Recrystallization from EtOH gave 30 mg of colorless needles, mp 89°, $[\alpha]_D$ $+106°$ ($c=0.0214$, $l=1$, EtOH) (lit.[3] mp 89°, $[\alpha]_D$ $+104°$ (EtOH)). Mixed melting point with a sample of L-laudanosine did not depress. IR ($CHCl_3$) spectra were also identical.

Acknowledgement The authors wish to thank Professors M. Tomita of Kyoto College of Pharmacy and T. Ikeda of Mukogawa Women's University for their interest in this work. They are also indebted to Professor F.R. Stermitz of Utah State University for the sample of natural romneine hydrobromide, to Dr. T. Shingu of Kyoto University for NMR measurements, and to Miss A. Sakamoto of Mukogawa Women's University for elemental analyses.

[Chem. Pharm. Bull. 16(2) 367—370 (1968)]

UDC 547.831.2.04.07

Chichibabin Reaction. III.[1] Chichibabin Reaction of 7-Methylquinoline and Migration of the Methyl Group in Friedel-Crafts Reaction of N-(*m*-Tolyl)- and N-(*p*-Tolyl)-β-chloropropionamide (Studies on the Syntheses of Heterocyclic Compounds. CCXV[2])

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(Received May 2, 1957)

In the previous paper,[1] it has been reported that the Chichibabin reaction of 8-methylquinoline (I) in dimethylaniline with sodium amide afforded our expected abnormal product, namely, 2-amino-3,4-dihydro-8-methylquinoline (II) as in case of the Chichibabin reaction of quinoline.[4] Furthermore, the formation of 3,4-dihydro-5-methylcarbostyril (III) besides the normal product, 3,4-dihydro-8-methylcarbostyril was observed by the migration of methyl group in case of Friedel-Crafts reaction of N-(*o*-tolyl)-β-chloropropionamide with aluminum chloride, whose reaction was found to be different from the results reported by Mayer, *et al.*[5]

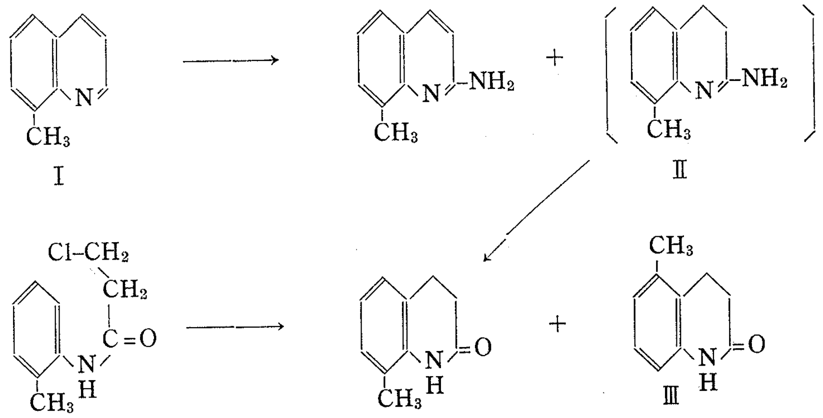

Chart 1

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[1] Part II: T. Kametani and H. Nemoto, *Chem. Pharm. Bull.* (Tokyo), **15**, 1910 (1967).
[2] Part CCXIV: *Chem. Pharm. Bull.* (Tokyo), **16**, 296 (1968).
[3] Location: *Kita-4-bancho, Sendai.*
[4] T. Kametani, K. Kigasawa, Y. Iwabuchi, and T. Hayasaka, *J. Heterocyclic Chem.*, **2**, 330 (1965).
[5] F. Mayer, L. von Zuetphen, and H. Phillips, *Ber.*, **60**, 858 (1927).

The purpose of the present investigation is to study the Chichibabin reaction of 7-methylquinoline (IV) under the same conditions as above and Friedel–Crafts reaction of N-(*m*-tolyl)- and N-(*p*-tolyl)-β-chloropropionamide in order to obtain an authentic sample as an abnormal product formed in case of the above Chichibabin reaction, leading eventually to the formation of the migrated compound (Vb) of methyl group in case of IX.

Recrystallization of the picrate of 7-methylquinoline (IV), which was obtained according to the literature,⁶⁾ was held repeatedly in order to obtain a pure free base (IV) as a starting material. The Chichibabin reaction of IV in dimethylaniline with sodium amide at 120—130° gave our expected 2-amino-3,4-dihydro-7-methylquinoline (Va) as an abnormal product, whose separation was so difficult that its hydrolysis was examined to give 3,4-dihydro-7-methylcarbostyril (Vb), mp 160—161°, as colorless needles in 4.3% yield. In this case attempts to separate a normal product, 2-amino-7-methylquinoline, resulted in failure perhaps due to its poor yield.

In order to characterize the above compound (Vb), an authentic sample was prepared as follows. Oxidation of IV with hydrogen peroxide in acetic acid gave N-oxide (VI), which was tosylated in chloroform with tosyl chloride to give 7-methylcarbostyril (VII). Furthermore, catalytic hydrogenation of VII in the presence of palladium-charcoal afforded colorless needles, mp 160—161°,⁷⁾ which was identical with the above compound (Vb) by mixed melting point test and infrared spectrum. This fact revealed that the formation of 2-amino-3,4-dihydro-7-methylquinoline was recognized in case of the Chichibabin reaction of 7-methylquinoline under the above conditions.

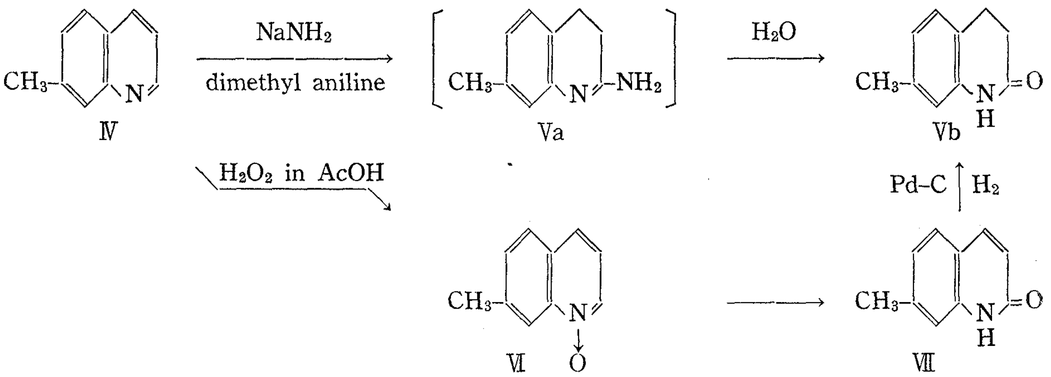

Chart 2

On the other hand, since the abnormal migration of methyl group has been recognized in Friedel–Crafts reaction of N-(*o*-tolyl)-β-chloropropionamide, cyclization of N-(*m*-tolyl)-(VIII) and N-(*p*-tolyl)-β-chloropropionamide (IX) with aluminum chloride under the Mayer's condition was investigated to give the same compound, mp 160—161°. That is, the compound, mp 160—161°, formed in the former case in 63.42% yield, was identical with the substance, which was obtained in the latter case in 50.7% yield, from the point of admixed melting point test and spectral comparison. Furthermore, the infrared spectra (in KBr) of these compounds as above were superimposable on that of the product (Vb) obtained by Chichibabin reaction of IV.

It is obviously reasonable that Friedel–Crafts reaction of VIII affords the expected product (Vb), but the formation of Vb in case of cyclization of IX seems to be abnormal. Perhaps the simplest mechanism to explain the formation of Vb in the latter case would initially involve the cation-formation of cationoid form as (XI) *via* an intermediate (X) and migration of the methy group at C_6-position to C_7-position through methyl anion shift to

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6) L. Brandford, T.J. Elliott, and F.M. Rowe, *J. Chem. Soc.*, **1947**, 437.
7) G.S. Sidhu, G. Thyagarajan, and S. Ansari, *Ann.*, **627**, 218 (1959).

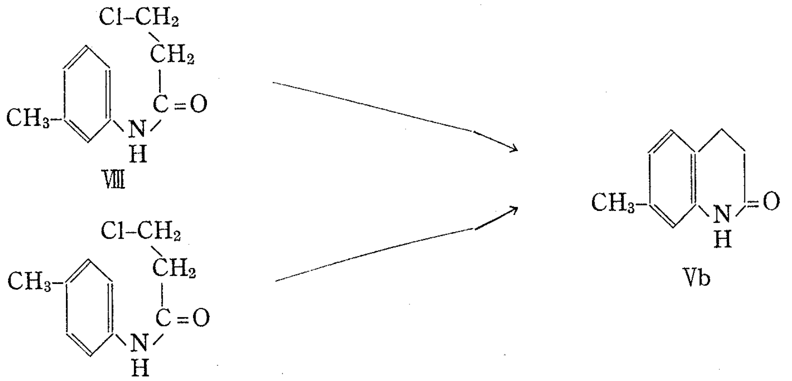

Chart 3

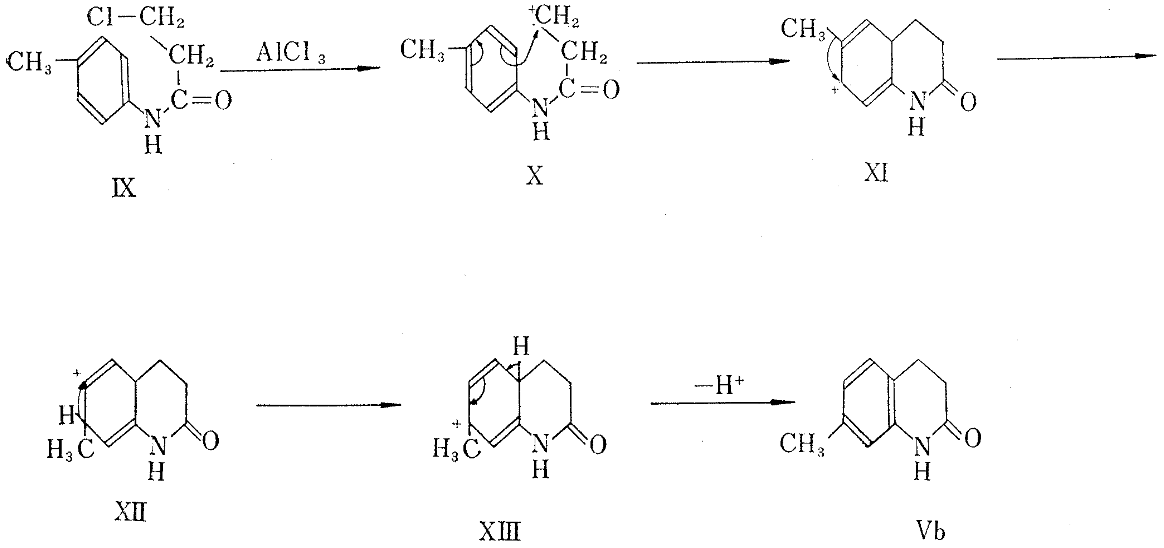

Chart 4

form the intermediate (XII), whose hydride shift from C_7-position to C_6-position, followed by deprotonation, would afford the compound (Vb).

Experimental[8]

The Chichibabin Reaction of 7-Methylquinoline (IV)——A suspension of 3.3 g of $NaNH_2$ in 20 g of dimethylaniline was added dropwise at 120—130° with stirring to 8 g of 7-methylquinoline within 20 min. After the addition, the reaction mixture was stirred for 3 hr, and an excess of water was added to the above mixture, which was heated on a water bath for 3 hr. After cooling, the reaction mixture was extracted with ether. The extract was treated as usual and distilled to give a syrup, which was chromatographed on silica gel using a mixture of benzene, hexane and MeOH (2:2:1) to give dimethylaniline as the first eluate. Removal of the second eluate afforded the solid, whose recrystallization from ether gave 378.2 mg (4.3%) of 3,4-dihydro-7-methylcarbostyril (Vb) as colorless needles, mp 160—161° (lit.,[7] mp 162—163°). *Anal.* Calcd. for $C_{10}H_{11}ON$: C, 74.51; H, 6.88; N, 8.69. Found: C, 75.09; H, 6.79; N, 8.70. IR cm^{-1} (KBr): ν_{NH} 3420, $\nu_{C=O}$ 1680 (amide). NMR (τ) (in $CDCl_3$): 7.72 (3H, singlet, $-C\underline{H}_3$), 6.90—7.55 (4H, multiplet, $C_3\underline{H}_2$-C_4-$\underline{H}_2$), 2.85—3.14 (3H, multiplet, aromatic proton).

7-Methylcarbostyril (VII)——A mixture of 2 g of 7-methylquinoline, 4.2 ml of AcOH, and 1.26 ml of 29% H_2O_2 was then added to the above mixture, which was further heated at 65—70° for 6 hr. Removal of the solvent from the reaction mixture under reduced pressure gave the residue, which was made basic with hot saturated Na_2CO_3 aq. solution and extracted with $CHCl_3$. The extract was treated as usual and distilled to give a syrup which was allowed to stand at room temperature. The crystals precipitated were collected by filtration and washed with on a filter with ether to give 1.1 g of 7-methylquinolin-1-oxide (VI).

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[8] All melting points were not corrected.

To a solution of 1.1 g of the about N-oxide in 6.6 ml of $CHCl_3$ was added 1.3 g of tosyl chloride with occasional shaking, and the mixture was heated under reflux on a water bath for 10 min. After cooling, the reaction mixture was made basic with 10% Na_2CO_3 aq. solution and extracted with $CHCl_3$. The extract was washed with water, dried on Na_2SO_4, and distilled to give the crude solid, whose recrystallization from MeOH gave 520 mg (2.3%) of 7-methylcarbostyril (VII) as colorless needles, mp 190—198° (lit.,[7] mp 198°). *Anal.* Calcd. for $C_{10}H_9ON$: C, 75.43; H, 5.69; N, 8.79. Found: C, 75.49; H, 5.96; N, 8.88. IR cm^{-1} (KBr): ν_{NH} 3390, $\nu_{C=O}$ 1660 (amide).

Catalytic Hydrogenation of 7-Methylcarbostyril (VII)——A mixture of 200 mg of 7-methylcarbostyril (VII) and 20 ml of EtOH was hydrogenated in the presence of 200 mg of 40% Pd-C in a current of H_2, a calculated amount of H_2 being absorbed within 30 hr. Filtration of the catalyst and evaporation of the filtrate gave the solid, which was recrystallized from ether to give 192 mg (95%) of 3,4-dihydro-7-methylcarbostyril (Vb) as colorless needles, mp 160—161°. This compound was identical with the sample formed in case of Chichibabin reaction of IV from the points of admixed melting point test and infrared spectral comparison.

Friedel-Crafts Reaction of N-(*m*-Tolyl)-*β*-chloropropionamide (VIII)——To 5.8 g of VIII heated at 100° was added portionwise with stirring 12 g of $AlCl_3$ within 5 min. After the addition the mixture was stirred at 100° for 3 hr and the resultant mixture was decomposed with water and extracted with ether. The extract was treated as usual and distilled to give 2.98 g (63.42%) of 3,4-dihydro-7-methylcarbostyril (Vb) as colorless needles, mp 160—161°, whose IR spectrum was identical with that of the above sample (Vb).

Friedel-Crafts Reaction of N-(*p*-Tolyl)-*β*-chloropropionamide (IX)——To 6.25 g of fused substance (IX) at 140° was added in small protions with stirring 13 g of $AlCl_3$ within 5 min. After the addition the stirring was continued for 2 hr. The reaction mixture was decomposed with water, treated as usual and extracted with ether. The extract was washed with water, dried on Na_2SO_4, and distilled to afford the solid whose recrystallization from ether gave 2.84 g (50.7%) of Vb as colorless needles, mp 159.5—160.5°. The IR spectrum of this compound was identical with that of the above sample.

Acknowledgement We thank Miss R. Kobayashi and Miss R. Hasebe for microanalyses.

[Chem. Pharm. Bull.
16(2) 370—373 (1968)]

UDC 547.94.04 : 615.783.19-011

Studies on Morphine Alkaloids. III.[1] Indolinocodeine. II. 9*α*-Methoxyindolinocodeine

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(Received May 5, 15)

In a previous paper,[1] we reported that on sodium borohydride reduction of 14*β*-bromocodeinone (I) in aqueous methanol solution, neopine (III), isoneopine (IV), and indolinocodeine (VIa) are produced *via* 14*β*-bromocodeine (II), the first reduction product, and discussed the mechanisms of this rather complicated reaction. The present studies deal with the isolation and characterization of 9*α*-methoxyindolinocodeine (VII), the fourth product of the above reaction.

This product is most nonpolar and eluted first from sillica gel column with pure benzene to furnish colourless needles, mp 139—140° (from methanol), $[\alpha]_D^{20}=+146°$ (c=1.21 in EtOH),

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[1] Part II: S. Okuda, S. Yamaguchi, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **13**, 1092 (1965).

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