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Studies on Tetrahydroisoquinolines. X.*,[1] A Stereospecific Synthesis of (±)-Cataline[2]

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A diastereomeric mixture (IV) obtained previously was separated chromatographically into (±)-4α- and (±)-4β-acetoxy-O-acetylthaliporphine (IVa and IVb).

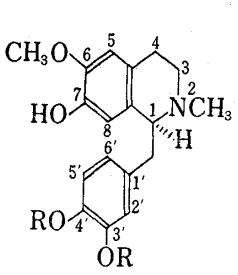
Furthermore, the lead tetraacetate oxidation of (±)-thaliporphine (VII) in acetic acid was found to afford stereospecifically in quantitative yield amorphous (±)-4β-acetoxy-thaliporphine (XI), whose hydrolysis and successive methylation produced (±)-cataline (IX) in overall 86.5% yield.

It has been previously reported that the lead tetraacetate [$(Pb(OAc)_4$] oxidation of (±)-codamine (I)[4,5] or (±)-1,2,3,4-tetrahydro-7-hydroxy-6-methoxy-2-methyl-1-(3′,4′-methylenedioxybenzyl)isoquinoline (II) followed by acid treatment (Ac_2O–conc. H_2SO_4) produces (±)-O-acetylthaliporphine (III)[5] together with diastereomeric mixture of (±)-4-acetoxy-O-acetylthaliporphine (IV)[5] or (±)-O-acetyldomesticine (V),[1] (±)-4α- and (±)-4β-acetoxy-O-acetyldomesticine (VIa and VIb),[1] respectively and that hydrolysis of III or V affords (±)-thaliporphine (VII)[4c,5,6] or (±)-domesticine (VIII).[2,7] In continuation of our studies on the synthesis of aporphine alkaloids, our interest was attracted toward separation of a diastereomeric mixture (IV)[5] into (±)-4α- and (±)-4β-acetoxy-O-acetylthaliporphine (IVa and IVb) and also toward the facile preparation of the latter (IVb) or the related compound, since IVb would be a key compound for the synthesis of (+)-cataline (IX), a new type of 4-hydroxyaporphine, which was recently isolated from *Glaucium flavum* Cr. var. *vestitum* by Ribas, Sueiras, and Castedo.[8] The present paper is concerned with successful separation of two diastereomers (IVa and IVb) and the first stereospecific synthesis of (±)-cataline (IX).

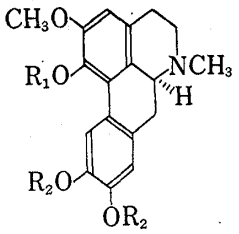
The same treatment with Ac_2O–conc. H_2SO_4 of the *p*-quinol acetate (X) obtained from (±)-codamine (I)[4b] (mp 103—105°) as noted previously[5] gave an amorphous mass, whose purification by preparative thin layer chromatography (TLC) led to three kinds of products (A, B, and C) (their moving rates decreased in the following order; A>B>C). The nuclear magnetic resonance (NMR) spectra of the product (A), mp 195.5—196°, and (B), mp 257—259°

* Dedicated to the memory of Prof. Eiji Ochiai.

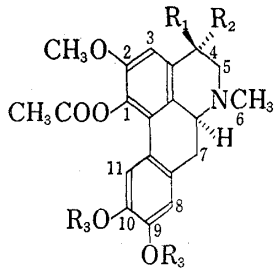
1) Part IX: O. Hoshino, H. Hara, N. Serizawa, and B. Umezawa, *Chem. Pharm. Bull.*(Tokyo),23 2048(1975).
2) The preliminary communication of this work will appear in O. Hoshino, H. Hara, M. Ogawa, and B. Umezawa, *J.C.S. Chem. Commun.*, **1975**, 306.
3) Location: *12, Ichigaya Funagawara-machi, Shinjuku-ku, Tokyo, 162, Japan.*
4) *a*) M. Onda, *Yakugaku Zasshi*, **74**, 931 (1954); *b*) B.K. Cassels and V. Deulafen, *Tetrahedron*, Suppl. **8**, 485 (1966); *c*) M. Shamma and W.A. Slusarchyk, *ibid.*, **23**, 2563 (1967).
5) O. Hoshino, T. Toshioka, and B. Umezawa, *Chem. Commun.*, **1971**, 1533; *idem*, *Chem. Pharm. Bull.* (Tokyo), **22**, 1302 (1974).
6) R.J. Spangler and D.C. Boop, *Tetrahedron Letters*, **1971**, 4851; T. Kametani, S. Shibuya, and S. Kano, *J. Chem. Soc. Perkin I*, **1973**, 1212; S.M. Kupchan and P.F. O'Brien, *J.C.S. Chem. Commun.*, **1973**, 915.
7) T. Kametani, K. Fukumoto, and T. Sugawara, *Tetrahedron Letters*, **1968**, 5459; *idem*, *J. Chem. Soc.* (*C*), **1969**, 801; S.V. Kessar, S. Batra, and S.S. Gandhi, *Indian J. Chem.*, **1970**, 468; T. Kametani, S. Shibuya, H. Sugi, O. Kusano, and K. Fukumoto, *J. Chem. Soc.* (*C*), **1971**, 2446; T. Kametani, S. Shibuya, K. Kigasawa, M. Hiiragi, and O. Kusama, *ibid* (*C*), **1971**, 2712; S.M. Kupchan and A.J. Liepa, *J. Am. Chem. Soc.*, **95**, 4062 (1973).
8) I. Ribas, J. Sueiras, and L. Castedo, *Tetrahedron Letters*, **1972**, 2033.



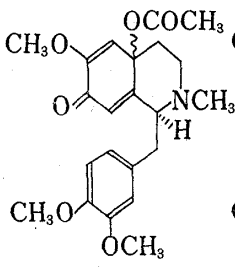
I: $R=CH_3$
II: $R+R=CH_2$



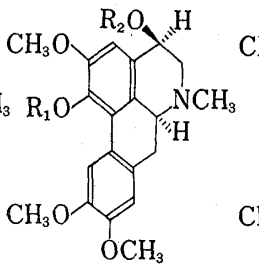
III: $R_1=COCH_3$, $R_2=CH_3$
V: $R_1=COCH_3$, $R_2+R_2=CH_2$
VII: $R_1=H$, $R_2=CH_3$
VIII: $R_1=H$, $R_2+R_2=CH_2$



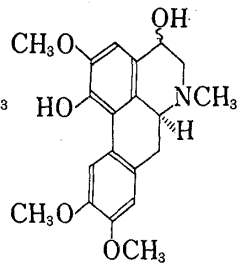
IVa: $R_1=H$, $R_2=OCOCH_3$, $R_3=CH_3$
IVb: $R_1=OCOCH_3$, $R_2=H$, $R_3=CH_3$
VIa: $R_1=H$, $R_2=OCOCH_3$ $R_3+R_3=CH_2$
VIb: $R_1=OCOCH_3$, $R_2=H$, $R_3+R_3=CH_2$



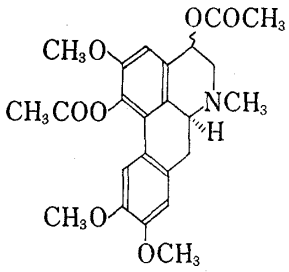
X



IX: $R_1=CH_3$, $R_2=H$
XI: $R_1=H$, $R_2=COCH_3$
XII: $R_1=R_2=H$



XIII



IV

Chart 1

(decomp.), showed one proton double doublet (J=6.3, 10 Hz) at δ 6.13 and one proton broad triplet (half-band width 5.0 Hz) at δ 5.92 due to a hydrogen at 4-position, respectively. Infrared (IR) spectrum of the former (A) exhibited absorption bands for an aromatic and an aliphatic acetoxyl group at 1760 and 1735 cm^{-1}, and IR spectrum of the latter (B) at 1765 and 1725 cm^{-1}. Furthermore, they had the same molecular formula ($C_{24}H_{27}O_7N$) as supported by their mass spectra [m/e: 441 (M^+)] and elemental analyses. Hence, the structures of the product (A) and (B) were proved to be (±)-4α- and (±)-4β-acetoxy-O-acetylthaliporphine [IVa (5% yield) and IVb (8.1% yield)], respectively.

The product (C), mp 156—157°, was identical with (±)-O-acetylthaliporphine (III)[5] (32.4% yield) by comparison of spectral data.

Thus, it was found that a diastereomeric mixture (IV) was separated readily and that IVb possessed the same stereochemical feature as that of (+)-cataline.

On the basis of the above result, moreover, the compound (IV)[5] [mp 236—238° (decomp.)] described previously must be a diastereomeric mixture enriched with IVb, which was eventually less soluble than IVa in the recrystallizing solvent and careful re-inspection of its NMR spectrum revealed that a hydrogen at 4-position appeared at δ 5.98 (half-band width 5.0 Hz) besides δ 6.20 (q, J=7.5, 10 Hz).[9]

The above method was by no means satisfactory for effective preparation of IVb, the key compound leading to (±)-cataline (IX). Therefore, an alternating route to IVb was next investigated. Among others, the direct oxidation of (±)-thaliporphine (VII) was most attractive.

A solution of VII in acetic acid (AcOH) was oxidized with $Pb(OAc)_4$ (1.2 eq.) at room temperature for 0.5 hr and usual work-up of the mixture gave an amorphous mass, whose NMR spectrum showed three proton singlet at δ 2.10 due to an acetoxyl group and one proton broad triplet (half-band width 5.0 Hz) at δ 5.90 due to a hydrogen at 4-position. Its IR spectrum

9) This coupling constant should read (dd, J=6.3, 10 Hz).

exhibited absorption bands due to a hydroxyl and an aliphatic acetoxyl group at 3510 and 1720 cm^{-1}, respectively. Successive acetylation with Ac_2O–pyridine of the amorphous mass, without further purification, gave in 79.2% yield (±)-4β-acetoxy-O-acetylthaliporphine (IVb) as a sole product, which was identical in all respects with an authentic sample obtained above. Hence, the structure of the amorphous product was proved to be (±)-4β-acetoxythaliporphine (XI).

Thus, it was found that XI was formed stereospecifically in good yield from VII.

Accordingly, XI was converted into (±)-cataline (IX) as follows. Namely, hydrolysis of XI in 10% hydrochloric acid at room temperature for 0.5 hr afforded in quantitative yield (±)-4β-hydroxythaliporphine (XII), mp 167—168°, whose NMR spectrum showed one proton broad triplet (half-band width 5.0 Hz) at δ 4.44 due to a hydrogen at 4-position. Furthermore, re-acetylation of XII with Ac_2O–pyridine gave exclusively IVb. Thereupon, acid hydrolysis of XI was proved to proceed without any configurational change of the hydroxyl group at 4-position. Mathylation of XII in methanol with diazomethane–ether (excess) at room temperature (overnight) produced in 86.5% yield (±)-cataline (IX), mp 149—150° (decomp.), which was identical with natural (+)-cataline by comparison of each IR and TLC.

Thus, the first stereospecific synthesis of (±)-cataline (IX) was accomplished from (±)-thaliporphine (VII).

In consideration of the finding that the oxidation of VII led to (±)-4β-acetoxythaliporphine (XI) and of the fact[10] that treatment with trifluoroacetic acid (CF_3COOH) of the *p*-quinol acetate (X) in methylene chloride (CH_2Cl_2) gave VII in a good yield, the similar reaction of (±)-codamine (I) in the presence of CF_3COOH was suggested to give (±)-4-hydroxythaliporphine (XIII). In fact, the oxidation of I in CH_2Cl_2 containing CF_3COOH followed by hydrolysis furnished (±)-4β-hydroxythaliporphine (XII) (20% yield) accompanied with VII (10% yield).

The mechanistic pathway on the formation of XI would be visualized in Chart 2.

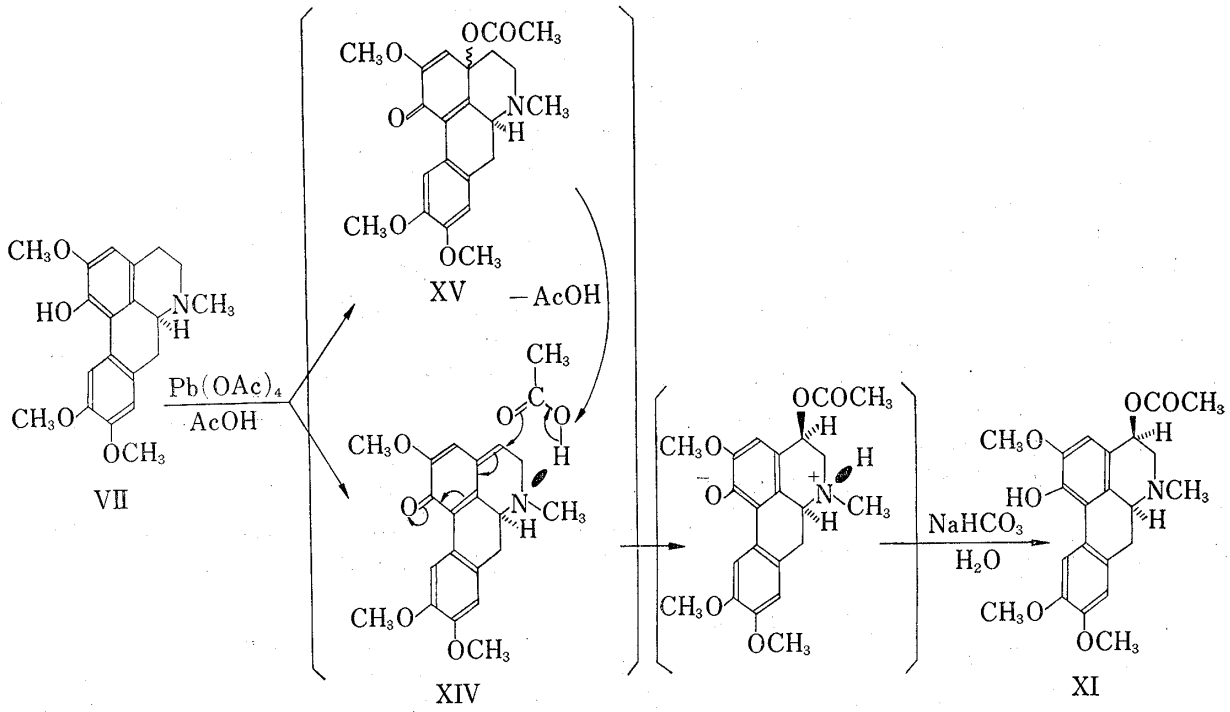


Chart 2

10) H. Hara, O. Hoshino, and B. Umezawa, *Chem. Pharm. Bull.* (Tokyo), "submitted."

Namely, the oxidation of VII would produce a quinone methide (XIV) directly or through the *p*-quinol acetate (XV) and a hydrogen bonded AcOH to nitrogen atom would make an attack on a carbon at 4-position leading to XI. This explanation found its closely related precedent as the Henbest rule[11] in epoxidation of cyclic allyl alcohols.

On the other hand, from the finding that the oxidation of I led to the *p*-quinol acetate (X) exclusively, the 4-acetoxyaporphine (IV) was undoubtedly formed through the *p*-quinol acetate (X). Accordingly, the formation of IV would be picturized in Chart 3.

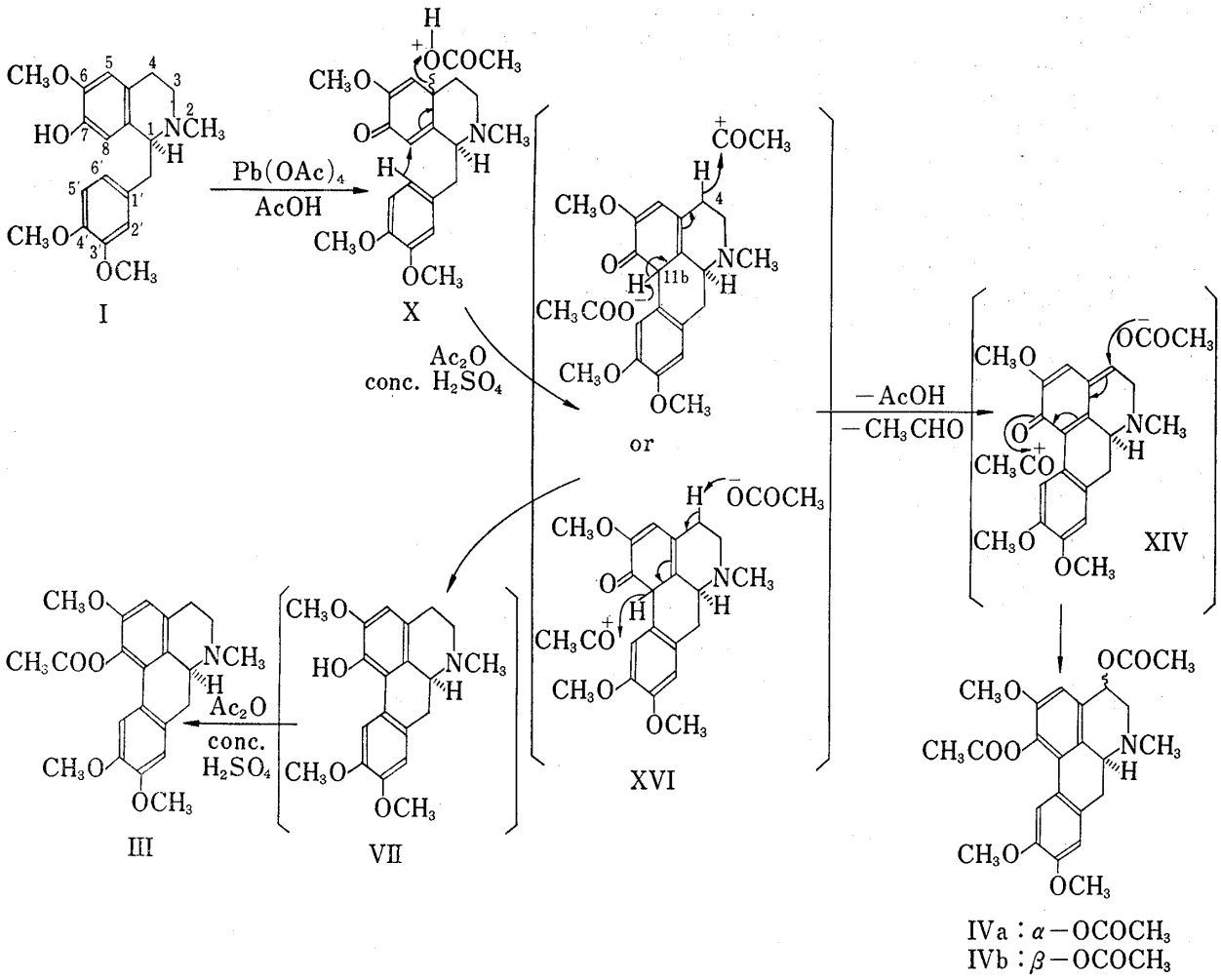


Chart 3

Firstly, detachment of an acetoxyl group followed by carbon-carbon bond formation at 8- and 6′-position would furnish an intermediate (XVI). Secondly, abstraction of ahydrogen at 4- or 11b-position and concerted deprotonation by acetylium and acetoxy ions would take place leading to the quinone methide (XIV). Finally, acetylation and acetoxylation of XIV with the foregoing ions would give rise to the 4-acetoxy products.

Moreover, the formation of (±)-O-acetylthaliporphine (III)[5] would be reasonably interpreted by assuming acetylation of (±)-thaliporphine (VII) formed probably from the intermediate (XVI). This assumption would be supported also by the finding that the oxidation of I in the presence of CF_3COOH gave VII and XII, respectively.

Contrary to the stereospecific formation of XI, however, the reason for the formation of IVa and IVb was mechanistically uncertain.

Further mechanistic details on the formation of 4-acetoxyaporphines are in progress.

11) H.B. Hembest and R.A.I. Wilson, *J. Chem. Soc.*, **1957**, 1958.

Experimental[12]

(±)-Codamine (I)——A mixture of (±)-O-benzylcodamine[4a,c,5] (4.33 g), 2% $PdCl_2$ (7.0 ml), and active carbon (0.5 g) in CH_3OH (100 ml) was shaken in an atmosphere of H_2 at room tempt., until uptake of H_2 ceased. After filtration of catalyst, removal of the solvent gave an oily residue, to which was added conc. NH_4OH, and the product was taken up in ether. The ether extract was washed with brine and dried over anhydrous K_2CO_3. Removal of the solvent led to an amorphous mass (I) (3.21 g, 93.6%), which was recrystallized from ether affording colorless prisms (2.95 g, 86%), mp 97—99°, and an analytical sample had mp 103—105° (lit.[4b] mp 106—108°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3525 (OH). *Anal.* Calcd. for $C_{20}H_{25}O_4N$: C, 69.95; H, 7.33; N, 4.08. Found: C, 69.84; H, 7.29; N, 3.91.

(±)-4α- and (±)-4β-Acetoxy-O-acetylthaliporphine (IVa and IVb), and (±)-O-Acetylthaliporphine (III)——To a stirred solution of I (500 mg, 1.46 mmoles) in AcOH (10 ml) was added in one portion $Pb(OAc)_4$ (775 mg, 1.75 mmoles) at room tempt. and stirring was continued at the same tempt. for 0.5 hr. The same work-up of the mixture as described previously[5] gave a crude *p*-quinol acetate (X) (582 mg). To an ice-cooled, stirred solution of the *p*-quinol acetate (X) (582 mg) in Ac_2O (5 ml) was added dropwise a mixture of conc. H_2SO_4 (0.2 g) in Ac_2O (0.4 ml) over a period of 10 min and the whole was stirred at room tempt. for 1 hr. The mixture was poured into ice-water and washed ether. The acidic solution was basified carefully with $NaHCO_3$ (powder) and the product was taken up in ether. The ether extract was washed with brine and dried over anhydrous K_2CO_3. Evaporation of the solvent gave an amorphous mass (383 mg), which was purified by preparative TLC (developing solvent; benzene–ethyl acetate (3:5)] giving three kinds of products (A, B, and C) (their moving rates decreased in the following order; A>B>C). Elution of the absorbent for the product (A) with $CHCl_3$–CH_3OH (10:1) produced (±)-4α-acetoxy-O-acetylthaliphorphine (IVa) (32 mg, 5.0%), mp 180—187°, which was recrystallized from ether affording colorless prisms (19 mg, 3.0%), mp 191—193°, and an analytical sample had mp 195.5—196°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (arom. $OCOCH_3$), 1735 (aliph. $OCOCH_3$). NMR δ: 2.13, 2.29 (each 3H, s, 2×$OCOCH_3$), 2.51 (3H, s, NCH_3), 3.80, 3.86, 3.87 (each 3H, s, 3×OCH_3), 6.13 (1H, dd, J=6.3, 10 Hz, 4-H), 6.79 (2H, s, 2×arom. H), 7.54 (1H, s, 11-H). *Anal.* Calcd. for $C_{24}H_{27}O_7N$ (mol. wt.=441.46): C, 65.29; H, 6.16; N, 3.17. Found: C, 65.51; H, 6.19; N, 3.19. Mass Spectrum *m/e*: 441 (M^+). The same work-up of the absorbent for the product (B) as noted above afforded (±)-4β-acetoxy-O-acetylthaliporphine (IVb) (52 mg, 8.1%), mp 240—243° (decomp.), which was recrystallized from benzene–*n*-hexane yielding colorless prisms (42 mg, 6.5%), 247—249° (decomp.), and an analytical sample had mp 257—259° (decomp.). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 (arom. $OCOCH_3$), 1725 (aliph. $OCOCH_3$). NMR δ: 2.14, 2.29 (each 3H, s, 2×$OCOCH_3$), 2.51 (3H, s, NCH_3), 3.80, 3.86, 3.88 (each 3H, s, 3×OCH_3), 5.92 (1H, bt, $W1/2$=5.0 Hz, 4-H), 6.80, 6.89 (each 1H, s, 2×arom. H), 7.53 (1H, s, 11-H). *Anal.* Calcd. for $C_{24}H_{27}O_7N$ (mol. wt.=441.46): C, 65.29; H, 6.16; N, 3.17. Found: C, 65.45; H, 6.22; N, 3.24. Mass Spectrum *m/e*: 441 (M^+). The same work-up of the absorbent for the product (C) as noted above furnished (±)-O-acetylthaliporphine (III) (181 mg, 32.4%), mp 147—150°, which was recrystallized from benzene–*n*-hexane leading to colorless prisms (146 mg, 26.2%), mp 156—157°. It was identical in all respects with an authentic sample.[5]

$Pb(OAc)_4$ Oxidation of (±)-Thaliporphine (VII)——To a stirred solution of VII (100 mg, 0.293 mmole) in AcOH (2 ml) was added in one portion the oxidant (156 mg, 0.352 mmole) at room tempt. and the whole was stirred at the same tempt. for 0.5 hr. The acidic solution obtained on addition of the mixture into ice-water was carefully basified with $NaHCO_3$ (powder) and the product was taken up in $CHCl_3$. The $CHCl_3$ extract was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent gave a dark brown amorphous (±)-4β-acetoxythaliporphine (XI) (117 mg, quantitative yield) [(IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3510 (OH), 1720 ($OCOCH_3$); NMR δ: 2.10 (3H, s, $OCOCH_3$), 2.55 (3H, s, NCH_3), 3.87 (6H, s, 2×OCH_3), 3.91 (3H, s, OCH_3), 5.90 (1H, bt, $W1/2$=5.0 Hz, 4-H), 6.80 (2H, s, 2×arom. H), 8.08 (1H, s, 11-H)], which was treated with Ac_2O (1.5 ml) and pyridine (3 ml) at room tempt. overnight, The mixture was basified with 5% $NaHCO_3$ and the product was taken up in ether. The ether extract was washed with 10% $CuSO_4$ and brine, and dried over anhydrous K_2CO_3. Removal of the solvent gave (±)-4β-acetoxy-O-acetylthaliporphine (IVb) (103 mg, 79.2%), mp 231—233° (decomp.), which was recrystallized from benzene–*n*-hexane yielding pale yellow needles (82 mg, 63%), mp 256—257° (decomp.). It was identical in all respects with an authentic sample obtained above.

(±)-4β-Hydroxythaliporphine (XII)——The same treatment of VII (200 mg, 0.587 mmole) and the oxidant (312 mg, 0.704 mmole) in AcOH (4 ml) as described above afforded (±)-4β-acetoxythaliporphine

12) All melting points were uncorrected and measured on a Büchi melting point measuring apparatus. NMR spectra were taken with a JEOL Model JNR-4H-100 spectrometer (100 MHz) in $CDCl_3$ solution (5—10%) by using $(CH_3)_4Si$ as internal standard. Following abbreviations were used; s: singlet; dd: double doublets; bt: broad triplet; $W1/2$: half-band width. IR spectra were measured with a Hitachi Model 215 spectrometer, unless otherwise noted. Mass spectra were taken with a Hitachi Model RMU-7M mass spectrometer. UV spectrum was measured on a Hitachi Model 323 spectrometer. Preparative thin-layer chromatographies were performed over Silica gel GF_{254} (Merck).

(XI) (290 mg, quantitative yield), to which was added 10% HCl (40 ml) and the whole was stirred at room tempt. for 0.5 hr. The mixture was basified with $NaHCO_3$ (powder) and the product was taken up in ether. The ether extract was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent produced (±)-4β-hydroxythaliporphine (XII) (213 mg, quantitative yield), mp 148—149° (decomp.), which was recrystallized from benzene–*n*-hexane giving pale brown needles (155 mg, 73.8%), mp 149—150° (decomp.) and an analytical sample had mp 167—168° (decomp.) (ether). IR[13] ν_{max}^{KBr} cm^{-1}: 3375 (bonded OH). NMR δ: 2.51 (3H, s, NCH_3), 3.86 (3H, s, OCH_3), 3.89 (6H, s, $2\times OCH_3$), 4.44 (1H, bt, $W1/2=5.0$ Hz, 4-H), 6.76, 6.81 (each 1H, s, $2\times$arom. H), 8.06 (1H, s, 11-H). *Anal.* Calcd. for $C_{20}H_{23}O_5N$ (mol. wt.=357.39): C, 67.21; H, 6.49; N, 3.92. Found: C, 66.97; H, 6.62; N, 3.90. Mass Spectrum *m/e*: 357 (M^+), 339 (M^+-18), 338, 337 (base peak), 332.

Acetylation of (±)-4β-Hydroxythaliporphine (XII)——A mixture of the crude (±)-4β-hydroxy base (XII) (52 mg) [obtained by the same treatment of VII (50 mg) as noted above] and Ac_2O (0.5 ml) in pyridine (1.5 ml) was kept at room tempt. overnight. The same work-up of the mixture as mentioned above gave (±)-4β-acetoxy-O-thaliporphine (IVb) (53 mg, 81.5%), mp 230—236° (decomp.), which was recrystallized from benzene–*n*-hexane yielding pale yellow needles (28 mg, 43%), mp 250—251°(decomp.). It was identical in all respects with an authentic sample obtained above.

(±)-Cataline (IX)——A solution of XII (100 mg) in CH_3OH (4 ml) was treated with CH_2N_2–ether (excess) at room tempt. overnight. Removal of the solvent under reduced pressure gave an amorphous mass (98 mg), which was triturated in *n*-hexane producing (±)-cataline (IX) (90 mg, 86.5%), mp 137—140° (decomp.). Recrystallization from ether–*n*-hexane furnished colorless needles (72 mg, 69.2%), mp 147—149° (decomp.) and an analytical sample had mp 149—150° (decomp.). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520 (OH). UV $\lambda_{max}^{C_2H_5OH}$ nm (log ε): 283 (4.18), 304 (4.15). NMR δ: 2.51 (3H, s, NCH_3), 3.57, 3.86 (each 3H, s, $2\times OCH_3$), 3.88 (6H, s, $2\times OCH_3$), 4.46 (1H, bt, $W1/2=5.0$ Hz, 4-H), 6.73, 6.88 (each 1H, s, $2\times$arom. H), 8.06 (1H, s, 11-H). *Anal.* Calcd. for $C_{21}H_{25}O_5N$ (mol. wt.=371.42): C, 67.90; H, 6.78; N, 3.77. Found: C, 67.61; H, 6.71; N, 3.54. Mass Spectrum *m/e*: 371 (M^+), 370 (M^+-1), 356, 340, 328 (base peak). It was identical with natural (+)-cataline by comparison of each IR ($CHCl_3$) and TLC [Silica gel GF_{254} (Merck); developing solvent, a) $CHCl_3$–C_2H_5OH (9: 1) and b) benzene–ethyl acetate–diethylamine (7: 2:1), and aluminum oxide G (type E) (Merck); developing solvent, a) acetone–petrol. ether (7: 3) and (1: 1)].

$Pd(OAc)_4$ Oxidation of (±)-Codamine (I) in the Presence of CF_3COOH——To a stirred solution of I (100 mg, 0.292 mmole) and CF_3COOH (0.5 ml) in CH_2Cl_2 (10 ml) was added in one portion the oxidant (324 mg, 0.73 mmole) at room tempt. and the whole was stirred at the same tempt. for 1 hr. The mixture was washed with 5% $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent gave an amorphous mass (97 mg), which was treated with 10% HCl (10 ml) under stirring at room tempt. for 0.5 hr. The acidic mixture was basified with $NaHCO_3$ (powder) and the product was taken up in ether. The ether extract was washed with brine and dried over anhydrous K_2CO_3. Evaporation of the solvent gave a dark brown amorphous mass (51 mg), which was purified by preparative TLC (developing solvent; $CHCl_3$–CH_3OH–conc. NH_4OH (10: 1: 0.05)] yielding two kinds of products (A and B) (moving rate; A>B). Elution of the absorbent for the product (A) with $CHCl_3$–CH_3OH (10: 1) furnished (±)-thaliporphine (VII) (10 mg, 10%), mp 167—170° (decomp.), whose IR spectrum ($CHCl_3$) was completely superimposable on that of an authentic sample.[5] The same work-up of the product (B) as described above afforded (±)-4β-hydroxythaliporphine (XII) (21 mg, 20.2%), mp 149—151° (decomp.), which was identical with an authentic sample obtained above by comparison of each IR spectrum ($CHCl_3$) and TLC.

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13) IR spectrum was obtained with a Hitachi Model 225 spectometer.