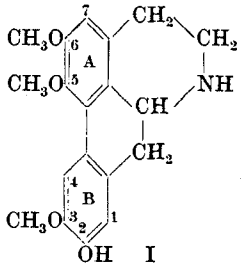
103. The constitution of Actinodaphnine

by T. P. Ghose, S. Krishna and E. Schlittler[1]).

(26. VI. 34.)

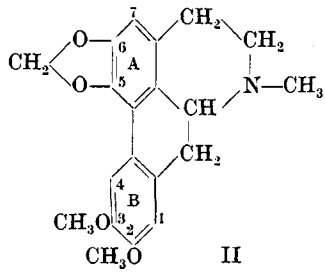
Greshoff[2]) discovered the wide distribution of the alkaloid laurotetanine in the N. O. Lauraceae. He isolated it first from Litsea chrysocoma, but also mentions its presence in the genera Tetranthera (T. citrata Nees), Notaphoebe, Aperula and Actinodaphne (A. procera *Nees*). Although laurotetanine seems to be widely distributed in this order, *Greshoff*'s work leaves some doubt as to whether it was always laurotetanine which he isolated.

Chopra[3]) mentions that in British India alone about 50 species of Litsea are still uninvestigated so that the discovery of a new alkaloid actinodaphnine from Actinodaphne *Hookeri* (N. O. Lauraceae) by *Krishna* and *Ghose* was of interest in this connexion[4]).



I

laurotetanine = 2-hydroxy-3-5-6-trimethoxy-nor-aporphine.



II

dicentrine = 2-3-dimethoxy-5-6-methylenedioxy-aporphine.

This base was certainly different from laurotetanine (I) and the authors discussed a similarity with bebeerine without adopting any final conclusions[5]). On the other hand it seemed to be more likely that actinodaphnine was closely related to laurotetanine, the latter having been isolated from another species of the same genus. With that view in mind we started again to work on the constitution of actinodaphnine and with a large supply of the base were able to determine its constitution apart from a slight doubt as to the respective positions of the methoxy and the phenolic hydroxy-group.

[1]) Actinodaphnine has been extracted from the plant-material by *T. P. Ghose* and *S. Krishna* in the Forest Research-Institute in Dehra-Dun, British India; the constitution of the base was elucidated by *E. Schlittler* working in the Medical Chemistry Dept., University Edinburgh (Prof. *Barger*).

[2]) B. **23**, 3537 (1890).

[3]) Indigenous Plants of India, Calcutta 1933, p. 504.

[4]) J. Indian Chem. Soc. **9**, 429 (1932).

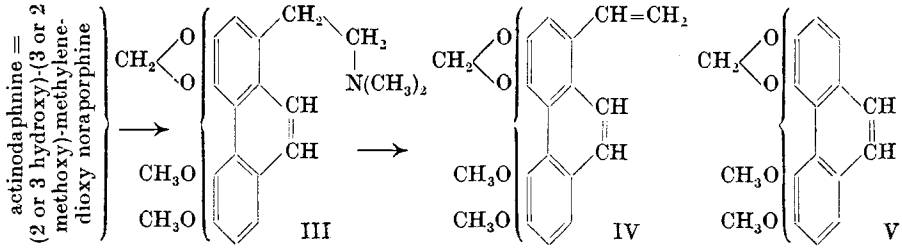
[5]) comp. *Späth, Leithe* and *Ladek*, B. **61**, 1704 (1928).

The micro-analyses of the free base and also of a large number of degradation products led us to prefer $C_{18}H_{17}O_4N$ to the formula $C_{18}H_{19}O_4N$ recorded earlier; also the methoxyl-estimation indicated one methoxyl-group. There was no evidence for a N—CH_3-group.

The two O-atoms previously not accounted for are present in a methylenedioxy-group (*Gaebel*'s test). We obtained positive evidence that actinodaphnine is a secondary base by the formation of a phenyltiocarbamide[1]).

The *Hofmann* degradation did not offer any difficulties; after twice treating with methyliodide and caustic soda the nitrogen was eliminated as trimethylamine thus showing that the nitrogen belongs to one ring only. The methine base was optically inactive and beautifully crystalline, the latter feature indicating that our new alkaloid must be related to glaucine or laureline as these bases yield the only two crystalline methine-bases known[2]).

The melting points of the methine (III), the vinyl-product and the corresponding phenanthrene were exceptionally high, suggesting a relationship to the aporphine alkaloid dicentrine (II). Dicentrine possesses the highest melting point of all the fully methylated aporphine alkaloids, probably due to the symmetrical arrangement of its substituents. So far as we could trace the results of a *Hofmann* degradation on dicentrine have never been published[3]) but we assumed that its degradation products would probably also have rather high melting points.



methine-base | vinyl-product | methylenedioxy-dimethoxyphenanthrene.

The oxidation of actinodaphnine gave interesting results. Nitric acid acting on aporphine alkaloids themselves does not give any well-defined products. *Warnat* first showed that mellophanic acid may be obtained if the nitrogen ring has previously been opened[2]).

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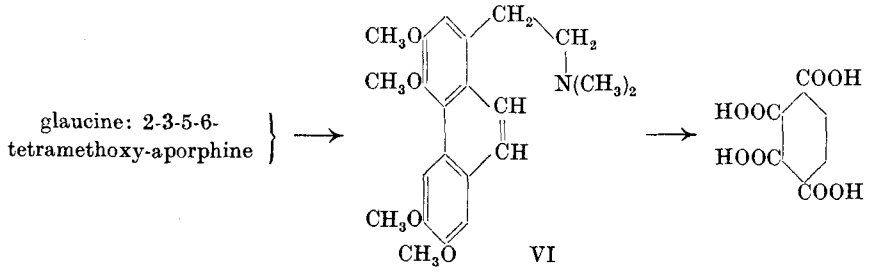
[1]) comp. *Filippo*, Arch. Pharm. **236**, 616 (1898).

[2]) comp. *Warnat*, B. **58**, 2773 (1925); *Barger* and *Girardet*, Helv. **14**, 503 (1931).

[3]) Meanwhile published by *Manske*, Canad. J. Res. **8**, 595 (1933).



glaucine methine. mellophanic acid.

A good many such oxidations on new aporphine alkaloids have been carried out, as the formation of mellophanic acid is conclusive for the aporphine structure[1]). The nitrogen ring may be opened by a *Hofmann* degradation or by means of ethyl-chlorocarbonate, a reagent of particular specificity for the tetrahydro-isoquinoline ring[2]). We then oxidized actinodaphnine methine with concentrated nitric acid and indeed isolated mellophanic acid whose tetramethylester was identical with an authentic specimen prepared from pukateine.

In the previous communication it has already been stated that actinodaphnine contains one methoxyl and one phenolic hydroxyl-group[3]). It was therefore likely that alkaline potassium permanganate would destroy first the benzene-nucleus which contains the hydroxyl-group with the possible formation of a methylenedioxy-phthalic or a methylenedioxy-hemimellitic acid. A benzene-nucleus containing a methylenedioxy-group is usually less stable towards oxidizing agents than a nucleus containing only methoxyl-groups. By oxidizing the fully methylated actinodaphnine we expected to obtain a dimethoxy-phthalic acid. Oxidation of the free base indeed gave rise to a substituted benzene-tricarboxylic acid, identified by its trimethylester as methylenedioxy-hemimellitic acid. This acid has been prepared previously by *Späth* and *Kuffner*[4]) from bulbocapnine. For identification we prepared the same acid from pukateine. Oxidation of the fully methylated base yielded m-hemipinic acid, isolated as ethylimide which was compared with an authentic specimen.

These results left little doubt about the constitution of actinodaphnine and at this stage we accepted the following formula:

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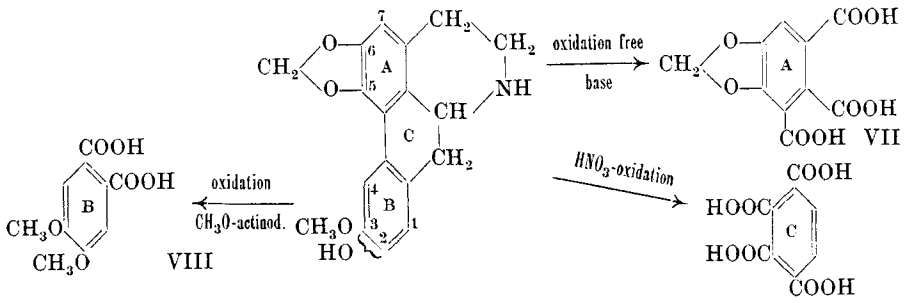
[1]) comp. e.g. *Späth* and *Strauhal*, B. **61**, 2395 (1928); *Barger* and *Girardet*, Helv. **14**, 498 (1931).

[2]) *Gadamer* and *Knoch*, Arch. Pharm. **259**, 146 (1921).

[3]) J. Indian Chem. Soc. **9**, 429, (1932).

[4]) B. **64**, 377 (1931).



The methylenedioxy-group is certainly in ring A, but an arrangement in 6—7 instead of 5—6 might still be possible since such a combination is considered to be present in domesticine[1]). The methoxyl- and hydroxyl-group must be in ring B, for only positions 2—3 can give rise to m-hemipinic acid. For the time being we preferred CH_3O in 3- and OH in 2-position, so that actinodaphnine would be a derivative of isovanillin. This hypothesis, first used by *Späth* and *Strauhal*[2]), was recently found to be correct in both laurotetanine and boldine[3]).

The position of the substituents in ring A was easily determined by the fact that on methylation actinodaphnine gave dicentrine. The melting points were identical and the same as that of a mixture, all the intermediate products of the *Hofmann* degradation proved to be identical. We are much indebted to Prof. *Asahina* of Tokyo and to Dr. *Manske* of Ottawa for supplying specimens of dicentrine from which we prepared all other products for comparison.

The relative positions of the hydroxyl- and the methoxyl-group in ring B proved to be more difficult to determine. We hoped to ethylate the phenolic hydroxyl-group thus differentiating it from the methoxyl-group originally present. We then intended to split off the methylenedioxy-group with 50% sulphuric acid and phloroglucinol, a method worked out in detail by *Späth* and *Quietensky*[4]) and subsequently employed with success by *Späth* and co-workers[5]).

The results with O-ethyl-actinodaphnine (IX) or O-ethyl-actinodaphnine-methine (X) did not prove to be satisfactory, but better results were obtained with O-ethyl-N-methyl-actinodaphnine (XI).

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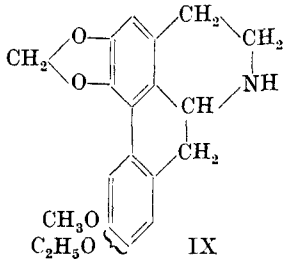
[1]) *Kitasato*, Acta Phytochim. **3**, 175 (1927).

[2]) B. **61**, 2395 (1928).

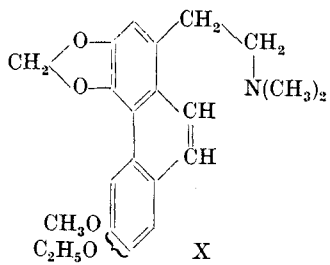
[3]) *Barger, Eisenbrand, Eisenbrand* and *Schlittler*, B. **66**, 450 (1933); *Späth* and *Tharrer*, B. **66**, 904 (1933).

[4]) B. **60**, 1882 (1927).

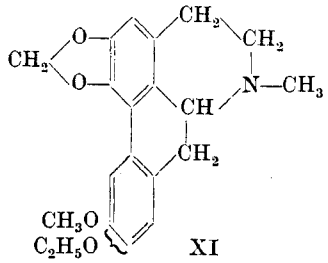
[5]) *Späth* and co-workers, B. **58**, 2279 (1925); **59**, 1498 (1926); **60**, 1895 (1927); **64**, 2044 (1931); *Kitasato*, Proc. Imp. Acad. Tokyo **2**, 124 (1926); *Osada*, J. Pharmac. Soc. Japan **48**, 85 (1928).



IX

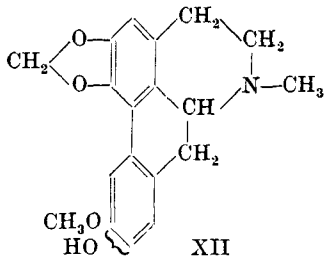


X

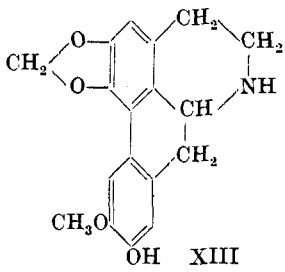


XI

In spite of the poor yield, we prepared O-ethyl-N-methyl-actinodaphnine, because we suspect it to be the ethylether of an alkaloid (XII) which we hope soon to demonstrate in the crude alkaloid-mixture from the bark of Actinodaphne *Hookeri*.

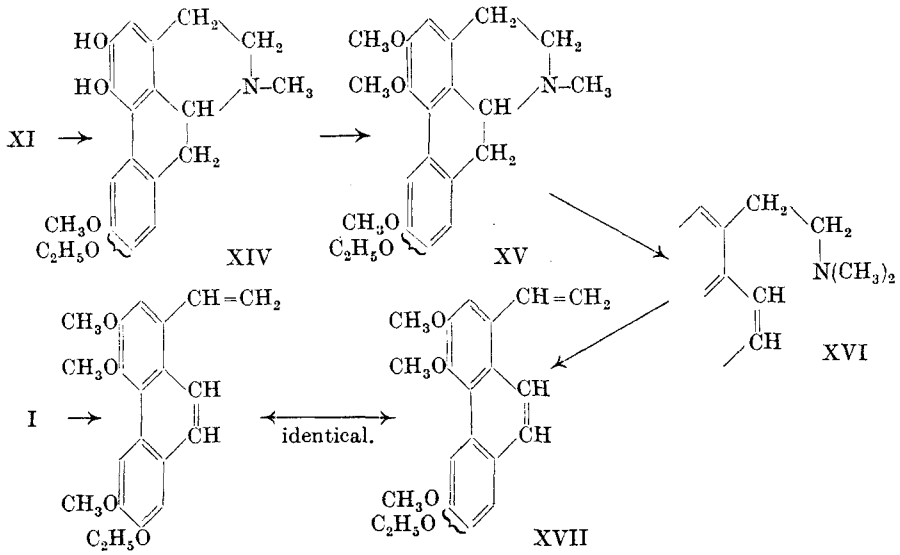


XII



XIII

The methylenedioxy-group was split off, the resulting dihydroxy-compound being beautifully crystalline. Owing to scarcity of material we did not prepare it in an analytically pure state but at once methylated with diazomethane thus obtaining a ethoxy-trimethoxy-aporphine. We next effected a *Hofmann* degradation and finally obtained an ethoxy-trimethoxy-8-vinyl-phenanthrene, m. p. 134° (owing to scarcity of material further purification was impossible), which when mixed with 2-ethoxy-3-5-6-trimethoxy-8-vinyl-phenanthrene from laurotetanine (m. p. 142°) melted at 135°. When mixed with 3-ethoxy-2-5-6-trimethoxy-8-vinyl-phenanthrene a strong depression in the melting point occurred.



Formula XIII is therefore proposed, actinodaphnine being 2-hydroxy-3-methoxy-5-6-methylene-dioxy-nor-aporphine. As our synthetic product (XVII) gave a very slight depression with an authentic specimen from laurotetanine, we are engaged in the synthesis of product XI ($C_2H_5O = 2$; $CH_3O = 3$) which synthesis will be the final test of the correctness of our view.

Experimental.

1) *Analyses of actinodaphnine:*

4.006 mg. subst. gave 10.20 mg. CO_2 and 2.00 mg. H_2O *(Roth)*
5.432 mg. subst. gave 0.227 c.c. N_2 (753 mm., 26°) *(Roth)*
4.658 mg. subst. gave 3.81 mg. AgJ *(Roth)*
5.003 mg. subst. gave 12.75 mg. CO_2 and 2.47 mg. H_2O *(Schoeller)*

$C_{18}H_{19}O_4N$	calc.	C 69.01	H 6.07	N 4.47% (Orignal formula)
$C_{18}H_{17}O_4N$	calc.	„ 69.45	„ 5.47	„ 4.50 CH_3O 10.0%
	found	„ 69.44	„ 5.52	„ 4.62 „ 10.8% *(Roth)*
	found	„ 69.52	„ 5.48% *(Schoeller)*	

2) *Methylenedioxy-group:* Actinodaphnine (20 mg.) and phloroglucinol (60 mg.) were heated with 40% sulphuric acid (5 c.c.) in a water-bath. Simultaneously tests with methyl-pukateine, glaucine and a blank were carried in the same vessel. After 20 minutes the test-tubes containing actinodaphnine and methylpukateine showed a bulky red precipitate while glaucine and the blank test showed merely a yellow coloration.

3) *Nitrogen atom:* The *Herzig-Meyer* estimation was absolutely negative. We then concluded that actinodaphnine was a secondary base like laurotetanine. The free base (22 mg.) was dissolved in

abs. alcohol and phenyl-iso-thio-cyanate (10 mg.) in a little alcohol was added. After two hours no crystals had formed, the solution was therefore concentrated to half its volume where upon the product soon began to crystallize. The crystals were very similar to the phenyl-thio-carbamide of laurotetanine.
M. p. 181° from alcohol.

5.052 mg. subst. gave 2.456 mg. $BaSO_4$
S cal. 7.41; found 6.67%

4) *Phenolic hydroxyl-group:* The phenolic hydroxyl-group previously recorded can easily be methylated with diazomethane. Actinodaphnine (2.16 gr.) was suspended in abs. methyl alcohol and a concentrated ethereal solution of diazomethane (from 7 c.c. of nitroso-N-methyl-urethane) was added. After standing for eight hours the diazo-methane and ether were distilled off, ether again added and the basic compounds extracted with 2-N. HCl. The hydrochloride of the methylated base is sparingly soluble and usually separated during the extraction. The non-phenolic base was removed by ether from a sodium hydroxide solution. It is a yellow oil which inclines to crystallize. We did not prepare it in a pure state, but transformed this compound at once into the sparingly soluble hydrochloride or sulphate, which was recrystallized from either alcohol or water. There was no evidence that diazomethane also methylated the nitrogen[1]).

5) *Hofmann degradation:* O-methyl-actinodaphnine (1,336 gr.) was dissolved in methyl alcohol (30 c.c.), methyl iodide (13,4 c.c.) was added and after every two hours sodium methoxide (9,8 c.c. of 0,023-N. solution) three times in all. After standing for two days the solvent was evaporated under reduced pressure and the residue dissolved in hot water. To the filtered solution was added potassium iodide and some ethyl-alcohol whereupon the methiodide separated in almost colourless crystals. Recrystallized from water or better from ethyl alcohol, they melted at 214° without decomposition.

The methiodide (1,272 gr.) was dissolved in boiling water (80 c.c.) and then solid caustic potash (15 gr.) was added. The whole was boiled under reflux for an hour, the methine soon began to separate in crystalline form while the mother-liquor was coloured slightly red. Conc. hydrochloric acid was added until the solution was only slightly alkaline, the precipitate of the methine was filtered, well washed with water and dried. The methine shows a blue fluorescence in acetone and a strong orange coloration with conc. sulphuric acid. Recrystallized twice from ethyl alcohol, m. p. 158—159°. The methine hydrochloride is sparingly soluble in water.

4.008 mg. subst. gave 10.51 mg. CO_2 and 2.35 mg. H_2O
$C_{21}H_{23}O_4N$ (III) calc. C 71.39 H 6.52%
found „ 71.51 „ 6,56%

[1]) comp. *Späth* and *Strauhal*, B. **61**, 2395 (1928); also *Orechoff*, B. **67**, 879 (1934).

The methine (from 0,2 gr. of hydrochloride) was dissolved in a few c.c. of methyl alcohol and an excess of methyl iodide added. The solution was heated under reflux for 5 minutes and then left standing for two hours. Boiling water (50 c.c.) was added and the organic solvent removed by heating on the water-bath. Freshly prepared silver-chloride was added, the solution heated on the water-bath for another 30 minutes and the precipitate of silver-chloride and iodide filtered off. The clear solution was concentrated to about 7 c.c. and solid caustic potash (3 gr.) was added. A brisk evolution of trimethylamine took place. As soon as it had stopped, the alkaline solution was extracted with chloroform, the chloroform washed with dilute hydrochloric acid and water, dried and evaporated. The crystalline residue (0.131 gr.) was recrystallized several times from chloroform-abs. alcohol. It is very sparingly soluble in abs. alcohol and ether. M. p. 205.5—206°.

3.995 mg. subst. gave 10.84 mg. CO_2 and 1.78 mg. H_2O

$C_{19}H_{16}O_4$ (IV) calc. C 74.02 H 5.20%

found „ 74.00 „ 4.99%

To the above vinyl-compound (0.074 gr.), dissolved in acetone (20 c.c.) and chloroform (20 drops), was added a solution of potassium permanganate (0.13 gr.) in acetone (30 c.c.), on the following day the manganese-dioxide was filtered off and well washed with hot water. Washings were added to the acetone solution and the organic solvent was evaporated. The acidified solution was repeatedly shaken with ether, leaving 0.041 gr. of a crystalline substance which was recrystallized once from benzene but was not obtained analytically pure.

The above phenanthrene-carboxylic acid (0.025 gr.) was heated with copper-powder (0.19 gr.) in quinoline (2 c.c.) for 30 minutes. After dilution with ether the copper was filtered off, the ethereal solution extracted about ten times with dilute hydrochloric acid, then twice with dilute caustic soda. The ether residue was sublimed in high-vacuum at 165—175° and had a m. p. of 204—205°. The pale yellow substance was recrystallized from ether-petrolether and then melted at 206—208°.

2.808 mg. subst. gave 7.410 mg. CO_2 and 1.305 mg. HO_2

$C_{17}H_{14}O_4$ (V) calc. C 72.34 H 4.96%

found „ 71.97 „ 5.20%

6) *Oxidation experiments:*

a) Oxidation of O-methyl-actinodaphnine-methine to mellophanic acid: The methine (0.889 gr.) was oxidized with conc. nitric acid. The tetramethyl-ester of the resulting acid mixed with tetramethyl-mellophanate from pukateine melted without depression at 129°.

b) Oxidation of actinodaphnine with potassium permanganate: Crude actinodaphnine (1.599 gr.) was dissolved in very dilute hydrochloric acid and sodium carbonate added until slight turbidity occurred. A 4% solution of potassium permanganate was added in volumes of 4.26 c.c. ($\frac{1}{8}$ O) at a time. About 12 atoms of oxygen were used up at room temperature, the oxidation was then completed on the water-bath, requiring 28 atoms of oxygen in all. The filtered solution was concentrated in vacuo to about 20 c.c., the filtered manganese dioxide added again and the whole heated on the water-bath with caustic potash (5 gr.) for 6 hours. Basic vapours with amine like odour were evolved copiously. When the evolution had stopped the manganese dioxide was dissolved by sulphur dioxyde and large amounts of inorganic matter filtered off. The solution was then acidified with conc. hydrochloric acid and after 17 hours extraction with ether in a continous extractor the ether was evaporated and the residue thoroughly dried in a desiccator. The dried crystals were suspended in a little ether and a concentrated solution of diazomethane was added. After a few hours the excess of diazomethane was destroyed by acid, the ether washed with a little very dilute sodium-carbonate to remove unchanged acid, and then evaporated. The ester distilled at 170—180°/0,07 mm. The distillate was dissolved in methyl alcohol, on cooling a small amount of a much higher melting substance (190—195°) separated first which was removed by filtration. A very small amount of water was added, after a short time the desired substance, the trimethyl-ester of methylenedioxy-hemimellitic acid separated. After two recrystallizations from slightly diluted methyl alcohol the m. p. was 128—129°. The ester gave a positive reaction for a methylene-dioxy-group when heated with phloroglucinol and sulphuric acid.

4.129 mg. subst. gave 8,08 mg. CO_2 and 1.56 mg H_2O

$C_{13}H_{12}O_8$ (VII) calc. C 52.70 H 4.05%

found „ 53.37 „ 4.24%

c) Oxidation of pukateine: In order to obtain an authentic specimen of methylenedioxy-hemimellitic acid, we oxidized pukateine in the same way. After several recrystallizations the m. p. of the trimethyl-ester was 124°. Mixed with the trimethyl-ester of the acid from actinodaphnine it softened at 124° and melted at 127—128°, so there was no actual depression.

d) Oxidation of O-methyl-actinodaphnine: By oxidation of O-methyl-actinodaphnine with potassium permanganate m-hemipinic acid was obtained. The oxidation was carried out as described for diethyl-boldine in an earlier paper[1]). The m-hemipinic

[1]) *Schlittler*, B. **66**, 988 (1933).

acid was identified as its ethyl-imide, mixed with an authentic specimen[1]) it did not show a depression of its m. p. (230.5°) (VIII).

6) *Formation of dicentrine by methylation of actinodaphnine:* The oily O-methyl-actinodaphnine (2.121 gr.) was dissolved in acetone (70 c.c.) and methyl iodide (4 c.c.) added. After 20 hours the crystals which had separated were filtered off and dried (2.35 gr.). They were dissolved in a large amount of water, made alkaline with potassium hydroxide and extracted with ether. Thus tertiary and unchanged secondary base were separated from quaternary salt. The ether left on evaporation an oil (1.125 gr.) which was dissolved in freshly distilled acetic anhydride (8 c.c.) and left at room temperature for 7 hours. Water (60 c.c.) and concentrated hydrochloric acid (6 c.c.) were added, after complete decomposition of the acetic anhydride the solution was repeatedly extracted with large amounts of ether to remove the acetyl-compound of the secondary base which had escaped methylation. The ether solution was repeatedly washed with sodium hydroxide, dried over calcium chloride and evaporated. The crystalline residue of O-methyl-N-acetyl-actinodaphnine (0.527 gr.) was recrystallized from little ethyl alcohol, m. p. 222—224°, blue fluorescence in alcohol and ether.

4.158 mg. subst. gave 10.435 mg. CO_2 and 2.285 mg. H_2O
$C_{21}H_{21}O_5N$ calc. C 68.66 H 5.72%
found „ 68.44 „ 6,11%

The solution after the removal of the O-methyl-N-acetyl-actinodaphnine was made alkaline with potassium hydroxide and extracted with much ether. This left 0.343 gr. of a crystalline substance which after two recrystallizations from alcohol melted at 169°.

3.971 mg. subst. gave 10.30 mg. CO_2 and 2.16 mg. H_2O
2.676 mg. subst. gave 0,106 c.c. N_2 (758 mm., 19°)
$C_{20}H_{21}O_4N$ (II) calc. C 70.79 H 6.19 N 4.13%
found „ 70.74 „ 6.09 „ 4.62%

Dicentrine, kindly supplied by Prof. *Asahina* and Dr. *Manske*, had the same m. p., a mixed melting point did not show a depression. We then compared also the intermediate products of the *Hofmann* degradation (methine and vinyl-product) with authentic specimens from dicentrine and found them to be identical.

8) *Derivatives of O-ethyl-actinodaphnine:* In the same way as described above for dicentrine we prepared O-ethyl-N-methyl-actinodaphnine (a) (with diazoethane and methyl iodide) and O-ethyl-N-ethyl-actinodaphnine (b) (with diazoethane and ethyl iodide).

a) Recrystallized twice from alcohol, m. p. 198—199° (rather sparingly soluble in alcohol).

[1]) We have to thank Prof. *Robinson* for a large supply of m-hemipinic acid.

4.008 mg. subst. gave 10.51 mg. CO_2 and 2.35 mg. H_2O

$C_{21}H_{23}O_4N$ (XI)	calc.	C 71.38 H 6.51%
	found	„ 71.51 „ 6.56%

b) Recrystallized twice from ethyl alcohol, m. p. 213—214°, fine needles with strong refraction (sparingly soluble in alcohol; 0.168 gr. dissolve in 40 c.c. of boiling alcohol).

4.102 mg. subst. gave 10.825 mg. CO_2 and 2.41 mg H_2O

$C_{22}H_{25}O_4N$	calc.	C 71.93 H 6.81%
	found	„ 71.97 „ 6.57%

In analogy to the preparation of dicentrine we obtained O-ethyl-N-acetyl-actinodaphnine as a by-product. It was recrystallized from dilute alcohol but could not be obtained in an analytically pure state. As already mentioned earlier, there is some evidence of N-methyl-actinodaphnine occurring naturally, we therefore effected a *Hofmann* degradation on O-ethyl-N-methyl-actinodaphnine in the way described above for O-methyl-N-methyl-actinodaphnine (dicentrine).

O-ethyl-actinodaphnine-methine (X) was recrystallized from little alcohol; after three recrystallizations it melted at 142—144°.

4.070 mg. subst. gave 10.86 mg. CO_2 and 2,375 mg. H_2O

$C_{22}H_{25}O_4N$	calc.	C 71.93 H 6,81%
	found	„ 72.77 „ 6,53%

The methine base was converted into the quaternary iodide and trimethylamine split off by means of potassium hydroxide. The crystalline vinyl-product which separated was extracted with chloroform and recrystallized twice from alcohol, m. p. 186—187°.

3.985 mg. subst. gave 10.785 mg. CO_2 and 1.965 mg. H_2O

$C_{20}H_{18}O_4$	calc.	C 74.53 H 5,59%
	found	„ 73.81 „ 5.52%

9) *Positions of the CH_3O- and OH-groups in ring B:* O-ethyl-N-methyl-actinodaphnine (XI, 0.095 gr.), phloroglucinol (0,095 gr.) conc. sulphuric acid (0.67 gr.) and water (1.2 c.c.) were heated to gentle boiling for 5 minutes and the reaction mixture afterwards heated on the water-bath for 6 hours. Boiling water (14 c.c.) was added, the bulky precipitate of dark red phloroglucinol-condensation products filtered off and the aqueous solution extracted with ether for 12 hours. The acid solution was neutralised with sodium bicarbonate and rapidly extracted with much ether. The ethereal solution was dried over potassium carbonate leaving behind 40 mg. of the dihydroxy-compound (XIV). Colourless crystals, decomposing from about 160°, giving only a slight precipitate with *Mayer*'s reagent. Alcoholic ferric chloride gave a dark-blue coloration slowly turning into dark-green.

The dihydroxy-compound (40 mg.) was dissolved in a few drops of methyl alcohol and an ethereal solution of diazomethane added. After standing for ten hours, the methylation-products were worked up as usual, yielding 30 mg. of non-phenolic base which was an oil (XV). The solution of this base in hydrochloric acid gave a bulky precipitate with *Mayer*'s reagent.

The oily base was dissolved in a few drops of acetone and a few drops of methyl iodide were added. After standing for nine hours the acetone and the excess methyl iodide were removed under reduced pressure but the quaternary iodide proved very difficult to crystallize. It was therefore dissolved in water (5 c.c.), solid caustic potash was added and the solution was refluxed for an hour. Isolated by extracting with ether, the methine base was a yellow oil (22 mg., XVI) which could not be crystallized.

The yellow oil was therefore dissolved in 2 c.c. of methyl alcohol, the second step of the *Hofmann* degradation being effected in the same way as in the case of O-methyl-actinodaphnine-methine (dicentrine-methine, comp. p. 926).

The crude vinyl-compound (10 mg.) was dissolved in ethyl alcohol (4 c.c.), concentrated to a volume of 1 c.c. and then two drops of water added, the vinyl-product then crystallized spontaneously (XVII). M. p. 134°, m. p. after mixing the corresponding vinyl-phenanthrene from laurotetanine (XVIII, m. p. 142°) was 135° (softening at 132°).

Also the form of the crystals was exactly the same. There is extremely strong evidence that the two products are identical; owing to want of material it was impossible to obtain a micro-analysis for product XVII. As already mentioned we hope to remove any doubt of the correctness of our proposed structure by synthetical experiments which are already in progress.

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