compared with that when insulin alone was given.

This result shows that insulin was degraded by Pronase P *in vitro*. Nevertheless, it is interesting that Pronase P showed hypoglycemic activity.

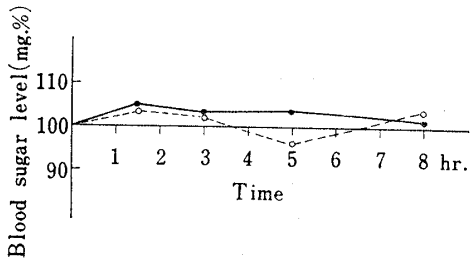

Fig. 3. Effect of Trypsin on Hypoglycemic Activity of Insulin

●——● trypsin 0.15 mg./kg.
○---○ mixture of insulin (0.3 u/kg.) and trypsin (0.15 mg./kg.), after incubation for 1 hr.

As shown in Fig. 3, when insulin was incubated with trypsin, trypsin entirely counteracted hypoglycemic activity of insulin and trypsin only was ineffective on blood sugar level in a dose of 0.15 mg./kg. It will be worth notice that a difference of physiological activity exists between the two proteases.

Recently, Dixit, *et al.*[3] reported that acid-alcohol extracts of larval foods of the honeybee showed insulin-like activity. This report shows the possibility that such active substances can be taken out of invertebrates.

The pattern of curve of hypoglycemic activity of Pronase P was analogous to that of insulin. It is not yet known, however, whether or not Pronase P itself shows insulin-like activity or activates the enzyme participating in insulin-activity.

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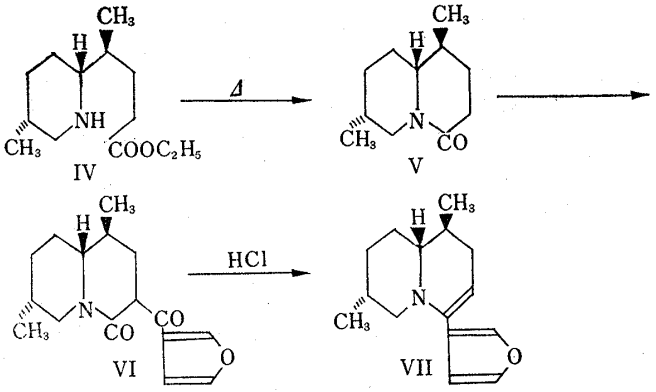
Dehydro-deoxynupharidine : A New Alkaloid of *Nuphar japonicum* DC.

A new unstable base, $C_{15}H_{21}ON$ (I) was isolated from the root of *Nuphar japonicum* DC., and designated as dehydro-deoxynupharidine. It formed a crystalline perchlorate, m.p. 159~161°, $[\alpha]_D$ +130.1° ($CHCl_3$) (*Anal.* Calcd. for $C_{15}H_{22}O_5NCl$: C, 54.28; H, 6.69; N, 4.22. Found: C, 54.19; H, 6.77; N, 4.41). The infrared spectrum of the perchlorate in chloroform showed bands at 877, 1510 and 3128 cm^{-1} attributable to the furan ring, and at 1640 cm^{-1} due to the iminium salt which conjugates with the furan ring, while its nuclear magnetic resonance spectrum contained three signals (δ 8.09, 7.56, 6.82), each corresponding to one proton, which were obviously attributable to the furan ring.

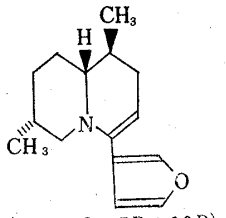
Sodium borohydride reduction of the perchlorate of I afforded an oily amine, II, $b.p_3$ 125° (oil bath temp.), $[\alpha]_D$ −114.1° ($CHCl_3$), IR ν_{max}^{liquid} 2764, 2792 (*trans*-quinolizidine) 874, 1032, 1505, 3140 cm^{-1} (furan). II formed a perchlorate, m.p. 203~204.5° (*Anal.* Calcd. for $C_{15}H_{24}O_5NCl$: C, 53.49; H, 7.18; N, 4.16. Found: C, 53.58; H, 7.33; N, 4.11), and a picrate, m.p. 154.5~155.5° (*Anal.* Calcd. for $C_{15}H_{23}ON \cdot C_6H_3O_7N_3$: C, 54.54; H, 5.67; N, 12.12. Found: C, 54.68; H, 5.67; N, 12.27). II was identical with an authentic specimen

of (−)-deoxynupharidine[1,2] (Ⅲ) by the mixed melting point determination of the perchlorates and by the comparision of the infrared spectra of the free bases. The action of sodium borohydride on I, as expected, also reduced to form (−)-deoxynupharidine (Ⅲ).

These results suggest that dehydro-deoxynupharidine is respresented by the formula (I). Furthermore, its correctness was confirmed by a synthesis as shown in the following schema :

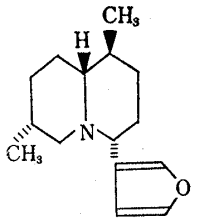


(±)-1,7-Dimethyl-octahydro-4*H*-quinolizinone (V) derived from an amino acid ester[3] which forms a picrolonate, m.p. 156~158°, was condensed with ethyl 3-furoate to afford Ⅵ. Ⅵ was converted to an enamine (Ⅶ) which forms a perchlorate, m.p. 145.5~147° (*Anal.* Calcd. for $C_{15}H_{22}O_5NCl$: C, 54.28; H, 6.69; N, 4.22. Found : C, 54.45; H, 6.78; N, 4.19). The infrared spectra of the perchlorates of the synthetic (Ⅶ) and the natural (I) bases,



(1*S* : 5*S* : 7*R* : 10*R*)

I



(1*S* : 4*R* : 5*S* : 7*R* : 10*R*)

III

both in chloroform solution, were completely indistinguishable. Since the absolute configuration[4] of (−)-deoxynupharidine (Ⅲ) is known, structure (I) respresents the structure and the absolute configuration of dehydro-deoxynupharidine.

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