The fraction, b.$p_{0.4}$ 130～134°, m.p. 56°, weighing 5.0 g., was identical with an authentic sample of N-benzylformamide by comparison of the IR spectra and by mixed melting point test. Crystallization from ether gave crystals, m.p. 60°. *Anal.* Calcd. for C_8H_9ON: C, 71.09; H, 6.71; N, 10.39. Found: C, 69.87; H, 6.72; N, 10.38. The second fraction, b.$p_{0.4}$ 160～164°, was shown to be composed of N,N-dibenzylformamide and tribenzylamine. The fraction was dissolved in dry benzene and dry HCl was introduced into the solution, whereupon tribenzylamine hydrochloride precipitated. Filtration gave crystals, m.p. 214～221°, weighing 0.3 g. This was identical with an authentic sample by comparison of the IR spectra and by mixed melting point test. Recrystallization from EtOH gave crystals, m.p. 226～227°. *Anal.* Calcd. for $C_{21}H_{22}NCl$: C, 77.87; H, 6.85; N, 4.32. Found: C, 77.79; H, 6.71; N, 4.01. The benzene solution was washed with $KHCO_3$ and dried over Na_2SO_4. Removal of benzene gave solid residue, m.p. 47～49°, weighing 4.0 g. This material was identical with an authentic N,N-dibenzylformamide by comparison of the IR spectra and by mixed melting point test. Crystallization from ether gave crystals, m.p. 51～52°. *Anal.* Calcd. for $C_{15}H_{15}ON$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.90; H, 6.60; N, 6.29.

Hydrogenolysis of N,N′-Benzylidenebisacetamide——From the reaction mixture obtained from the general procedure (reaction temperature 75～85°; reaction period 4.5 hr.) AcOH and $AcNH_2$ were distilled off under reduced pressure. The AcOH distillate was shown to contain a small amount of toluene, which was isolated and identified in the same manner as in the experiment with N,N′-benzylidenebisformamide. The residue was further distilled under higher reduced pressure to give a solid distillate, b.p_2 151～154°, m.p. 58～59°, weighing 10.1 g. This material was identical with an authentic N-benzylacetamide by comparison of the IR spectra and by mixed melting point test. Crystallization from ether gave crystals, m.p. 61°. *Anal.* Calcd. for $C_9H_{11}ON$: C, 72.45; H, 7.43; N, 9.39. Found: C, 72.66; H, 7.42; N, 9.50.

Hydrogenolysis of N,N′-Benzylidenebispropionamide——From the reaction mixture obtained from the general procedure (reaction temperature 75～85°; reaction period 3.7 hr.) AcOH and propionamide were removed by distillation under reduced pressure. The former distillate was shown to contain a small amount of toluene, which was isolated and identified in the same manner as in the experiment with N,N′-benzylidenebisformamide. The residue was further distilled under higher reduced pressure to give a solid distillate, b.p_{12} 151～156°, m.p. 48～50°, weighing 9.3 g. This material was identical with an authentic N-benzylpropionamide by comparison of the IR spectra and by mixed melting point test. Crystallization from benzene-petr. ether gave crystals, m.p. 50～51°. *Anal.* Calcd. for $C_{10}H_{13}ON$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.51; H, 7.89; N, 8.41.

Hydrogenolysis of N,N′-Benzylidenebisbenzamide——From the reaction mixture from the general procedure (reaction temperature 75～85°; reaction period 2.7 hr.) AcOH was removed by distillation under reduced reduced pressure. From the AcOH distillate a small amount of toluene was isolated in the same manner as in the experiment with N,N′-benzylidenbisformamide. Further distillation under higher reduced pressure gave a fraction of benzamide and then a solid fraction, b.p_2 200～201°, m.p. 105～107°, weighing 14.3 g. The latter fraction was identical with an authentic N-benzylbenzamide by comparison of the IR spectra and by mixed melting point test. Crystallization from benzene gave crystals, m.p. 107°.

The authors are indebted to Mr. K. Narita of this college for elementary analyses.

[Chem. Pharm. Bull. 15(2) 240～242 (1967)]

UDC 546.271.04 : 547.834.2.07

Takehisa Kunieda and Shun-ichi Yamada: Chemistry of Sodium Borohydride and Diborane. Ⅲ.[*1] Synthesis of (+)-Lupinine by Hydroboration Reaction.

(*Faculty of Pharmaceutical Sciences, University of Tokyo*[*2])

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Although the chemistry of lupinine, the simplest compound among the so-called lupine alkaloids, has been studied in detail,[1] no report has been found concerning the synthesis of optically active lupinine from optically active compound.

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*1 Part Ⅱ: This Bulletin, **14**, 1389 (1966).

*2 Hongo 7, Tokyo (国枝武久, 山田俊一).

1) N. J. Leonard: "The Alkaloids" edited by R. H. F. Manske, Vol. Ⅶ, 263 (1960), Academic Press, New York and London.

The present investigation was undertaken to prepare the optically active lupinine (Ⅲ) stereoselectively by the hydroboration reaction of (+)-1-methylenequinolizidine (Ⅱ), which was synthesized in a good yield by the application of the Wittig reaction to (+)-hexahydro-2*H*-quinolizin-1(6*H*)-one (Ⅰ).[2] The absolute configuration of (+)-Ⅱ has

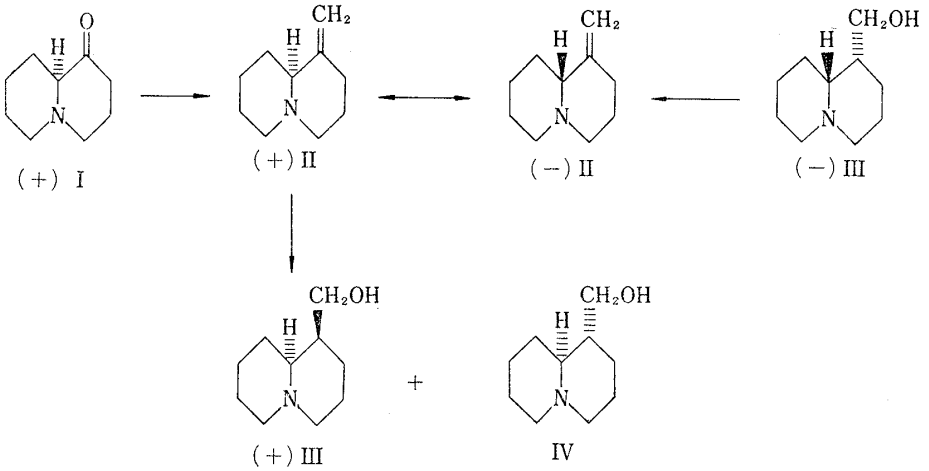

Chart 1.

been known as shown in Chart 1, by the correlation of (−)-Ⅱ with (−)-lupinine (Ⅲ)[3] by Karrer, *et al.*[4] S (+)-Ⅱ, α_D+ 2.787° (l=1 cm, neat), which was considered to be of about 60% optical purity in comparison with the data of α_D −11.57° (l=2.5 cm, neat) reported by Karrer,[4] was subjected to the hydroboration reaction using an excess of diborane in diglyme solution at room temperature and then the reaction mixture was oxidized with alkaline hydrogen peroxide in the usual manner to yield (+)-lupinine, which was characterized as methiodide, m.p. 288~290°, $[\alpha]_D$ −6.3° (MeOH).

This sample was identified with an enantiomer of the natural (−)-lupinine methiodide, m.p. 294°, $[\alpha]_D$ +11.2° (MeOH) in comparison with their melting points and infrared spectra (KBr). Gas chromatographic data of the hydroboration-oxidation reaction product indicated the existence of both lupinine (Ⅲ) and epilupinine (Ⅳ) in the ratio of about 10:1.

The stereoselectivity of this reaction might be explained as follows. The preferential conformation of Ⅱ is considered to be the trans chair (Ⅱ) from the fact that the presence of Bohlmann absorption[5] is distinct in its infrared spectrum. The first

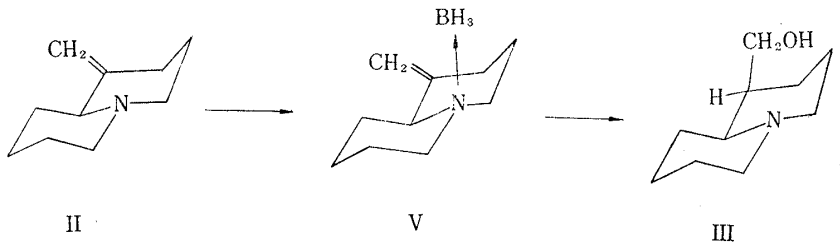

Chart 2.

electrophilic addition of borane takes place to the bridge-head nitrogen to give amine-borane (Ⅴ) and then another borane adds to the double bond from the less hindered

2) S. Yamada, T. Kunieda : This Bulletin, in press.
3) R.C. Cookson : Chem. & Ind. (London), **1953**, 337; S. Okuda, H. Kataoka, K. Tsuda : This Bulletin, **13**, 487 (1965).
4) P. Karrer, A. Vogt : Helv. Chim. Acta, **13**, 1073 (1930).
5) F. Bohlmann : Ber., **91**, 2157 (1958).

equatorial side predominantly. The similar explanation was made in the reaction of benzomorphan system by H. Kugita, *et al.*[6]

Experimental*3

(+)-Lupinine Methiodide——To the 100 ml. flask was added 0.7 g. (0.0046 mole) of S(+)-1-methylene-quinolizidine, α_D^{26} +2.787°(l=1 cm., neat)[2] and 0.3 g. (0.0075 mole) of $NaBH_4$ in 20 ml. of diglyme. A solution of 1.4 g. (0.01 mole) of borontrifluoride etherate in 20 ml. of diglyme was added dropwise to the stirred reaction mixture over a period of 40 min. under N_2 atmosphere, while the temperature was maintained at 5~7°. The mixture was kept for 1 hr. at this temperature and then 1 hr. at room temperature. An excess of hydride was then decomposed by careful dropwise addition of 1 ml. of H_2O. The organoborane is oxidized by the addition of 4 ml. of 3*N* NaOH, followed by 4 ml. of 30% H_2O_2. The inorganic compound precipitated was filtered off, the filtrate acidified with dil. HCl and evaporated to dryness *in vacuo*. The residue was basified with K_2CO_3 and extracted with benzene. The extract was dried and evaporated *in vacuo* to leave 0.6 g. of colorless viscous liquid, a part (0.3 g.) of which was chromatographed on neutral alumina (Woelm activity Ⅲ) to give 110 mg. of colorless oil. This was proved to be a mixture (10:1) of lupinine (Ⅲ) and epilupinine (Ⅳ) by gas chromatographic analysis using a 3% carbowax 20*M* column at 174°. The methiodide was formed in benzene and recrystallized several times from EtOH to afford colorless needles, m.p. 288~290°, $[\alpha]_D^{15}$ −6.3°(c=0.72, MeOH). $[\alpha]_{260}^{15}$ −45°. *Anal.* Calcd. for $C_{11}H_{22}ONI$: C, 42.58; H, 6.78; N, 4.52. Found: C, 42.61; H, 6.79; N, 4.66. The IR spectrum (KBr) was identical with that of the authentic methiodide, m.p. 294°, $[\alpha]_D^{15}$ +11.2°(c=1, MeOH), prepared from natural(−)-lupinine. The epilupinine methiodide could not be isolated.

The authors express their deep gratitude to Professor S. Shibata and Dr. U. Sankawa of Tokyo University for the generous gift of natural lupinine and epilupinine. They are also grateful to the members of the Central Analysis Room of this Faculty for elemental analysis and measurement of IR spectra.

*3 Melting points are uncorrected.

6) H. Kugita, M. Takeda: This Bulletin, **12**, 1166, 1172 (1964).

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UDC 615.778 : 581.19 : 582.628

Tetsuro Ikekawa,*1 E. Lin Wang, Masa Hamada, Tomio Takeuchi, and Hamao Umezawa: Isolation and Identification of the Antifungal Active Substance in Walnuts.

(*Institute of Microbial Chemistry**2)

The substance in walnuts of *Juglans regia* Linn. and *J. Sieboldiana* Maxim. exhibiting growth inhibition of *Trichophyton mentagrophytes* has been isolated, and it is confirmed that the active substance is identical with juglone (5-hydroxy-1,4-naphthoquinone).

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Pericarps of walnuts have been known since earlier days as a crude drug for treatment of Trichophytiasis,[1] but no report has been published about the active agent inhibiting *Trichophyton*.

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1) S. J. Lee: Honzo Komoku, **30**, 100.