 gm.

3. Hydrolysis.

The nitrile (10 gm) was heated under reflux with alcoholic potassium hydroxide solution (15 gm in 50 ccs) for 15 hours when evolution of ammonia was complete. The product was steam distilled to remove alcohol and unchanged nitrile and amide, washed with ether, acidified and extracted with ether. On drying the extract and evaporating the ether the product was obtained and distilled.

Yield : 6.5 gm

B.P. 118-118.5°C at 0.55 mm

Optical Rotation (in 5 cm tube at 21°C for sodiumlight) : +3.0°

Refractive Index : 1.4561 at 21.5°C.

These properties are in remarkably good agreement with those of "callitrol" (p.14), except of course that in that case the optical rotation was in the laevo direction.

d-Citronellic Acid Anilide.

d-Citronellic acid (2 gm) was treated with thionyl chloride (3 ccs), the reaction being completed by warming for a few minutes on the water bath. The excess thionyl chloride was then removed on the water bath at 25 mm. The acid chloride was then dissolved in ether (5 ccs) and a solution of aniline in ether added until there was no further reaction. The aniline hydrochloride was then removed with water and the excess aniline with dilute HCl. The ethereal extract was then washed with water, dried and the ether removed. The product was crystallised from aqueous methyl alcohol and then 3 times from petroleum ether.

Yield : 0.5 gm.

M.P. 75-6° C. (Constant).

A mixture with equal weight of "callitrol" anilide, crystallised together from aqueous methyl alcohol had M.P. 51-2° C.

Analysis.

5.105 mgm gave 0.255 ccs nitrogen at 29°C and 754 mm

5.080 mgm gave 0.256 ccs nitrogen at 29°C and 754 mm

i.e. N : 5.64 , 5.68 %

Calculated for $C_{16}H_{23}ON$, N : 5.71 %

d-Citronellic Acid p-Toluidide.

This was prepared by adding a solution of p-toluidine in ether to the acid chloride solution prepared as described above.

M.P. 93-4°C. (Constant).

Analysis.

5.222 mgm gave 0.245 ccs nitrogen at 28°C and 754 mm

4.810 mgm gave 0.234 ccs nitrogen at 29°C and 754 mm

N : 5.32 , 5.39 %

Calculated for $C_{17}H_{25}ON$, N : 5. 41 %

Comparison of properties of "Callitrol" and d-Citronellic acid.

Substance	Rotation (5 cm t).	R.I.	Amide M.P.°C	Anilide M.P.°C	p-Toluidide M.P.°C.
d-Citronellic Acid	3.0°	1.4561	84-5	75-6	93-4
"Callitrol"	-2.81°	1.4563	84-5	76	93-4
d-Dihydrocitronellic Acid			108-9	91	
"Dihydrocallitrol"	-2.0°	1.4365	108-9	90-1	

Nonene (2) 1-carboxylic Acid. (Schneegans, Ann. 227, 87).

(a). Hexyl Paraconic Acid.

Oenanthaldehyde (25 gm), sodium succinate (35.5 gm) and acetic anhydride (25 gm) were heated together at 120-30°C for 24 hours. Water and ether were then added and the ethereal extract removed and extracted with sodium carbonate solution. This solution was then acidified and the acid extracted with ether.

Yield : 5 gm of a liquid acid.

– – –

Oenanthaldehyde (10 gm), freshly prepared sodium succinate (14.2 gm) and acetic anhydride (10 gm) were heated together at 120-30°C for 20 hours. Water and ether were then added, the ethereal extract separated and extracted with sodium carbonate solution. On acidification the acid crystallised and was recrystallised from hot water.

Yield : 2 gm. M.P. 86-8°C.

(b). Distillation.

Hexyl paraconic acid (2 gm) was distilled from a 5 cc distilling flask at atmospheric pressure, the temperature of the bath being allowed to rise slowly to 330°C. The liquid product was then treated with ether and 5% sodium carbonate solution, the alkaline solution being removed, acidified and extracted with ether.

Yield : 0.7 gm. B.P. 125-7°C at 1.2 mm.

This acid was a colourless liquid which readily decolourised bromine water and permanganate solution.

2-Methyl octene (1) carboxyllic acid.

[illegible]

The ethyl ester of this acid had been prepared by Bouveault and Blanc (Bull.Soc.Chim., 1904, 1208) but it was found that better results were obtained by the following slightly modified method.

Methyl Hexyl Ketone.

Capryl alcohol (50 gm) was added slowly with vigorous stirring to a solution containing sodium bichromate (100 gm) and sulphuric acid (150 gm) in water (500 ccs). The temperature was maintained at 35-40°C. After the addition was complete (45 minutes) the stirring was continued for a further 1 hour, when the mixture was steam distilled and the oil separated.

Yield : 46 gm.

This was shaken with 250 ccs saturated sodium bisulphite solution and the product filtered and washed with alcohol.

Yield : 25 gm.

The bisulphite compound was then decomposed by heating for 15 minutes on the water bath with 200 ccs 10% sodium carbonate solution. The ketone was then extracted with ether and distilled.

Yield : 10 gm. B.P. 170-3° C.

Condensation.

Methyl hexyl ketone (12.8 gm) and bromacetic ester (16.7 gm) were dissolved in pure dry benzene (50 ccs) and 7 gm zinc added.

The mixture was then heated under reflux, on the water bath, for 8 hours with the addition of a little ethyl acetate. At the end of this time about 0.5 gm zinc remained unattacked and the solution beceme semi-solid on cooling. Water (100ccs) and concentrated HCl (20 ccs) were then added and the product extracted with ether and distilled.

Yield : 4.8 gm. B.P. 142-8° C at 20 mm.

Dehydration.

The above product (4.8 gm) and anhydrous potassium bisulphate (15 gm) were heated together to 180-200°C for 5 hours. On cooling water was added and the product extracted with ether.

Yield : 3.2 gm. B.P. 128-30°C at 22 mm.

Hydrolysis.

The ester (3.2 gm) obtained from the dehydration was refluxed with 20% aqueous KOH (100 ccs) for 30 minutes. The solution was then washed with ether ,acidified and extracted with ether.

Yield : 1.5 gm. B.P. 125-8° C at 0.3 mm.

Isobutyl bromide and Diethyl Malonate.

Sodium (11.5 gm) was dissolved in ethyl alcohol (150 ccs) and diethyl malonate (66 gm) added. On warming for 30 mins. the sodium salt had completely separated. Isobutyl bromide (70 gm) was then added and the mixture refluxed for 5 hours. The excess alcohol was then distilled and water and ether added. The product from the ethereal extract was distilled:-

1. B.P. 220-245°C	5.5 gm
2. B.P. 245-255°C	1.0 gm.

Isobutyl iodide and Diethyl Malonate.

Sodium (3 gm) was dissolved in ethyl alcohol (100 ccs) and diethyl malonate (20 gm) added. After separation of the sodium salt, isobutyl iodide (26 gm) was added and the mixture refluxed for 5 hours. The excess alcohol was then distilled and water and ether added. The product obtained from the ethereal extract was distilled :-

Yield : 1.5 gm. B.P. 220-230°C.

Isobutyl bromide and Ethyl Cyanacetate.

Sodium (4.6 gm) was dissolved in ethyl alcohol (100 ccs) and ethyl cyanacetate added.(22.4 gm). On warming for a few minutes the sodium salt had separated. Isobutyl bromide (30 gm) was then added and the mixture refluxed for 4 hours. Water was then added and the product extracted with ether.

Yield : 18 gm. B.P. 115-130° at 17 mm.

Isobutyl bromide and Ethyl Isobutyl-cyanacetate.

(a). Ethyl isobutyl cyanacetate was added to a solution of
(18 gm)
sodium (2.5 gm) in alcohol (75 ccs), and after precipitation of the sodium salt, isobutyl bromide (20 gm) was added and the mixture refluxed for 4 hours. Water was added and the product extracted with ether. An acid was also obtained from the aqueous portion.

Yield : 5 gm. B.P. 134-7°C at 17 mm.
Acid : 10 gm.

(b). On repetition of the above, the products obtained were :-

Unchanged ester : 9 gm. B.P. 120-133°C at 17 mm.
Acid : 6 gm.

(c). Using potassium (4.2 gm) in alcohol (50 ccs) instead of sodium ethoxide the products obtained were :-

Unchanged ester : 3 gm. B.P. 120-130°C at 21 mm
Acid : 8 gm.

Thus, although ethyl di-isobutyl-cyanacetate appeared to be obtained in the first case, its preparation could not be repeated.

Hydrolysis of "Unchanged ester".

The "unchanged ester" (3 gm) was refluxed for 18 hours with

35% aqueous KOH (50 ccs). The solution was washed with ether and acidified but the acid obtained could not be crystallised. This confirmed the fact that the second isobutyl group had not been introduced as di-isobutyl-cyanacetic acid is solid (M.P. 90-1°C -- Freylon, A. Ch. ser.8,19,562 and M.P. 85-6°C according to Hessler and Henderson-- J.A.C.S. 43,672.).

Acid with Methyl Alcohol and HCl.

The acid (10 gm) was dissolved in methyl alcohol (100 ccs) and HCl gas passed to saturation. On evaporating the alcohol ammonium chloride separated, so water and ether were added and the ethereal extract washed with sodium carbonate solution, dried, the ether removed and the product distilled.

Yield : 6 gm. B.P. 115-20°C at 18 mm.

This was apparently isobutyl malonic ester, so that the acid was isobutyl cyanacetic acid.

(B). "TASMANOL".

Robinson and Smoth in a paper in the Journal of the Royal Society of New South Wales (1914, 518) report the occurrence of a liquid"phenol" in the oils of those eucalypts which belong to ~~to~~ the cineol-phellandrene bearing class,notably the Tasmanian species Eucalyptus Risdoni and Eucalyptus linearis, and suggest the name "Tasmanol" for it.

The physical properties are described,the boiling point being 268-273°C at atmospheric pressure and 164°C at 12 mm,while it was optically inactive. It is reported as being soluble in ammonia,partly so in sodium carbonate solution and insoluble in sodium bicarbonate solution,while it gave a blood red colour with alcoholic ferric chloride. Robinsom and Smith state that it "contains one methoxyl group and appears to have two phenolic groups in para positions" but give no analytical figures or other data from which these conclusions are drawn.

In order that the constitution of this substance might be more fully investigated,50 kilograms of the leaves of Eucalyptus Risdoni were obtained from Tasmania,but on steam distillation in the apparatus previously described for the distillation of Callitris glauca timber,the amount of alkali soluble material obtained was rather disappointing,being only 0.012% (6 gm).

This was found to be mostly soluble in 6% sodium carbonate solution (75%) and of this portion 55% distilled over a range of 3° C under reduced pressure. The material obtained in this way appeared to be practically a pure substance but was redistilled again. This material gave a pronounced red colour with alcoholic ferric chloride, liberated methyl iodide with hydriodic acid and appeared to be an acid as the methyl derivative, obtained by treatment with methyl alcohol and hydrochloric acid gas, was readily hydrolysed with 20% aqueous potassium hydroxide solution.

Analyses showed it to have the constitution $C_{13}H_{22}O_3$, while a crystalline p-toluidide and a silver salt were obtained, but unfortunately in insufficient amount for analysis.

Examination of a specimen of "tasmanol" of unknown origin, prepared by the late H.G.Smith and which was found to be completely soluble in sodium carbonate solution, showed that although it could be esterified and the ester hydrolysed, no crystalline p-toluidide or silver salt could be obtained.

Although owing to scarcity of materials, definite conclusions could not be arrived at, it seems certain that "tasmanol" is an acid rather than the "phenol" suggested by Robinson and Smith, the material obtained recently having the constitution $C_{11}H_{18}(OMe)COOH$.

EXPERIMENTAL.

Alkali soluble oil obtained from 50 Kg E.Risdoni leaves : 10 gm

(containing a little benzene)

Soluble in sodium carbonate solution (6%)	4.5 gm	Red with FeCl$_3$
Insoluble " " " " " "	1.5 gm	Crimson with FeCl$_3$
	6.0 gm.	

Distillation of Soluble fraction.

1.	B.P. 110-113°at 0.5 mm	2.5 gm
2.	B.P. 115-125°at 0.5 mm	1 gm
3.	Residue	1 gm

Fraction 1 Redistilled.

a.	B.P. 80-105°C at 0.5 mm	0.25 gm
b.	B.P. 107-9° C at 0.5 mm	2.25 gm

Analysis. (Fraction 1.b.).

0.0786 gm gave 0.1988 gm CO_2 and 0.0685 gm H_2O

0.0769 gm gave 0.1960 gm CO_2 and 0.0680 gm H_2O

C : 69.0 , 69.4 %

H : 9.69 , 9.83 %

Calculated for $C_{13}H_{22}O_3$: C : 69.00 %

H : 9.71 %

Demethylation with HI.

"Tasmanol" (from E.Risdoni) (0.3 gm) was treated with hydriodic acid (constant boiling;10 ccs),the mixture being refluxed for 3 hours. Methyl iodide was evolved,as evidenced by the precipitation of silver iodide from alcoholic silver nitrate solution. Water was added to the residue which was then extracted with ether.

The product gave a distinct red colour with ferric chloride.

Methylation of "Tasmanol"

"Tasmanol" (0.25 gm) was dissolved in methyl alcohol (10 ccs), saturated with HCl and refluxed for 1 hour. Water and ether were added,the ethereal extract being washed with 5% sodium carbonate solution. The ethereal extract on evaporation yielded 0.2 gm of an oil,which gave no colour with ferric chloride and was insoluble in sodium hydroxide solution in the cold.

"Tasmanol" recovered : 0.05 gm.

Hydrolysis.

The methylation product (0.2 gm) was refluxed for 2 hours with 20% aqueous KOH (10 ccs). The product was then washed with ether,acidified and extracted with ether.

Yield : 0.2 gm.

Red colour with ferric chloride.

p-Toluidide.

"Tasmanol" (0.1 gm) was treated with thionyl chloride (0.5 cc), excess of the latter removed and the residue taken up in ether and treated with excess of p-toluidine in ether. The ethereal solution was the washed with dilute HCl and water and the ether removed. The crystalline product thus obtained was purified by recrystallisation from petroleum ether.

Yield : 0.04 gm M.P.88-9°C.(Constant).

Silver Salt.

"Tasmanol" (0.1 gm) was dissolved in the minimum amount of 0.5% ammonia and excess silver nitrate solution added. A copious white precipitate of the silver salt was obtained.

Yield : 0.1 gm.

H.G.Smith's specimen of "Tasmanol" was now examined.

Redistilled. B.P. 115-122°C at 1.4 mm.

Completely soluble in sodium carbonate solution.

Pronounced red colour with ferric chloride.

p-Toluidide.

0.5 gm treated with thionyl chloride and then with p-toluidine in the usual way gave a product which was mainly oily, although it appeared to contain some crystalline material.

Silver Salt.

On treatment of a solution of the ammonium salt with silver nitrate solution, no precipitate of the silver salt could be obtained.

Methylation.

0.3 gm dissolved in methyl alcohol (10 ccs) was refluxed for 45 minutes with the addition of 2 drops of pure sulphuric acid. Water and ether were added and the ethereal extract washed with sodium carbonate solution.

Yield : 0.2 gm . No colour with ferric chloride.

Unchanged acid : 0.1 gm

Hydrolysis.

The above methylation product (0.2 gm) was refluxed for 2 hours with 10 ccs of 20% aqueous KOH. The solution was then washed with ether, acidified and extracted with ether.

Yield : 0.2 gm.

Red colour with ferric chloride.

In conclusion I wish to thank Mr. Dadswell of the Council for Scientific and Industrial Research for specimens of Callitris oils and toxicity determinations, the Departments of Forestry of N.S.W. and Queensland for timber and Mr. McLeod of the University of Tasmania for supplies of Eucalyptus Risdoni leaves.