The unusual bisnorditerpene skeleton[6] of II might be biogenetically derived from manool on oxidation of the vinyl group to an aldehyde followed by retroaldol condensation.

The pharmacological activities of these diterpenes (I) and (II) are still under investigation.

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Received September 22, 1980

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[Chem. Pharm. Bull. 28(11)3454—3456(1980)]

## The Chemical Transformation of Gardnerine to 2-Acylindole Alkaloid "Ochropine"

The absolute configuration and the geometry of ethylidene group of the 2-acylindole alkaloid "Ochropine" have been confirmed by the chemical transformation starting from "Gardnerine" whose absolute configuration is known.

**Keywords**——ochropine; gardnerine; absolute configuration; chemical transformation; ring opening reaction; 2-acylindole alkaloids; indole alkaloid

The 2-acylindole alkaloid, ochropine **1**, was isolated from *Ochrosia poweri* Bailey (Apocynaceae) by Doy and Moore in Australia in 1962.[1] From the chemical and physical studies, the structure **1** was posturated to ochropine in 1964.[2]

In this communication, we wish to report the chemical conversion to ochropine from gardnerine **2** which is a main alkaloid of *Gardneria nutans* Sieb. *et* Zucc. (Loganiaceae).[3,4] It should be stressed that this forms the first correlation of ochropine with the other natural indole alkaloids whose absolute configurations are known.

Thus, the primary alcohol group of Na-methylgardnerine **3** obtained from Na-methylgardnerine acetate[5] was oxidized to Na-methylgardneral **4** (mp 198°, in 76% yield) using N-chlorosuccinimide, $Me_2S$ and $Et_3N$ by Corey method.[6] Compound **4** was isomerized to Na-methyl-epi-gardnerinal **5** (mp 204°) by treatment with alumina or sodium hydroxide in methyl alcohol at 80°. The nuclear magnetic resonance (NMR) spectra of the both aldehydes **4** and **5** revealed the aldehyde protons at $\delta$ 9.07 and 9.56. In the former case the aldehyde group was shown to be shielded with indole skeleton. Normal (**6**, mp 267°) and epi-(**7**, mp 248°) oxime derivatives formed the both aldehydes were refluxed with acetic anhydride for 15 minutes under Ar atmosphere. The resulting nitriles **8** (mp 285°, $\delta$ 1.63 C=CHC$\underline{H}_3$) and **9** (mp 238°, $\delta$ 1.74 C=CHC$\underline{H}_3$) were obtained in the pure states with moderate yields by each

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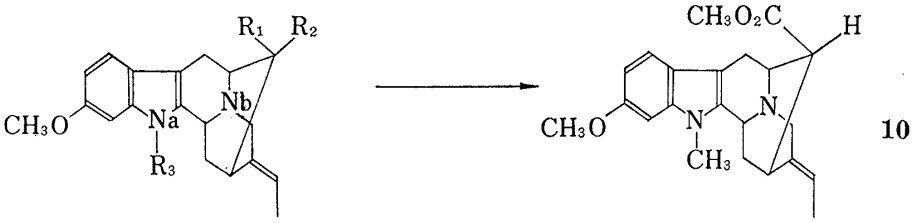

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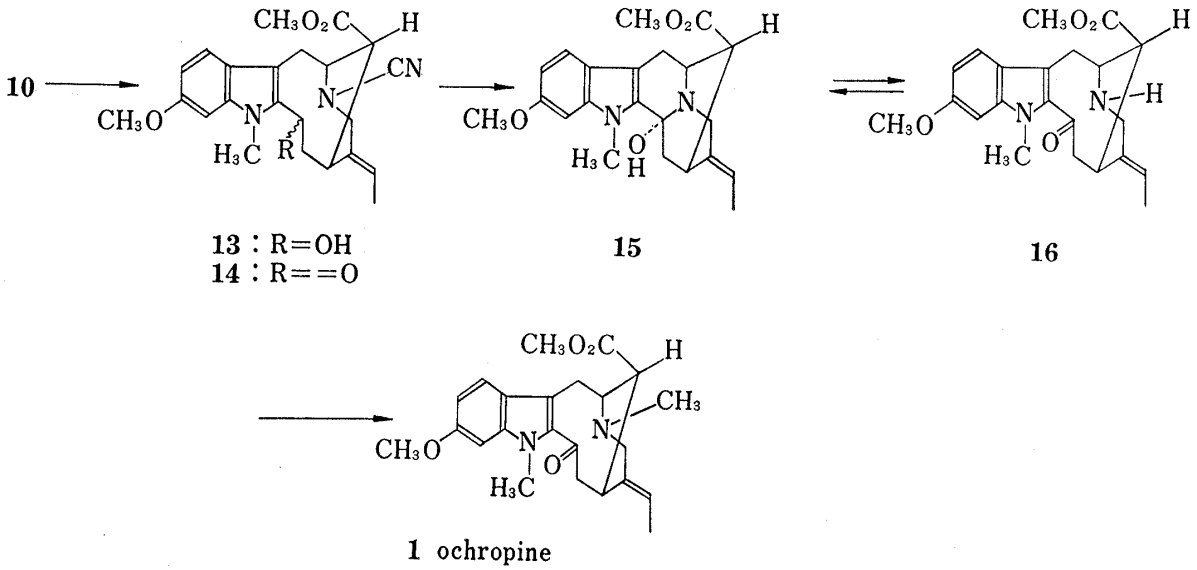
| Comp. No. | $R_1$ | $R_2$ | $R_3$ | Comp. No. | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|---|---|---|---|
| Gardnerine 2 | $CH_2OH$ | H | H | 7 | H | CH=N–OH | $CH_3$ |
| 3 | $CH_2OH$ | H | $CH_3$ | 8 | C≡N | H | $CH_3$ |
| 4 | CHO | H | $CH_3$ | 9 | H | C≡N | $CH_3$ |
| 5 | H | CHO | $CH_3$ | 11 | $CONH_2$ | H | $CH_3$ |
| 6 | CH=N–OH | H | $CH_3$ | 12 | H | $CO_2CH_3$ | $CH_3$ |



13 : R=OH
14 : R=O

15

16

1 ochropine

reaction. No isomerization between the two epimers was observed in this reaction. The nitrile **8** was converted to the methoxycarbonyl derivative **10** (mp 204°, in 50% yield) by methanolysis (absolute MeOH: $H_2SO_4$, 3: 1, 110°, 30 minutes) and to the amide **11** (mp 277°, in 50% yield) as another product. By the same method, 16-epi-methoxycarbonyl derivative **12** (mp 166°) was given rise to from 16-epi-nitrile **9**. The NMR spectrum of **10** presents a signal due to carbomethoxy group at $\delta$ 3.07 which exhibited a remarkable shielding effect of indole skeleton, compared with 16-epi-derivative **12** ($\delta$ 3.66). The spectral data of both methyl esters are: **10**,: UV (EtOH), $\lambda_{max}$ (log $\varepsilon$), 233 (4.57), 270 sh. (3.70), 280 (3.76), 298 (3.79); IR (KBr), $\nu_{max}$ $cm^{-1}$, 1730, 1625, 1590, 1575; NMR ($CDCl_3$), $\delta$ 1.59 (3H, d. of t. $J$=7 and 1 Hz), 3.07 (3H, s. ester $C\underline{H}_3$), 3.52 (3H, s. Na–$C\underline{H}_3$), 3.83 (3H, s. ether $C\underline{H}_3$), 4.19 (1H, broad d. $J$=8 Hz, H on C-3), 5.22 (1H, q. -like $J$=7 Hz); CD ($c$=0.482×$10^{-3}$, EtOH), $\lambda_{max}$ $\Delta\varepsilon$(nm), +0.63 (310), −0.57 (293), +1.70 (278), −3.39 (250), +1.51 (227), −5.40 (210); Mass, $m/e$ (%), 366 ($M^+$, 100), 365 (94), 351 (22), 307 (30), 213 (54), 212 (80) and **12**, UV (EtOH), $\lambda_{max}$ nm (log $\varepsilon$), 232.5 (4.60), 269 sh. (3.67), 280 (3.76) 297 (3.80); IR (KBr), $\nu_{max}$ $cm^{-1}$, 1730, 1640, 1625, 1585, 1570; NMR ($CDCl_3$), $\delta$ 1.58 (3H, d. of t. $J$=7 and 1 Hz), 3.59 (3H, s. Na–$C\underline{H}_3$), 3.66 (3H, s. ester $C\underline{H}_3$), 3.88 (3H, s. ether $C\underline{H}_3$), 5.33 (1H, q. -like $J$=7 Hz); CD ($c$=0.515×$10^{-3}$, EtOH) $\lambda_{max}$ $\Delta\varepsilon$ (nm), +0.53 (306), −0.71 (295), +1.18 (277), −4.94 (237), −1.41 (225), +0.82 (223), −1.06 (215); Mass, $m/e$ (%) 366 ($M^+$, 100), 365 (86), 351 (24), 307 (25), 213 (48), 212 (67). The both sarpagine-type alkaloids **10** and

**12** may be found in the future in natural plants. By the C/D ring opening reaction of **10** using BrCN–$Na_2CO_3$ in THF–$H_2O$ at room temperature for 30 minutes, the isomeric mixture of alcohols **13** (IR, $\nu_{CN}$ 2215 $cm^{-1}$) was formed.[5] The alcohols **13** were converted into the corresponding ketone **14** (amorphous, UV $\lambda_{max}$ nm, 223 sh., 237 sh., 260 sh., 340) with pyridine-$CrO_3$–$H_2O$ in 60% yield from **10**. Decyanation of **14** using 5% aq.AcOH–$AcONH_4$ (refluxing 3 hr. at 120°) gave a crystalline amine **15** (mp 186°, des-Nb-methylochropine, in 57% yield) which showed an equilibrium state with 2-acylindole derivative **16**. Especially an addition of acid to the solution produced mainly 2-acylindole **16** as observed on UV spectra. The structure of this base **15** corresponds to Na-methyl-11-methoxy perivine[7] which may be found in the near future in natural plants. The spectral data for **15** are: UV (EtOH), $\lambda_{max}$ nm (log $\varepsilon$), 233 (4.48), 270 sh. (3.70), 301 (3.80), 339 (3.89); IR (KBr), $\nu_{max}$ $cm^{-1}$ 1725 (ester CO), 1625, 1585, 1570; NMR ($CDCl_3$), $\delta$ 1.59 (3H, broad d. $J$=7 Hz), 2.84 (3H, s. ester $CH_3$), 3.56 (3H, s. Na–C$\underline{H}_3$), 3.83 (3H, s. ether C$\underline{H}_3$), 5.25 (1H, q. -like $J$=7 Hz); CD ($c=0.269\times10^{-3}$, EtOH) $\lambda_{max}$ $\Delta\varepsilon$(nm), −3.24 (325), +1.35 (278), −2.25 (259), −0.34 (245), −0.66 (240), +4.84 (228); Mass, $m/e$ (%), 382 ($M^+$, 100), 365 (27), 323 (18), 281 (22), 229 (54), 228 (75), 216 (42), 166 (17). Finally, the base **15** was methylated using formaldehyde and palladized charcoal with hydrogen in a dioxane solution by a usual method.[8]

Synthesized compound **1** (mp 143—145° from MeOH–$H_2O$) was formed by the methylation in 42% yield. This compound was identified as ochropine by mixture melting point determination with an authentic sample and by comparison of their physical properties including optical rotation, TLC, UV, NMR, IR and Mass spectra.

**Acknowledgement** We thank Dr. B.P. Moore, Division of Entomology, CSIRO, Canberra, Australia, for generous gift of ochropine. This research was supported by a Grant-in-Aid for Special Project Research of "Chemical Research in Development and Utilization of Nitrogen-Organic Resources" from the Ministry of Education, Science and Culture, Japan, which is gratefully acknowledged.

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Received September 26, 1980

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