The Aconite Alkaloids. XXVI. On Lucaconine and Monoacetyllucaconine*

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In Part XXIII⁽¹⁾ of this series, it was reported that a new alkaloid, lucaconine, $C_{21}H_{33}O_6N$, was isolated from the roots of *Aconitum lucidusculum*, Nakai and it was suggested that it had two methoxyl, four hydroxyl, and a secondary amino group. One of the present authors with Amiya⁽²⁾ found that diacetyllucaconine had two active hydrogens. Therefore, *N*-alkyl and other functional groups had to be determined more precisely. As the results of repeated examinations, it was found that the base had an *N*-ethyl and three methoxyl groups, and, therefore, the older molecular formula of lucaconine, $C_{21}H_{33}O_6N$, should be revised to $C_{24}H_{39}O_7N$***.

On the other hand, a new alkaloid was isolated from the roots of the above mentioned *Aconitum* species, viz., on the basis of the difference of solubility in benzene from the crude bases containing lucaconine. The content of the base was about one-tenth of that of lucaconine and was about 0.012 per cent that of dried roots. The new alkaloid was purified through a perchlorate, from which the free base was liberated and recrystallized from ethanol. The purified base had m.p. 187°, $[\alpha]_D^{18}+42.7°$, and molecular formula $C_{26}H_{41}O_8N$. On hydrolysis with alcoholic potassium hydroxide it split off one mole of acetic acid and produced the alkamine, lucaconine.

$$C_{26}H_{41}O_8N+H_2O\rightarrow CH_3COOH+C_{24}H_{39}O_7N$$

Therefore, this new base was named monoacetyllucaconine.

Acetylation of lucaconine I and monoacetyllucaconine II with acetic anhydride gave the same diacetyl compound, diacetyllucaconine III, $C_{28}H_{43}O_9N$, m. p. 124°, $[\alpha]_D^{16}+15.3°$, which afforded lucaconine on hydrolysis with alcoholic potassium hydroxide.

From these results the formulae of lucaconine I and monoacetyllucaconine II may be extended as follows:

$$C_{19}H_{21}\left\{\begin{array}{l}(OCH_3)_3\\(OH)_4\\N\text{-}C_2H_5\end{array}\right. \qquad C_{19}H_{21}\left\{\begin{array}{l}(OCH_3)_3\\OCOCH_3\\(OH)_3\\N\text{-}C_2H_5\end{array}\right.$$

Lucaconine (I) Monoacetyllucaconine (II)

Lucaconine and monoacetyllucaconine are assumed to have hexacyclic structure based on the skeletal formula, $C_{19}H_{29}N$⁽³⁾.

Experimental

Isolation of Lucaconine.—As described in the previous reports⁽¹,⁴⁾, 293.6 kg. of dried roots of *Aconitum lucidusculum*, Nakai was treated. The percolate thus obtained was divided into three fractions, which were named fraction I, fraction II, and fraction III as previously described⁽⁴⁾. The yield of fraction III was 1,062 g. (0.36% of dried roots). Treatment of fraction II with acetone gave 357 g. of crystalline material, which was recrystallized from ethanol to give 210 g. of crude lucaconine, melting at 197°.

From 5.5 g. of this crude lucaconine, 6.8 g. of crystalline perchlorate was prepared, which was recrystallized from ethanol to give 5.1 g. of pure perchlorate, m. p. 210° (decomp.). From this salt, 3.9 g. of a free base melting at 198° was liberated; on three recrystallizations from ethanol, the base melted at 200°, and showed no depression of the melting point on admixture with an authentic sample of lucaconine⁽¹⁾. $[\alpha]_D^{14}+57.1°$ (chloroform).

Anal. Found: C, 63.48; H, 8.39; N, 3.55; OCH_3, 20.86; (N)-C_2H_5, 6.59. Calcd. for $C_{24}H_{39}O_7N$: C, 63.55; H, 8.45; N, 3.09; 3-OCH_3, 20.53; (N)-C_2H_5, 6.19%.

Determination of N-ethyl group⁽⁵⁾.—Lucaconine was treated in the usual manner for Willstätter's *N*-alkyl determination. Trimethyl ethyl ammonium iodide thus obtained was analyzed.

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* Part XXV, H. Suginome and S. Kakimoto, This Bulletin, **32**, 352 (1959).

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1) H. Suginome, S. Kakimoto, J. Sonoda and S. Noguchi, *Proc. Japan Acad.*, **22**, 122 (1946).

2) H. Suginome and T. Amiya, unpublished work.

*** The compositions calculated for these two formulae are nearly identical as follows: Calcd. for $C_{21}H_{33}O_6N$: C, 63.77; H, 8.41; N, 3.57%. Calcd. $C_{24}H_{39}O_7N$: C, 63.55; H, 8.45; N, 3.09%.

3) H. Suginome and K. Ohno, *J. Fac. Sci., Hokkaido Univ., Ser. III. Chem.*, **4**, 36 (1950).

4) H. Suginome, S. Furusawa, Y. Chiba and S. Kakimoto, ibid., **4**, 1 (1950).

5) R. Willstätter and M. Utzinger, *Ann.*, **382**, 148(1911); R. Majima and K. Tamura, ibid., **526**, 116 (1936).

Anal. Found: I, 60.38. Calcd. for $(CH_3)_3(C_2H_5)NI$: I, 59.02%.

The pure lucaconine was also obtained by treatment of the crude base melting at 197° with ethanolic potassium hydroxide, followed by recrystallization from ethanol.

Perchlorate.—m. p. 210° (decomp.).

Anal. Found: C, 51.68; H, 7.08; Cl, 6.39. Calcd. for $C_{24}H_{39}O_7N \cdot HClO_4$: C, 52.01; H, 7.75; Cl, 6.36%.

Hydrochloride.—m. p. 216~217° (decomp.) (from abs. ethanol).

Anal. Found: C, 58.81; H, 8.31; Cl, 7.32. Calcd. for $C_{24}H_{39}O_7N \cdot HCl$: C, 58.80; H, 8.22; Cl, 7.24%.

Hydrobromide.—m. p. 223° (decomp.) (from abs. ethanol).

Anal. Found: C, 54.30; H, 7.54; Br, 14.81. Calcd. for $C_{24}H_{39}O_7N \cdot HBr$: C, 53.91; H, 7.54; Br, 14.93%.

Methiodide.—m. p. 174° (from water).

Anal. Found: C, 49.23; H, 7.29; OCH_3, 16.36; I, 19.51. Calcd. for $C_{24}H_{39}O_7N \cdot CH_3I$: C, 50.40; H, 7.11; 3-$OCH_3$, 15.91; I, 21.32%.

The methiodide readily returned to the original base by means of alkali.

Isolation of Monoacetyllucaconine. — On being left to stand in a refrigerator, the mother liquor, obtained by removal of the lucaconine-rich base, gave 90 g. of crystalline substance melting at 168~172°. This substance was recrystallized from benzene and then from ethanol to give a crystalline base melting at 186°. Yield 12.8 g. From this base perchlorate was obtained, which after three recrystallizations from ethanol showed m. p. 202~202.5° (decomp.). Yield, 9.0 g. Free base, obtained from this perchlorate, showed m. p. 187°, $[\alpha]^{18}_{D}+42.7°$ (ethanol) after recrystallization from ethanol. Yield, 3.75 g.

Anal. Found: C, 63.11; H, 8.22; N, 2.85; OCH_3, 18.90; (N)-C_2H_5, 5.05; $COCH_3$, 10.80. Calcd. for $C_{26}H_{41}O_8N$: C, 63.07; H, 8.34; N, 2.83; 3-OCH_3, 18.79; (N)-C_2H_5, 5.86; $COCH_3$, 8.68%.

This base, monoacetyllucaconine, was easily soluble in methanol and in ethanol and moderately so in benzene but sparingly so in water and in petroleum ether.

Perchlorate.—m. p. 202~202.5° (decomp.).

Anal. Found: Cl, 5.85. Calcd. for $C_{26}H_{41}O_8N \cdot HClO_4$: Cl, 5.95%.

Hydrobromide.—m. p. 190~191° (decomp.).

Anal. Found: H_2O, 2.42. Calcd. for $C_{26}H_{41}O_8N \cdot HBr \cdot 3/4H_2O$: H_2O: 2.29%.

Anal. (anhydrous) Found: Br, 13.21. Calcd. for $C_{26}H_{41}O_8N \cdot HBr$: Br, 13.85%.

Hydrolysis of Monoacetyllucaconine.— After monoacetyllucaconine was hydrolyzed with 0.5 N ethanolic potassium hydroxide, a crystalline substance was obtained. After recrystallization from ethanol, it was identified as lucaconine by the mixed melting point test.

Anal. Found: C, 63.34; H, 8.77. Calcd. for $C_{24}H_{39}O_7N$: C, 63.55; H, 8.45%.

Acetic acid produced on hydrolysis of monoacetyllucaconine was identified as silver salt.

Anal. Found: Ag, 64.67. Calcd. for CH_3CO_2Ag: Ag, 64.64%.

Diacetyllucaconine (III). — *a) From Lucaconine (I).*—Lucaconine was heated in acetic anhydride for 30 min., and the reaction mixture was treated in the usual manner. After recrystallization from dilute ethanol, diacetyllucaconine was obtained in colorless needles, m. p. 124°, $[\alpha]^{16}_{D}+15.3°$ (94% ethanol).

Anal. Found: C, 62.40; H, 8.01; N, 2.69; $COCH_3$, 15.93. Calcd. for $C_{28}H_{43}O_9N$: C, 62.55; H, 8.05; N, 2.61; 2-$COCH_3$, 15.9%.

b) From Monoacetyllucaconine (II).—Upon the same treatment as in the case of lucaconine described above, monoacetyllucaconine afforded the same diacetyllucaconine, m. p. and mixed m. p. 124°.

After being heated at 145° for 10 min. under reduced pressure (1×10^{-5} mmHg), diacetyllucaconine was recovered unchanged.

Hydrolysis of Diacetyllucaconine (III).— Diacetyllucaconine was hydrolyzed by heating with 0.5 N ethanolic potassium hydroxide. After removal of most of the ethanol, the reaction mixture was extracted with chloroform and then the chloroform extract was evaporated to give lucaconine, which melted at 198° after recrystallization.

Anal. Found: C, 63.58; H, 8.67; N, 3.44. Calcd. for $C_{24}H_{39}O_7N$: C, 63.55; H, 8.45; N, 3.09%.

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