[Chem. Pharm. Bull. 16(4) 688—694 (1968)]

UDC 547.94.04 : 547.833.04

Phenol Oxidation of Isoquinoline Alkaloids. III.[1] Oixdative Coupling of *dl*-4′-O-Methyl-N-methylcoclaurine

Masao Tomita,[2a] Yukio Masaki, Kazuyoshi Fujitani, and Yoshiro Sakatani

Faculty of Pharmaceutical Sciences, Kyoto University[2]

(Received July 17, 1967)

Potassium ferricyanide oxidation of *dl*-4′-O-methyl-N-methylcoclaurine (VII) afforded two species of diphenyl ether derivatives (Base A′ and Base B′), which were racemic and diastereoisomeric each to each. The yield was about 15%. Spectrometric studies of the dimerization product and their O-methyl ethers gave proof to their structures. The structures were confirmed by a synthesis of their O-methyl ethers *via* an alternative route. Configurations of the products were also assigned by the chemical correlation with fangchinoline, having (L,L)-configuration on the two asymmetric carbon atoms.

In the previous papers of this series,[1,3] the authors reported on the results of preliminary experiments in the biogenetic type synthesis of bisbenzylisoquinoline alkaloids. The potassium ferricyanide oxidation of corypalline (I) and its metho-salt resulted in the formation of biphenyl derivatives, 8,8′-bicorypallyl (II) and the corresponding diquaternary metho-salt respectively. On the other hand, *dl*-N-methylisosalsoline (III) gave rise to biphenyls (IV and V) and a diphenyl ether derivative (VI) when subjected to the potassium ferricyanide oxidation, and it was suggested that the bulkiness of substituent at 1-position of the isoquinoline nucleus would apparently affect the product development in the oxidative dimerization process.

In this paper, the authors report on the potassium ferricyanide oxidation of *dl*-4′-O-methyl-N-methylcoclaurine (VII), which bears *p*-methoxybenzyl group at the 1-position of the corypalline skeleton (see Chart 2).

The material, *dl*-4′-O-methyl-N-methylcoclaurine (VII) was prepared by a standard Bischler-Napieralski method *via dl*-7-O-benzyl-4′-O-methyl-N-methylcoclaurine and was obtained as colorless prisms, mp 88—89°.

VII was treated with potassium ferricyanide in a stirred two phase system of chloroform–0.1 N sodium carbonate at room temperature. The product was worked up in a usual manner, and two fractions of phenolic base were obtained in amorphous state by chromatographical separation on silicic acid.

One of the phenolic base fractions (Base A′) showed single spot on thin-layer chromatography (TLC) with samller *Rf* value than that of the starting material (VII). Homogeneity and dimeric character of this fraction (Base A′) were evidenced by its NMR sepctrum, which showed two N-methyl signals with equal intensity and four methoxyl singlets each corresponding to three protons. These NMR data suggested that it might be a diphenyl ether derivative. The signal pattern of the aromatic proton region was also found to be of a diphenyl ether derivative. Further, the NMR spectrum of the O-methyl ether(Base A), obtained by the methylation of Base A′ with diazomethane, showed a singanl for the newly introduced methoxyl group at higher field (by 0.05 ppm) than those of methoxyls of Base A′. The NMR spectra of Base A and A′ showed all N-methyl and O-methyl signals as singlets and suggested that they were

1) Part II: M. Tomita, Y. Masaki, and K. Fujitani, *Chem. Pharm. Bull.* (Tokyo), **16**, 257 (1968).
2) Location: *Yoshida-Shimoadachi-Cho, Sakyo-Ku, Kyoto*; *a*) Present address: *Kyoto College of Pharmacy, Yamashina-Misasagi, Higashiyama-Ku, Kyoto.*
3) M. Tomita, K. Fujitani, Y. Masaki, and K-H. Lee, *Chem. Pharm. Bull.* (Tokyo), **16**, 251 (1968).

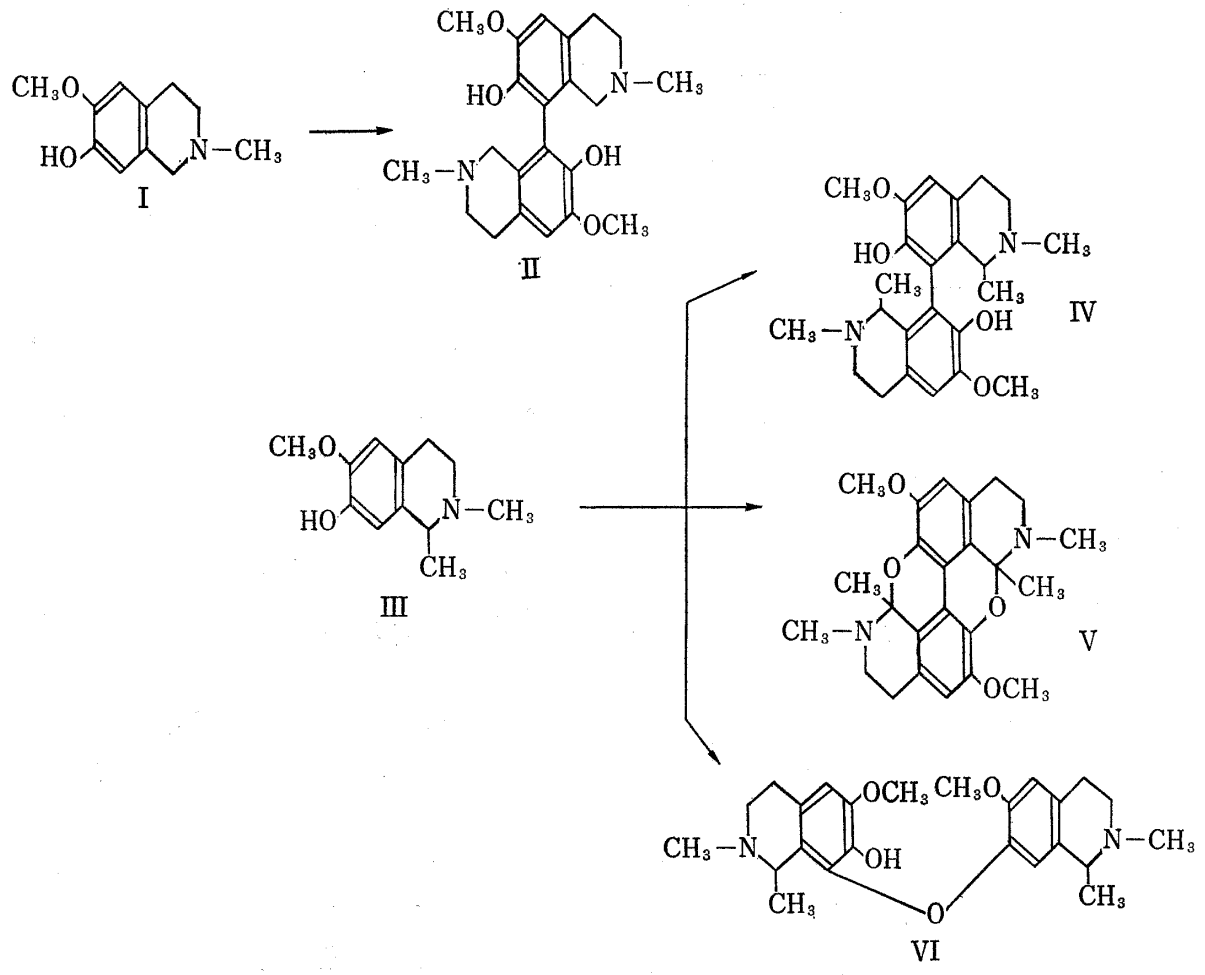


Chart 1

not diastereoisomeric mixtures but homogeneous. The authors already noticed that the NMR spectra of diastereoisomeric mixture of the diphenyl ether of this type (*e.g.* VI and its O–methyl ether) show a complicated appearance of N–methyl and O–methyl signal pattern.[1] With the spectra of Base A and A′, these complication could not be found and it was suggested that Base A′(and A) would be one of the diastereoisomers which were expected to be produced in almost equal amounts.

Therefore, it was assumed that the diastereoisomeric counterpart of Base A′ should be separated by the silicic acid chromatograhy and the second fraction with the same *Rf* value with the staring material (VII) was investigated.

The second fraction was methylated with diazomethane and a non–phenolic base (Base B) was obtained together with N,O,O–trimethylcoclaurine, the methylation product of the starting material (VII). The *Rf* value of Base B on TLC was larger than that of Base A, but IR spectrum in chloroform was superimposable with that of Base A. The NMR spectrum of Base B showed five methoxyl and two N–methyl singlets with the different chemical shifts from those of Base A. From these spectral data, it was made clear that Base A and B have the common two dimensional structural formula but they are diastereoisomeric each other. Therefore, it was understood that a dimeric product (Base B′) which is diastereoisomeric with Base A′ has the same *Rf* value on TLC with the starting material (VII).

The phenolic hydroxyl group of Base A′ and B′ should reasonably be placed at 7–position from the reaction mechanism and the NMR spectra of O–methyl derivatives (Base A and B) which showed up–field shift of their newly introduced methoxyl singlets.

The common planar structure of Base A and B were cofirmed by their synthesis through Ullmann condensation between VII and *dl*–8–bromo–N,O,O,–trimethylcoclaurine (VIII).

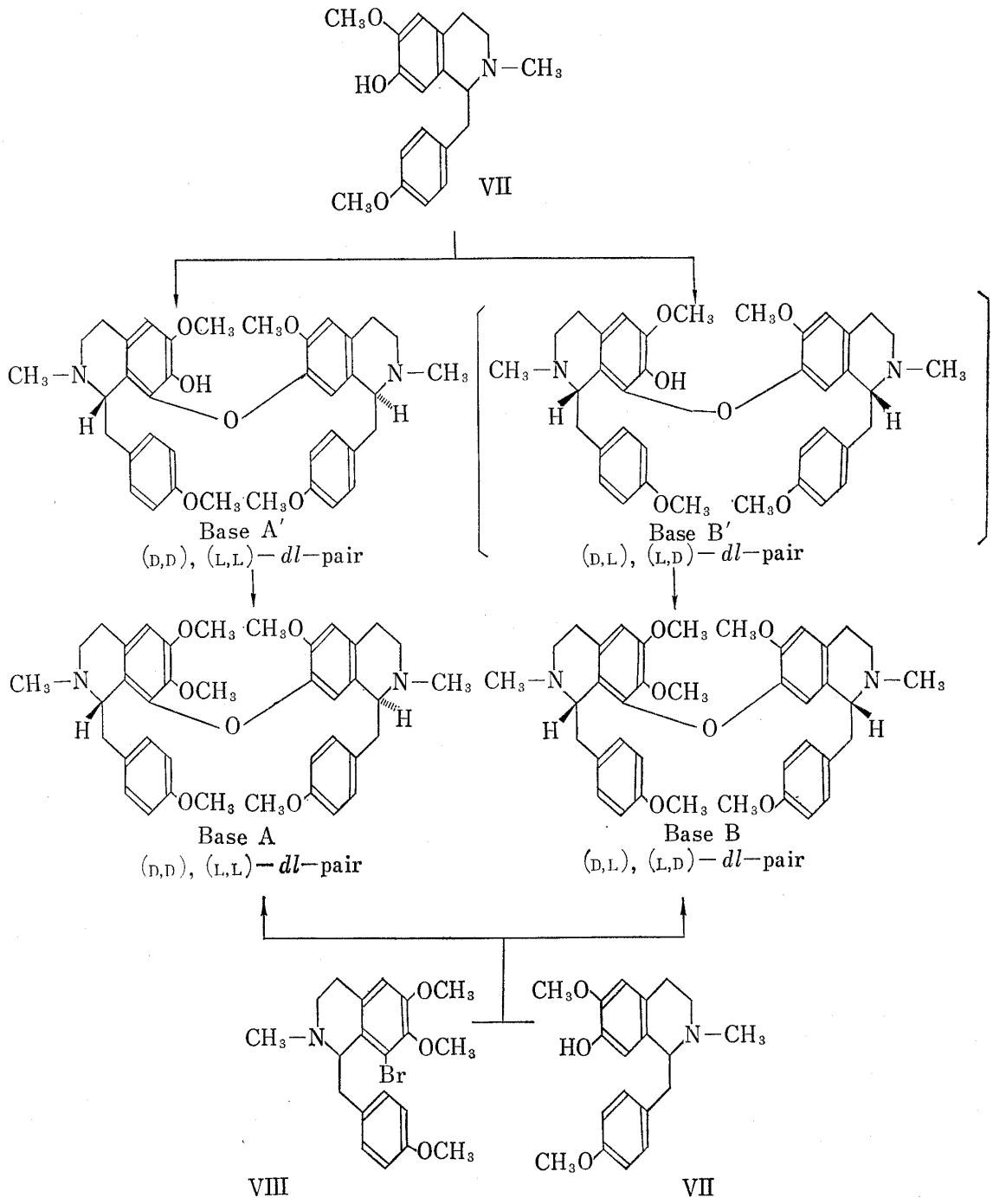
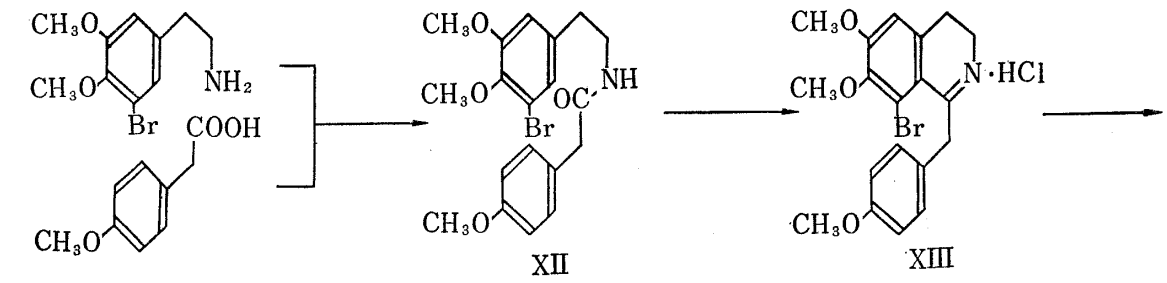


Chart 2

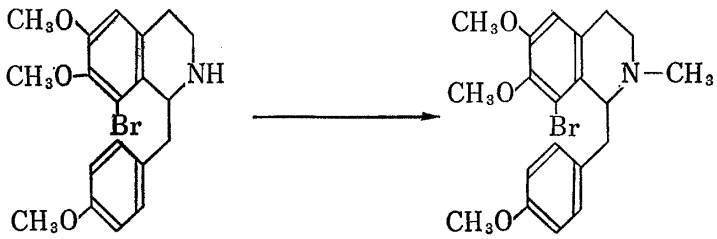
The latter material was prepared by a standard route shown in Chart 3. Ullmann condensation products were identified as Base A and B.

Additionally, the mass spectral data of Base B also gave the structural proof. Although the moelcular ion peak could not be detected, the peaks at *m/e* 396, 198, and 175, corresponding to ions $[M-2X(CH_2\cdot C_6H_4\cdot OCH_3)]^+$, $[M-2X(CH_2\cdot C_6H_4\cdot OCH_3)]^{++}$, and $[M-2X(CH_2\cdot C_6H_4\cdot OCH_3)-(CH_3)-(OCH_3)]^{++}$ respectively were observed, and the fragmentation pattern was found to be of a bisbenzylisoquinoline[4] possessing the diphenyl ether bond between two isoquinoline nuclei.

4) *a*) M. Tomita, T. Kikuchi, K. Fujitani, A. Kato, H. Furukawa, Y. Aoyagi, M. Kitano, and T. Ibuka, *Tetrahedron Letters*, **1966**, 857; *b*) M.P. Cava, D.C. Dejongh, and S.R. Shrader, *J. Am. Chem. Soc.*, **88**, 1052 (1966); *c*) J. Baldas, Q.N. Porter, I.R.C. Bick, and M. Vernengo, *Tetrahedron Letters*, **1966**, 2059.

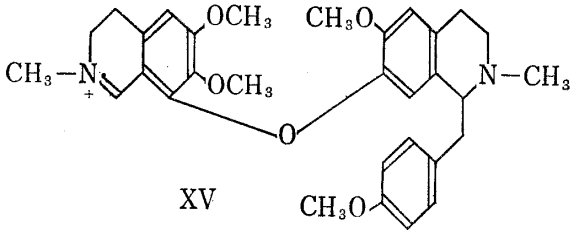


XII XIII

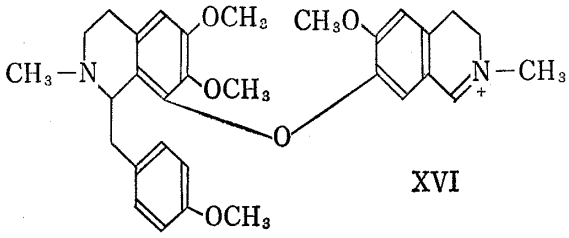


XIV VIII

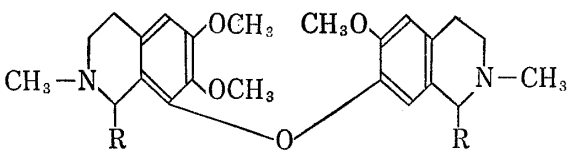
Chart 3



XV

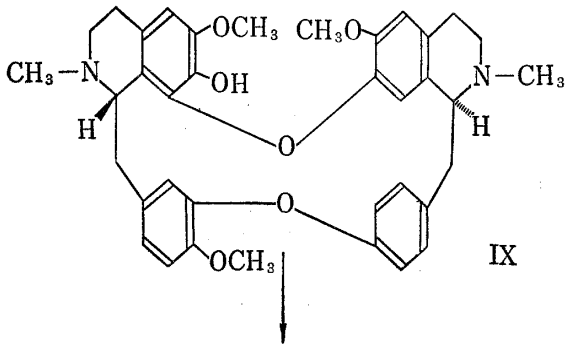


XVI

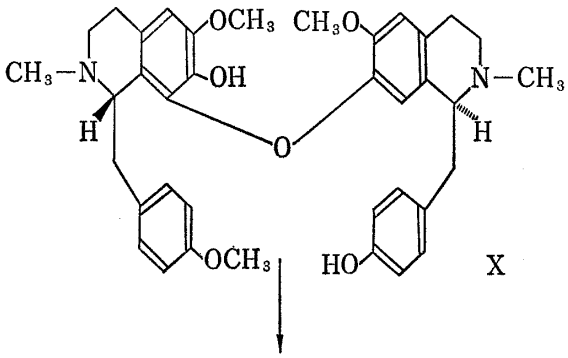


XVII

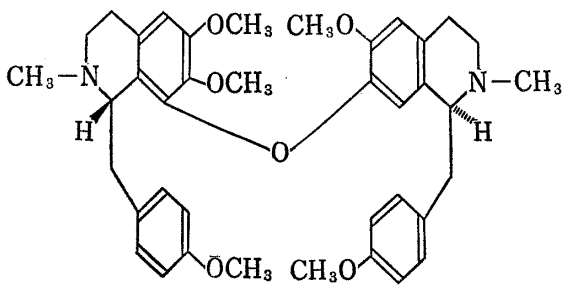
Chart 4



IX



X



XI

Chart 5

In the mass spectrum of Base B, a peak at *m/e* 517 was found to be the base peak, which seems to represent an ion $[M-(CH_2 \cdot C_6H_4 \cdot OCH_3)]^+$. Considering the fact that the reported mass spectra of isopilocereine (XVII, R=isobutyl)[5,6] and VI (XVII, R=methyl)[1] have their base peaks at *m/e* (M–R), the base peak at *m/e* 517 in the mass spectrum of Base B should have the structure XV and/or XVI, and seems to exemplify the characteristic strong intensity of $(M-R)^+$ of the mass spectral fragmentation of a dimeric base with general formula XVII having a diphenyl ether linkage only between two isoquinoline moieties.

From the results stated above, it was made clear that the potassium ferricyanide oxidation of *dl*–4′–O–methyl–N–methylcoclaurine (VII) affords the diphenyl ether derivatives (Base A′ and B′) which are diastereoisomeric each other with the same planar structure and are separable by chromatography.

Previously, Franck and Blaschke[7] reported that the potassium ferricyanide oxidation of *dl*–4′–O–methylmagnocurarine iodide and *dl*–magnocurarine iodide afforded the diphenyl ether derivatives but they did not refer to the stereoisomerism and configuration of the products. In the present study, as shown in Chart 5, the configurations of the products were determined by the chemical correlation with fangchinoline (IX) which has (L,L)–absolute configuration.[8] Frangchinoline (IX) was submitted to the sodium in liquid ammonia reduction to yield a diphenolic base (X) which in turn was methylated with diazomethane to give an optically active methyl ether (XI). The product (XI) and Base A behaved identically on TLC, and their IR ($CHCl_3$) and NMR spectra were found to be superimposable. From the above data, it could be concluded that Base A is a racemate with (D,D)– and (L,L)–configuration on the two asymmetric carbon atoms and consequently Base B would be (D,L)– and (L,D)–racemate.

Although the diphenyl ether formation from quaternary *dl*–4′–O–methyl magnocurarine iodide by oxidative coupling was already reported,[7] the present results seem to add an additional demonstration, as with the cases of reported oxidations of corypalline (I),[3] lophocerine,[5,9] reticuline[10] and its derivatives,[11,12] to the assumption that it would not always be necessary to quaternize the nitrogen atom in order to prevent the amine oxidations in the phenol oxidative coupling of isoquinoline bases.

Experimental[13]

***dl*-7-O-Benzyl-4′-O-methyl-N-methylcoclaurine**——To a solution of *dl*–7–O–benzyl–4′–O–methylcoclaurine[14] (13 g) in 250 ml of MeOH, formalin (3.5 g) was added dropwise at room temperature with stirring. After the mixture was stirring for 30 min, $NaBH_4$ (2 g) was added in samll portions to the reaction mixture at room temperature with stirring. Stirring was continued for additional 30 min, and the solvent was evaporated off *in vacuo*. To the residue was added 2% aq. NaOH and the liberated base was extracted with ether. The ethereal layer was dried over anhyd. K_2CO_3, and the solvent was evaporated to give an oily base (13 g). NMR ($CDCl_3$) τ: 2.70 (s. 5H, arom. H), 2.95—3.33 (A_2B_2 quartet, $J=9$ cps, 4H, arom. H),

5) B. Franck, G. Blaschke, and K. Lewejohann, *Ann.*, **685**, 207 (1965).
6) H. Budzikiewicz, C. Djerassi, and D.H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden–Day Inc., San Francisco, 1964, p. 173.
7) B. Franck and G. Blaschke, *Ann.*, **668**, 145 (1963).
8) The configurational symbols, D and L, in this paper correspond to Cahn–Ingold–Prelog's symbolism, R and S; that is D=R and L=S.
9) J.M. Bobbitt, R. Ebermann, and M. Schubert, *Tetrahedron Letters*, **1963**, 575.
10) W. Wan–Chiu Chan and P. Maitland, *J. Chem. Soc.* (C), **1966**, 753.
11) Sem M. Albonico, A.M. Kuck, and V. Deulofeu, *Ann.*, **685**, 200 (1965).
12) A.H. Jackson and J.A. Martin, *J. Chem. Soc.* (C), **1966**, 2061.
13) The melting points were determined on a Yanagimoto Micro Melting Point Apparatus and uncorrected. NMR spectra were taken on a Varian A–60 recording spectrometer in $CDCl_3$ with TMS as an internal standard. Chemical shifts are presented in τ values. Mass spectra were measured on a Hitachi Mass Spectrometer model RMU–6D.
14) M. Tomita, K. Nakaguchi, and S. Takagi, *Yakugaku Zasshi*, **70**, 152 (1950).

3.43 (s. 1H, arom. H), 3.88 (s. 1H, arom. H), 5.18 (s. 2H, $-CH_2-Ar$), 6.18 (s. 3H, OCH_3), 6.27 (s. 3H, OCH_3), 7.52 (s. 3H, NCH_3). From EtOH the base oxalate crystallized. Recrystallization from EtOH gave colorless microcrystal, mp 149°. *Anal.* Calcd. for $C_{26}H_{29}O_3N \cdot C_2H_2O_4 \cdot \frac{1}{2}H_2O$: C, 66.92; H, 6.43. Found: C, 66.40; H, 6.65.

***dl*-4′-O-Methyl-N-methylcoclaurine (VII)**——*dl*-7-O-Benzyl-4′-O-methyl-N-methylcoclaurine (13 g) was submitted to catalytic hydrogenation in EtOH (250 ml) over palladised charcoal catalyst (prepared from 20 ml of 1% $PdCl_2$ solution and 2g of active charcoal (Darco G 60)) under atmospheric pressure at room temperature. After uptake of hydrogen ceased, the catalyst was filtered off. The filtrate was treated by usual manner, and phenolic base was extracted with ether. The ethereal extract was dried over anhyd. K_2CO_3, and the solvent was evaporated to give an oily base (10 g), which crystallized after standing for several days. Recrystallization from benzene–ether (1:1) gave colorless prisms, mp 55—58°. The melting point of the base rose 88—89° on drying at 30° for 8 hr *in vacuo* (lit.[15]: colorless oil). *Anal.* Calcd. for $C_{19}H_{23}O_3N$: C, 72.82; H, 7.40. Found: C, 72.98; H, 7.63. IR ($CHCl_3$) cm^{-1}: ν_{OH} 3540. NMR ($CDCl_3$): superimposable on that of D-(−)-4′-O-methyl-N-methylcoclaruine.[16]

Potassium Ferricyanide Oxidation of *dl*-4′-O-Methyl-N-methylcoclaurine(VII), Fromation of 1-(4-Methoxybenzyl)-7-hydroxy-6-methoxy-2-methyl-8-[1(4-methoxybenzyl)-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yloxy]-1,2,3,4-tetrahydroisoquinoline (Base A′ and B′)—A mixture of the solution of *dl*-4′-O-methyl-N-methylcoclaurine (VII) (2.5 g) in $CHCl_3$ (200 ml) and the solution (pH 11.40) of $K_3Fe(CN)_6$ (5 g) in 0.1 N Na_2CO_3 (500 ml) was vigorously stirred for 6 hr at 15—17°. The $CHCl_3$ layer was separated and shaken with 2% HCl. The acidic aqueous layer was made alkaline with NH_4OH and the liberated base was extracted with ether. The ethereal layer was dried over anhyd. K_2CO_3 and the solvent was evaporated to give an amorphous powder (1.2 g). The product showed two spots on TLC.[17] One had the same *Rf* value as the starting material (VII) and the other had a smaller *Rf* value than VII. The crude basic product was separated to two fractions by silica gel column chromatography[18]; One(300 mg) was found to show the same behavior as VII on TLC, and the other (Base A′, 208 mg), which was obtained as an amorphous powder, showed single spot on TLC with smaller *Rf* value than VII. Base A′: IR ($CHCl_3$) cm^{-1}: ν_{OH} 3520. NMR ($CDCl_3$) τ: 6.10 (s. 3H, OCH_3), 6.11 (s. 3H, OCH_3), 6.28 (s. 6H, 2XOCH_3), 7.57 (s. 3H, NCH_3), 7.88 (s. 3H, NCH_3). Base B′ was not isolated in a pure state, but *Rf* value on TLC was the same with that of VII; the yield was about equal with that of Base A′. These were proved by the O-methylation described below.

1-(4-Methoxybenzyl)-6,7-dimethoxy-2-methyl-8-[1-(4-methoxybenzyl)-6-mtehoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yloxy]-1,2,3,4-tetrahydroisoquinoline (Base A and Base B)——i) Base A, (D,D), (L,L)-*dl*-pair: To the solution of Base A′ (50 mg) in MeOH (2 ml) and ether (20 ml), excess CH_2N_2-ether was added and the mixture was stood over night at room temperature. The reaction mixture was worked up in usual manner and the non-phenolic base was extracted with ether. The ethereal extract was dried over anhyd. K_2CO_3 and the solvent was evaporated to give a faint yellow oily base (Base A, 40 mg). NMR ($CDCl_3$) τ: 6.08 (s. 3H, OCH_3), 6.11 (s. 3H, OCH_3), 6.25 (s. 3H, OCH_3), 6.28 (s. 3H, OCH_3), 6.33 (s. 3H, OCH_3), 7.57 (s. 3H, NCH_3), 7.83 (s. 3H, NCH_3).

ii) Baes B, (D,L), (L,D)-*dl*-pair: The fraction (300 mg) showing the same behavior as VII on TLC, which was obtained in the chromatographical isolation of Base A′, was O-methylated by an analogous procedure with Base A′. The obtained crude non-phenolic base showed on TLC a main spot, which moved slower than N,O,O-trimethylcoclaurine and faster than Base A, and a spot corresponding to N,O,O-trimethylcoclaurine as impurity. The crude non-phenolic base was dissolved in $CHCl_3$ and shaken with 1% HCl. The acidic aqueous layer was made alkaline with dil. NaOH and the liberated base was extracted with ether. The ethereal layer was dried over anhyd. K_2CO_3 and the solvent was evaporated to give a faint yellow oily base (Base B, 170 mg), which showed on TLC a single spot different from N,O,O-trimethylcoclaurine produced by O-methylation of the starting materials (VII) and from Base A. The IR ($CHCl_3$) spectrum of Base B was found to be superimposable on that of Base A. Mass spectrum *m/e*: 517 (base peak), 396, 381, 206, 198, 175. NMR ($CDCl_3$) τ: 6.08 (s. 3H, OCH_3), 6.11 (s. 3H, OCH_3), 6.23 (s. 3H, OCH_3), 6.27 (s. 3H, OCH_3), 6.30 (s. 3H, OCH_3), 7.61 (s. 3H, NCH_3), 7.78 (s. 3H, NCH_3).

N-(β-3-Bromo-4,5-dimethoxyphenethyl)-4-methoxyphenylacetamide (XII)——A mixture of β-3-bromo-4,5-dimethoxyphenethylamine (10 g), *p*-methoxyphenyl acetic acid (7 g), and decalin (100 ml) was refluxed for 1 hr. After cooling the reaction mixture, decalin was decanted off, and the residual crude crystals was dissolved in $CHCl_3$. The chloroform extract was washed successivley with 2% HCl and 2% NaOH. Evaporation of the solvent after drying over anhyd. K_2CO_3 gave crude crystalline product (15 g). Recrystallization

15) H. Yamaguchi, *Yakugaku Zasshi*, **78**, 692 (1958).
16) M. Tomita, T. Shingu, K. Fujitani, and H. Furukawa, *Chem. Pharm. Bull.* (Tokyo), **13**, 921 (1965).
17) Thin-layer chromatography: Silica Gel G acc. to Sthal (E. Merck), MeOH–acetone (1:1) and Aluminium oxide G acc. to Sthal (E. Merck), $CHCl_3$–acetone (1:1), spots were adetected with iodine vapor and Dragendorff's reagent.
18) Silicic acid (Mallinckrodt Chemical Works), gradient elution system (from $CHCl_3$ to $CHCl_3$–acetone).

from MeOH gave colorless microcrystal, mp 101—102° (13 g). *Anal.* Calcd. for $C_{19}H_{22}O_4NBr$: C, 55.88; H, 5.43. Found: C, 55.99; H, 5.72. IR ($CHCl_3$) cm^{-1}: ν_{CO} 1660.

***dl*-8-Bromo-O,O-dimethylcoclaurine (XIV)**——A mixture of the amide (XII) (13 g), anhyd. toluene (100 ml), and $POCl_3$ (25 g) was refluxed for 2.5 hr. Excess of $POCl_3$ and toluene was removed off *in vacuo*, and the residue was dissolved in dil. HCl. After the solution was washed with ether the acidic aqueous layer was shaken with $CHCl_3$. The chloroform layer was dried over anhyd. $MgSO_4$, and the solvent was evaporated off to give crude oily 1-*p*-methoxybenzyl-8-bromo-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (XIII). To the solution of crude XIII in MeOH (200 ml), $NaBH_4$ (5 g) was added in small portions at room temperature with stirring. After the addition of $NaBH_4$, the mixture was stirring for additional 30 min. MeOH was removed off *in vacuo*, and the residue was extracted with ether after addition of aq. NaOH solution. Drying over anhyd. K_2CO_3 and evaporation of ether gave crude oily base (10 g). Recrystallization of the base oxalate from EtOH afforded colorless prisms, mp 185° (7 g). *Anal.* Calcd. for $C_{19}H_{22}O_3NBr \cdot \frac{1}{2}C_2H_2O_4 \cdot \frac{1}{4}H_2O$: C, 54.37; H, 5.36. Found: C, 54.37; H, 5.36.

***dl*-8-Bromo-N,O,O-trimethylcoclaurine (VIII)**——To a solution of XIV (6 g) in MeOH (100 ml), formalin (2.5 g) was added dropwise at room temperature with stirring and the mixture was stirred for additional 30 min. $NaBH_4$ (1.5 g) was then added in small portions to the mixture at room temperature with stirring. After the addition of $NaBH_4$, the mixture was stirred for 30 min. The solvent was evaporated off *in vacuo* and dil. NaOH was added to the residue. The liberated basic substance was extracted with ether. The ethereal layer was dried over anhyd. K_2CO_3 and the solvent was evaporated off to give crude crystal (6 g). Recrystallization from MeOH gave colorless prisms, mp 82—84°. *Anal.* Calcd. for $C_{20}H_{24}O_3NBr$: C, 59.11; H, 5.96. Found: C, 58.81; H, 6.17.

Ullman Condensation between *dl*-4′-O-Methyl-N-methylcoclaurine (VII) and *dl*-8-Bromo-N,O,O-trimethylcoclaurine (VIII). (Synthesis of Base A and Base B)——To the mixture of *dl*-4′-O-methyl-N-methylcoclaurine (VII) (1 g), *dl*-8-bromo-N,O,O-trimethylcoclaurine (VIII) (1 g), pyridine (6 ml), and anhyd. K_2CO_3 (1.5 g) was added CuO (500 mg) with stirring at 140° (oil bath) under N_2 stream. The mixture was refluxed for 4.5 hr with stirring at 140—150° under N_2 stream. After the completion of the reaction, $CHCl_3$ was added to the reaction mixture, and insoluble material was filetred off. The residue left after evaporation of the filtrate to dryness *in vacuo* was dissolved in $CHCl_3$, and the $CHCl_3$ solution was shaken with 2% HCl. The acidic aqueous layer was made alkaline with dil. NaOH and the liberated base was extracted with ether. The etheral extract was dried over anhyd. K_2CO_3 and the solvent was evaporated off to give crude oily non-phenolic base (750 mg), which showed two spots on TLC in about the ratio 1:1. The column chromatographical separation of the product on aluminium oxide[19] gave two basic substances in pure state, one was identified with Base A by TLC, and IR ($CHCl_3$) and NMR ($CDCl_3$) spectral comparisons; and the other with Base B by TLC and on the spectral data. The yields of Base A and Base B were 110 mg and 150 mg respectively.

Cleavage of Fangchinoline (IX) with Sodium in Liq. Ammonia (Formation of Diphenolic Base (X))——Metallic sodium (150 mg) and the solution of fangchinoline (IX) (250 mg) in anhyd. ether (50 ml) and anhyd. toluene (15 ml) was added alternately in small portions into the mixture of liq. NH_3 (250 ml) and anhyd. ether (50 ml) with stirring at −65°. After 2 hr, excess of metallic sodium was decomposed by adding crystalline NH_4Cl until the blue color of the reaction mixture disappears. The reaction mixture was allowed to stand overnight to evaporate ammonia. To the residue, dil. NaOH was added and the mixture was washed with ether. The alkaline aqueous layer was made ammoniacal with NH_4Cl to liberate the phenolic base. The liberated phenolic base was extracted with ether. The ethereal extract was dried ovr anhyd. K_2CO_3 and the solvent was evaporated to give crude crystal (160 mg). Recrystallization from EtOH gave colorless prisms, mp 110°, $[\alpha]_D^{18}$ −52.5° ($c=2$, in $CHCl_3$). *Anal.* Calcd. for $C_{37}H_{42}O_6N_2 \cdot H_2O$: C, 70.68; H, 7.05. Found: C, 70.48; H, 7.06. NMR ($CDCl_3$) τ: 6.10 (s. 3H, OCH_3), 6.13 (s. 3H, OCH_3), 6.28 (s. 3H, OCH_3), 7.57 (s. 3H, NCH_3), 7.90 (s. 3H, NCH_3).

O-Methylation of the Diphenolic Base (X) (Formation of XI)——Diphenolic base (X) (70 mg) was O-methylated in a mixture of MeOH (4 ml) and ether (20 ml) with CH_2N_2-ether, and a non-phenolic base was obtained as colorless oil (40 mg). $[\alpha]_D^{21}$ −29° ($c=1$, $CHCl_3$). This non-phenolic base was superimposable with Base A on TLC and in IR ($CHCl_3$) and NMR ($CDCl_3$) spectra.

Acknowledgement The authors wish to acknowledge Dr. T. Sningu for taking NMR spectra, A. Kato for mass measurements. They are also indebted to the members of Microanalytical Center of his University for elemental analysis.

19) Aluminium oxide standardized acc. to Brockmann, gradient elution system (from benzene to benzene–ether).