

## Lantadene A—The Active Principle of *Lantana camara* L. Part III.—Pyrolytic Distillation of Lantadene A.

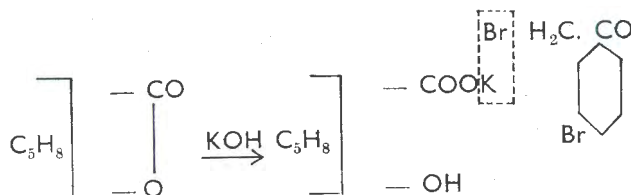
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WHEN the melting point of Lantadene A was determined, it was noticed that it melted with the generation of small bubbles while it turned orange-yellow in colour. Lantadene A was accordingly subjected to dry distillation in high vacuum.

It was found that when Lantadene A was heated above its melting-point temperature, a colourless liquid of a peculiar sweet odour distilled over. This liquid could be obtained in a good yield of approximately 20 per cent. of the weight of Lantadene A used. Analysis of this product, which boiled at 200° C., indicated its composition as C<sub>6</sub>H<sub>8</sub>O<sub>2</sub>. This compound, which was not an acid, could however be titrated in the cold with alcoholic potash, indicating that a lactone group was present. From the titration the molecular weight could be fixed at 115. (Compare Mol. wt. of C<sub>6</sub>H<sub>8</sub>O<sub>2</sub>: 112.)

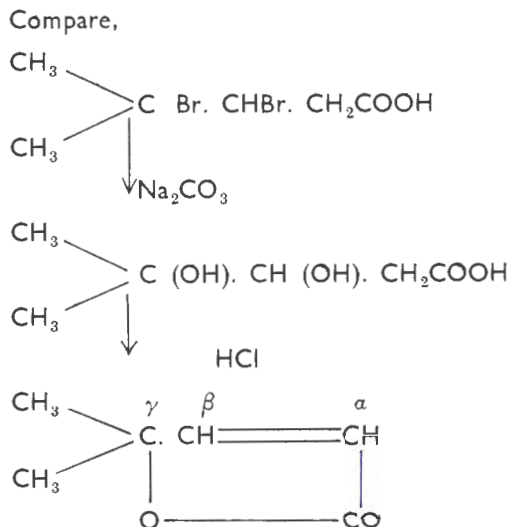
When this compound was hydrogenated in acetic acid solution, one ethylenic double bond could be determined. Treated with bromine in chloroform solution, it easily took up bromine. When this brominated product, an oily mixture, was left in the refrigerator, crystals were formed on the sides of the vessel. These crystals melted sharply at 130° C.

As the lactone itself did not give too good theoretical combustion values, the p. bromo-phenacylester was prepared by treating the potassium salt of the hydrolysed lactone with p. bromo-phenacyl bromide according to the method of Judefind and Reid (1920), e.g.



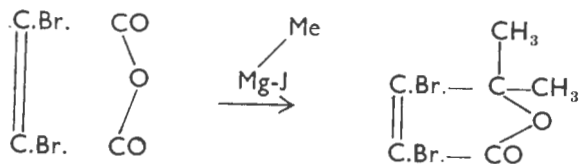
The ester has a melting point of 52° C. and gives C and H values which correspond very well with the theoretical values for C<sub>14</sub>H<sub>15</sub>O<sub>4</sub>Br, and accordingly fixes the formula for the lactone as C<sub>6</sub>H<sub>8</sub>O<sub>2</sub>.

Fittig and Geisler (1881) prepared a lactone  $C_6H_8O_2$  by treatment of  $\beta, \gamma$ -dibromisocaproic acid with sodium carbonate and hydrochloric acid, respectively. This lactone was called "Terelactone" ( $\gamma, \gamma$ -dimethyl  $\Delta \alpha, \beta$ -crotonlactone). It is a colourless liquid which is partly soluble in water and takes up bromine easily.



$\gamma, \gamma$  dimethyl  $\Delta \alpha, \beta$ -crotonlactone.  
(Terelactone)

Diels and Reinbeck (1910) synthesised the dibrom-derivative of terelactone by treating dibrom-maleic-anhydride with methylmagnesium iodide.



The dibrom-derivative has a M.P. of  $129-130^\circ \text{C}$ ., a peppermint smell, and sublimes readily, which corresponds with the properties of the bromolactone originating from Lantadene A.

From these data it is probable that the lactone obtained by distillation of Lantadene A, was "Terelactone".

For the further identification of this lactone it was hydrogenated. The product should then be iso-capro-lactone if the original lactone was "Terelactone". The acid amide of the saturated lactone was prepared according to the method of Ström (1893), but unfortunately the material did not suffice for a complete investigation. The product which was obtained differed in properties from those given by Ström for the amide of iso-capro-lactone.

Ström prepared iso-capro-lactone ( $C_6H_{10}O_2$ ) by dry distillation of terebic acid, and the amide of the lactone by heating it in a tube at  $100^\circ C$ . for four hours with a saturated solution of ammonia in alcohol at  $4^\circ C$ . The amide so obtained was slightly soluble in cold chloroform, almost insoluble in ether, insoluble in benzene and readily soluble in alcohol. It crystallised from chloroform in plates with M.P.  $101^\circ C$ .

The amide product of the saturated lactone prepared from Lantadene A was found to be very soluble in chloroform, ether, alcohol, and benzene, so that it could not be crystallised from these solvents. It was less soluble in ethyl acetate from which it crystallised in plates with M.P.  $70^\circ C$ . The material did not suffice for repeated recrystallisation, so that it is doubtful whether  $70^\circ C$ . is the true melting point of the amide.

During the distillation of Lantadene A, a crystalline product with M.P.  $125^\circ$  distilled. This product has not yet been investigated further.

After the lactone and the crystalline product had distilled over, the bath temperature was raised and with a vacuum of 2 mm. Hg. a beautiful yellow glassy material which became hard on cooling, distilled. This resinous product could not be crystallised from the ordinary solvents. It was obtained in small crystals with M.P.  $125^\circ C$ . from petroleum-ether (B.P.  $120-130^\circ C$ .). Analysis indicated the empirical formula as  $C_{17}H_{26}O_3$ .

This resin condensed readily with 2:4—dinitrophenylhydrazine and semi-carbazide, which indicated that a ketone group was still present.

It was hoped that this resinous compound would be a great help in the elucidation of the structure of Lantadene A, for example when treated with oxidising agents. Unluckily this resin only yielded resinous products on oxidation. However, on selenium-dehydrogenation of this resin, sapotalene and 1.2.6—trimethylpheanthrene were obtained, which cleared up the whole carbon skeleton of this breakdown product.

On distilling Lantadene A with zinc-dust a product with M.P.  $75^\circ C$ . and empirical formula  $C_{23}H_{32}O_2$  was obtained.

## EXPERIMENTAL.

### A. Dry Distillation.

27 gm. Lantadene A are gently heated in a 100 ml. Pyrex flask by means of a  $KNO_3/NaNO_3$  bath until a yellow melt is obtained. A vacuum distillation apparatus is now connected to the flask (ground-glass joints) and the contents fractionally distilled.

At  $280^\circ C$ . Lantadene A melts and gas bubbles escape.

#### Fraction I.

Bath temperature  $280-305^\circ C./2$  mm. Hg.

(a) 5 ml. colourless oily liquid distills.

(b) 1.10 gm. crystalline material collects in the connection tubes past the condenser and collection tube.

*Fraction II.*

Bath temperature 305-340° C./2 mm. Hg: Slow distillation of a yellow glassy resinous substance. Yield, 10 gm.

B. *Lactone.*

Fractional distillation of fraction I (a) yields a liquid with B.P. 200° C.

(1) *Properties.*

It is a colourless, oily liquid with a peculiar sweet and persistent odour. It is not a ketone nor an acid, but can be titrated in the cold with alcoholic potash.

Placed in a refrigerator the liquid crystallises. The crystals remelt at room temperature. The melting point is approximately 20° C., B.P. 200° C./650 mm. Hg.

(2) *Titration.*

134.5 mgm. lactone dissolved in 10 ml. alcohol is titrated with  $\frac{N}{10}$  alcoholic KOH using phenolphthalein as indicator.

ml.  $\frac{N}{10}$  KOH used = 11.66

$$\therefore \text{mol. weight of lactone} = \frac{10,000 \times 134.5}{11.66} \\ = 115.3$$

(3) *Analysis.*

(i) 2.169 mgm. substance: 4.972 mgm. CO<sub>2</sub>: 1.539 mgm. H<sub>2</sub>O

(ii) 2.604 mgm. substance: 5.979 mgm. CO<sub>2</sub>: 1.895 mgm. H<sub>2</sub>O

Calculated C<sub>6</sub>H<sub>8</sub>O<sub>2</sub>: C = 64.28%; H = 7.19%

Found: C = 62.60%; H = 8.14%

C = 62.52%; H = 7.94%

Mol. weight calculated C<sub>6</sub>H<sub>8</sub>O<sub>2</sub>: 112.124

Found: 115.3

(4) p. *brom-phenacyl ester.*

1 gm. lactone dissolved in 10 ml. absolute alcohol is titrated with  $\frac{N}{10}$  KOH. To the solution of the potassium salt of the hydroxy acid (solution about 20 ml.) 2 gm. p. brom-phenacylbromide dissolved in 25 ml. 70% alcohol is added and refluxed for 2 hours. On cooling a product with M.P. 52° C. crystallises in plates. Yield 1.5 gm.

*Analysis.*

3.677 mgm. substance: 6.927 mgm. CO<sub>2</sub>: 1.405 mgm. H<sub>2</sub>O

3.557 mgm. substance: 6.731 mgm. CO<sub>2</sub>: 1.365 mgm. H<sub>2</sub>O

Calculated C<sub>14</sub>H<sub>15</sub>O<sub>4</sub>Br: C = 51.39%; H = 4.62%

Found: C = 51.39%; H = 4.28%

C = 51.62%; H = 4.29%

(5) *Hydrogenation.*

1.033 gm. lactone dissolved in 100 ml. glacial acetic acid is shaken with 120 mgm.  $\text{PtO}_2$  in a current of hydrogen.

ml.  $\text{H}_2$  absorbed = 310

ml.  $\text{H}_2$  control = 95

Temp. =  $21^\circ \text{C}$ ; pressure =  $663.1 \text{ mm. Hg.}$

$$\therefore \text{ml. H}_2 \text{ absorbed at N.T.P.} = \frac{215 \times 643.1 \times 273}{294 \times 760} \\ = 169$$

Calculated for one double bond in 1.033 gm.  $\text{C}_6\text{H}_8\text{O}_2 = 206.3$  ml. at N.T.P.

(6) *Bromine-derivative.*

0.5 gm. lactone dissolved in 5 ml. chloroform is treated with a solution of bromine in chloroform in direct sunlight until the bromine colour persists. The chloroform is then evaporated leaving a brownish liquid with a pleasant peppermint odour. Left in a refrigerator the product crystallises in plates which readily re-dissolve in the mother liquor at room temperature. Colourless crystals form against the side of the vessel when this brominated product is left in the refrigerator. These crystals have M.P.  $130^\circ \text{C}$ .

Attempts to separate the bromine-derivative from the bromination mixture with the aid of solvents proved unsuccessful.

(7) *Amide of the Saturated Lactone.*

1.0 gm.  $\text{C}_6\text{H}_8\text{O}_2$ -lactone, dissolved in 100 ml. methanol was hydrogenated in a current of hydrogen using  $\text{PtO}_2$  as catalyst, when 175 ml. hydrogen was absorbed.

The solvent was removed by evaporation and a colourless product with B.P.  $200^\circ \text{C}$ . was obtained (B.P. of iso-capro-lactone, is  $200-202^\circ \text{C}$ .).

The product was treated with an excess of a saturated solution of ammonia in absolute alcohol at  $0^\circ \text{C}$ ., sealed in a tube and heated for four hours at  $100^\circ \text{C}$ . The product crystallised spontaneously when the solvent was evaporated.

*Solubilities.*

The crystalline product is very soluble in chloroform, ether, alcohol and benzene, readily so in ethyl acetate.

The product is dissolved in ethyl acetate and the solution then evaporated, as the product is too soluble to be crystallised from the solvent. In this manner colourless plates of melting point  $70^\circ \text{C}$ . are obtained. By washing these crystals with ethyl acetate, re-dissolving in ethyl acetate, and allowing the solution to evaporate slowly no rise in melting point of the product can be effected.

C. *Resin.*(1) *Properties.*

Very soluble in alcohol, ether, dioxane, chloroform, acetone, acetic acid, and petroleum ether. It is less soluble in methanol and insoluble in water.

It can not be crystallised from the ordinary solvents. From petroleum-ether (B.P. 120-130° C.) it can be obtained in micro-crystalline form with melting point 125° C.

(2) *Analysis.*

3.774 mgm. substance: 10.155 mgm. CO<sub>2</sub>: 3.052 mgm. H<sub>2</sub>O  
 Calculated C<sub>17</sub>H<sub>26</sub>O<sub>3</sub>: C=73.35%; H=9.42%  
 Found: C=73.40%; H=9.05%

(3) *Molecular Weight.*

0.501 mgm. in 4.474 mgm. camphor, Δ=13.1°  
 Found: 338.5  
 Calculated C<sub>17</sub>H<sub>26</sub>O<sub>3</sub>: 278.4

(4) The resin condenses easily with 2, 4—dinitrophenylhydrazine to give a hydrazone which crystallises from methanol and melts at 165-167° C.

*Analysis.*

1.622 mgm. substance: 0.174 ml. N<sub>2</sub> at 22° C. and 623 mm. Hg.  
 Calculated C<sub>23</sub>H<sub>30</sub>N<sub>4</sub>O<sub>6</sub>: N=12.21%  
 Found: N=12.49%

D. *Zinc Dust Distillation of Lantadene A.*

3 gm. Lantadene A are mixed with 20 gm. zinc dust and heated in a current of hydrogen by means of a KNO<sub>3</sub>/NaNO<sub>3</sub> bath. A colourless liquid (lactone previously described) begins to distil at 290° C. The temperature is slowly raised to 300° C. The distillation is stopped after five hours when no more liquid distills. On cooling, the reaction mixture is extracted with ether, the ether evaporated when a brown oily residue is obtained. This residue is subjected to fractional distillation in vacuum when a product distills at 80-100° C. and 5 mm. pressure. This yellow product is micro-crystalline and has a melting point of 75° C. It is very soluble in benzene, chloroform, alcohol, acetone, and petroleum ether, less so in methanol, and insoluble in water.

*Analysis.*

3.471 mgm. substance: 10.313 mgm. CO<sub>2</sub>: 2.908 mgm. H<sub>2</sub>O  
 Calculated C<sub>23</sub>H<sub>32</sub>O<sub>2</sub>: C=81.12%; H=9.47%  
 Found: C=81.03%; H=9.38%

*Molecular Weight.*

0.628 mgm. in 6.35 mgm. camphor, Δ=10.40°  
 Found: 376.6  
 Calculated C<sub>23</sub>H<sub>32</sub>O<sub>2</sub>: 340.4

## SUMMARY.

1. Lantadene A was subjected to dry distillation yielding:—

(a) A lactone, C<sub>6</sub>H<sub>8</sub>O<sub>2</sub>, B.P. 200°C./650 mm. Hg, probably "Terelactone".

(b) A crystalline product, M.P.  $125^{\circ}$  C. which has not yet been investigated further.

(c) A resinous compound  $C_{17}H_{26}O_3$ , M.P.  $125^{\circ}$  C.

2. Zinc-dust distillation of Lantadene A gives a product  $C_{23}H_{32}O_2$ , M.P.  $75^{\circ}$  C.

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