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Quinolizidines. XX.[1] Racemic and Chiral Syntheses of the *Alangium* Alkaloids 9-Demethylprotoemetinol and 10-Demethylprotoemetinol

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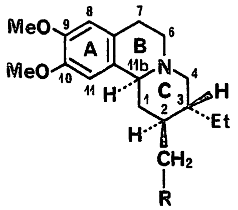
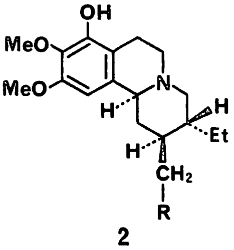
The synthesis of (±)-9-demethylprotoemetinol [(±)-**3d**] was accomplished by $LiAlH_4$ reduction of the tricyclic ester (±)-**5** and subsequent debenzylation of the resulting tricyclic alcohol (±)-**10**. Acetylation of (±)-**3d** with acetic anhydride and pyridine gave the diacetate (±)-**11**. The same sequence of reactions starting with (−)-**5** afforded (−)-9-demethylprotoemetinol [(−)-**3d**] and the diacetate (−)-**11** through (−)-**10**. Parallel synthetic routes starting with the isomeric tricyclic esters (±)-**9** and (−)-**9** produced (±)- and (−)-10-demethylprotoemetinols [(±)-**4d** and (−)-**4d**] and the corresponding diacetates [(±)-**13** and (−)-**13**] through (±)-**12** and (−)-**12**, respectively. The correctness of the structure and absolute stereochemistry of an *Alangium* alkaloid inferred to be 10-demethylprotoemetinol was confirmed by a direct comparison of its diacetate with synthetic (−)-**13**.

Keywords——*Alangium lamarckii* alkaloid; demethylprotoemetinol; racemic synthesis; chiral synthesis; lithium aluminum hydride ester reduction; benzyl ether hydrogenolysis; acetic anhydride–pyridine *O*-acetylation

In previous papers,[2,3] we have classified a number of benzo[*a*]quinolizidine alkaloids found in *Alangium lamarckii* Thw. (Alangiaceae)[4] into four groups (types **1**—**4**) (R = CH_2OH, CO_2H, or a heterocyclic ring)[5] according to their substitution patterns in the aromatic ring A. Prior to the present study, the isolation of the **1**-type alkaloids psychotrine (**1a**),[6-8] cephaeline (**1b**),[6-9] and tubulosine (**1c**),[8-12] accompanied with their demethylated bases (types **3** and **4**) such as 9-demethylpsychotrine (**3a**),[8,13,14] demethylcephaeline (**3b** or **4b**),[8,15] and 10-demethyltubulosine (**4c**),[12,13,16] from the same plant suggested the possibility of co-occurrence of the 9-demethylated (**3d**) and/or 10-demethylated (**4d**) bases of pro-



1



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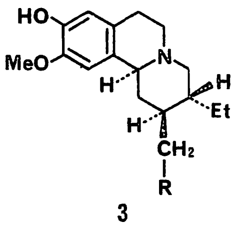

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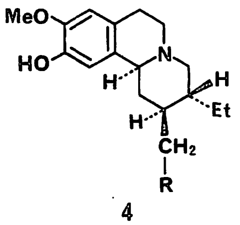
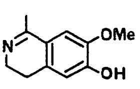
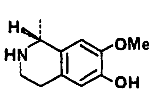


4

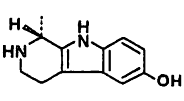
a : R =



b : R =



c : R =



d : R = CH_2OH

toemetinol (dihydroprotoemetine) (**1d**), which had also been encountered[9,17] in *A. lamarckii*. This suggestion seemed to be very probable because ankorine (**2d**),[18] the **2**-type alkaloid at the protoemetinol level (R = CH_2OH), had already been found[17,19] to occur in the same plant. If the two demethylprotoemetinols were available in advance by synthesis, searching for them as natural products would be greatly facilitated. Our previous work has shown that the racemic syntheses of all the alkaloids of **1**—**4**-types are possible through the "lactim ether route" or "3-acetylpyridine route" and the chiral syntheses, through the "cincholoipon-incorporating route" or "lactim ether route".[20] We therefore undertook the racemic and chiral syntheses of 9-demethylprotoemetinol (**3d**) and 10-demethylprotoemetinol (**4d**), based on these unified synthetic strategies.[21]

The first target selected for synthesis was (±)-9-demethylprotoemetinol [(±)-**3d**], which would be accessible from the known tricyclic ester (±)-**5**, a common key intermediate utilized in our previous syntheses of (±)-9-demethylpsychotrine [(±)-**3a**][22] and (±)-9-demethyltubulosine [(±)-**3c**].[23] The starting tricycle (±)-**5** was available from the lactim ether (±)-**6** by the previously reported 6-step synthesis[22] or from 3-acetylpyridine (**7**) by the recently reported multistep syntheses.[24] Reduction of (±)-**5** with $LiAlH_4$ in ether gave the tricyclic alcohol (±)-**10** in 98% yield. On debenzylation using hydrogen and Pd–C catalyst, (±)-**10** produced the first target (±)-**3d** in 93% yield. The diacetate (±)-**11** was prepared from (±)-**3d**

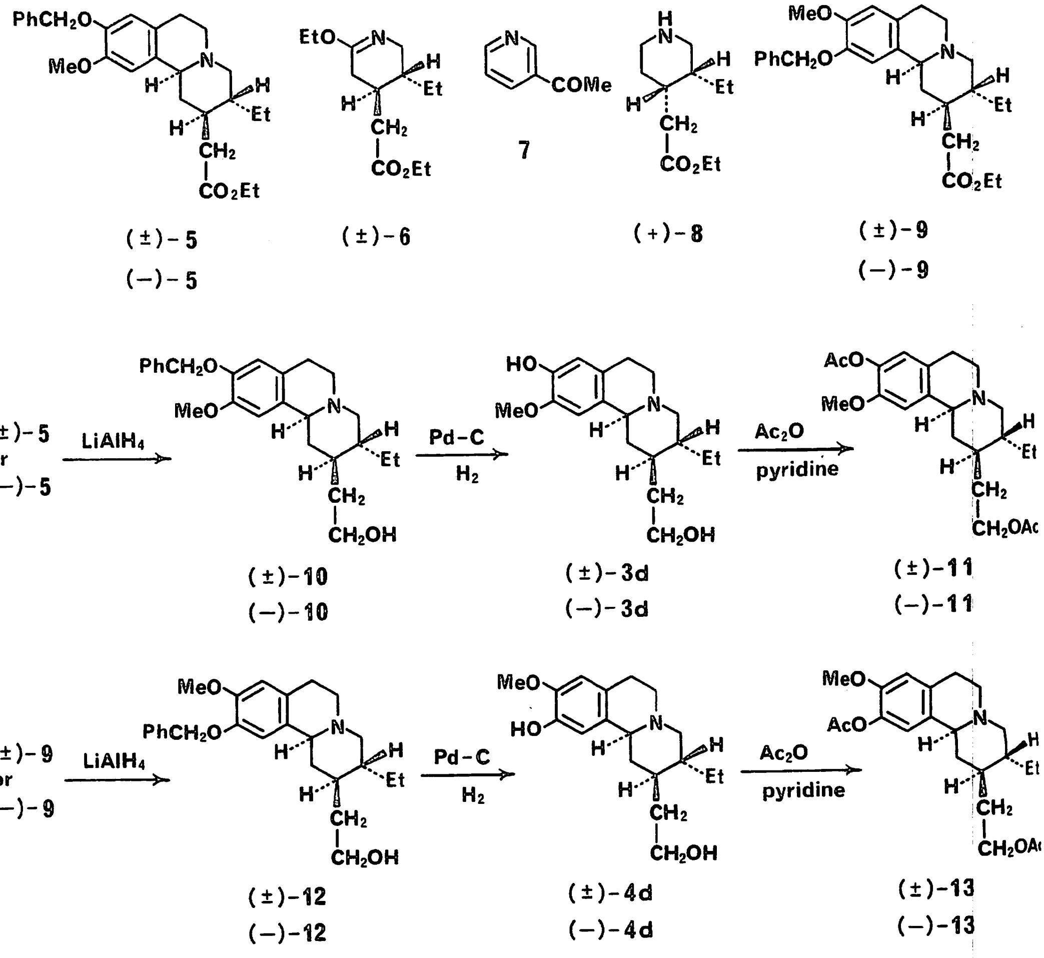


Chart 1

in 93% yield by acetylation with acetic anhydride and pyridine.

Our second target for synthesis was (−)-9-demethylprotoemetinol [(−)-**3d**], and the same sequence of reactions starting with (−)-**5** afforded (−)-**10**, (−)-**3d**, and (−)-**11** in excellent yields. The starting material [(−)-**5**], a common key intermediate in our recent unified syntheses of (+)-9-demethylpsychotrine [(+)-**3a**],[14] (−)-9-demethylcephaeline [(−)-**3b**],[15] and (−)-9-demethyltubulosine [(−)-**3c**],[1] was prepared from cincholoipon ethyl ester [(+)-**8**][25] according to the previously reported 10-step procedure.[14]

For the syntheses of (±)- and (−)-10-demethylprotoemetinols, the third and fourth targets, synthetic routes starting with the known tricyclic esters (±)-**9** and (−)-**9** and parallel to those employed for the above 9-demethyl series were separately followed. All reactions proceeded smoothly and compounds **12**, **4d**, and **13**, in both the (±) and (−) forms, were obtained in high yields. The racemic starting material [(±)-**9**], a common key intermediate used by us in the syntheses of (±)-10-demethylpsychotrine [(±)-**4a**][22] and (±)-10-demethyltubulosine [(±)-**4c**],[16] was prepared from (±)-**6** by the previously reported 6-step synthesis[22] or from **7** according to the "3-acetylpyridine method".[24c] The chiral starting material [(−)-**9**], a key intermediate used also in our recent synthesis of (−)-10-demethylcephaeline [(−)-**4b**],[15] was obtained from (+)-**8**[25] as described previously.[2]

In the meantime, Pakrashi's group isolated two new alkaloids from the seeds of *A. lamarckii* and, on the basis of spectral and chemical evidence, inferred them to be 9-demethylprotoemetinol (**3d**) and 10-demethylprotoemetinol (**4d**).[26] We thus tried to confirm the structures of these compounds by direct comparisons with our authentic samples. It was found that the infrared (IR), nuclear magnetic resonance (NMR), and mass spectra and chromatographic behavior of the diacetate of the second alkaloid were identical with those of synthetic (±)-10-demethylprotoemetinol diacetate [(±)-**13**] [hence with those of synthetic (−)-**13**]. The chiral identity of the diacetate of the natural base with synthetic (−)-**13** was shown by the same sign of their specific rotations, establishing that the second alkaloid was actually (−)-10-demethylprotoemetinol [(−)-**4d**]. On the other hand, a direct comparison of the other alkaloid, inferred to be 9-demethylprotoemetinol (**3d**), with synthetic (−)-**3d** at the diacetate or the original level was not possible on account of paucity of the natural base, thus leaving its chemistry incomplete.

In conclusion, the above results not only represent an extension of the scope of our unified synthetic strategies for benzo[*a*]quinolizidine-type *Alangium* alkaloids but also have unequivocally established the structure and absolute stereochemistry of the *Alangium* alkaloid (−)-10-demethylprotoemetinol [(−)-**4d**]. Interestingly, among the many benzo[*a*]quinolizidine-type *Alangium* alkaloids hitherto known, the tricyclic alcohol level is the only one that embraces all the **1**—**4**-types of alkaloids: protoemetinol (**1d**), ankorine (**2d**), 9-demethylprotoemetinol (**3d**), and 10-demethylprotoemetinol (**4d**). Though the very limited availability of the third of the four alkaloids at this moment precludes us from providing conclusive evidence to support the correctness of its structure, it is hoped that the knowledge obtained on the synthetic (±)-**3d** and (−)-**3d** or (±)-**11** and (−)-**11** will be of great help toward further isolation of this base from natural sources.

Experimental

General Notes——All melting points were determined by using a Yamato MP-1 capillary melting point apparatus and are corrected. See refs. 3 and 18*b* for details of instrumentation and measurements. Microanalyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br = broad, m = multiplet, s = singlet, sh = shoulder, t = triplet.

(±)-9-Benzyloxy-3α-ethyl-1,3,4,6,7,11bα-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizine-2β-ethanol [(±)-10]——To a stirred, ice-cooled suspension of $LiAlH_4$ (304 mg, 8 mmol) in dry ether (40 ml) was added dropwise a solution of (±)-**5**[22,24] (1.75 g, 4 mmol) in dry ether (40 ml) over a period of 15 min. After the mixture had been stirred at room temperature for 1 h, H_2O (0.3 ml), 10% aqueous NaOH (0.3 ml), and H_2O (0.7 ml) were successively added under ice-cooling. The insoluble material that resulted was filtered off and washed with three 15-ml portions of $CHCl_3$. The filtrate and washings were combined, dried over anhydrous K_2CO_3, and concentrated *in vacuo* to leave (±)-**10** (1.55 g, 98%) as a brown oil. The oil was crystallized from hexane–AcOEt (3 : 1, v/v) to afford an analytical sample as colorless pillars, mp 111.5—112 °C; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3640 (OH), 2820, 2760 (*trans*-quinolizidine ring);[27] ^1H-NMR ($CDCl_3$) δ: 0.91 (3H, t, J=6.5 Hz, $CCH_2\underline{Me}$), 1.78 (1H, s, OH), 3.78 (2H, br, $C\underline{H}_2OH$), 3.86 (3H, s, OMe), 5.10 (2H, s, $OC\underline{H}_2Ph$), 6.60 (1H, s, $H_{(8)}$ or $H_{(11)}$), 6.71 (1H, s, $H_{(11)}$ or $H_{(8)}$), 7.2—7.5 (5H, m, Ph). *Anal.* Calcd for $C_{25}H_{33}NO_3$: C, 75.92; H, 8.41; N, 3.54. Found: C, 75.81; H, 8.65; N, 3.49.

(2*R*,3*R*,11b*S*)-9-Benzyloxy-3-ethyl-1,3,4,6,7,11b-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizine-2-ethanol [(−)-10]——This was prepared in 93% yield from (−)-**5**[14] (1.53 g, 3.5 mmol) by reduction with $LiAlH_4$ (266 mg, 7 mmol) in dry ether (70 ml) in a manner similar to that described above for (±)-**10**. Purification by means of recrystallization from hexane–AcOEt (3 : 1, v/v) gave (−)-**10** as colorless needles, mp 103—104 °C; $[\alpha]_D^{25}$ −35.0° (c=0.50, EtOH). *Anal.* Calcd for $C_{25}H_{33}NO_3$: C, 75.92; H, 8.41; N, 3.54. Found: C, 75.91; H, 8.46; N, 3.80. The IR ($CHCl_3$) and ^1H-NMR ($CDCl_3$) spectra and thin-layer chromatographic (TLC) mobility of this sample were identical with those of the racemic modification [(±)-**10**] described above.

(±)-10-Benzyloxy-3α-ethyl-1,3,4,6,7,11bα-hexahydro-9-methoxy-2*H*-benzo[*a*]quinolizine-2β-ethanol [(±)-12]——To a chilled (0 °C), stirred solution of (±)-**9**[22,24c] (662 mg, 1.51 mmol) in dry ether (30 ml) was added $LiAlH_4$ (86 mg, 2.3 mmol) in small portions. The reaction mixture was stirred at room temperature for 1 h and then heated under reflux for 10 min. After successive additions of H_2O (2 drops) and anhydrous Na_2SO_4 at 0 °C, the resulting solid was filtered off and washed with $CHCl_3$. The filtrate and washings were combined and dried over anhydrous Na_2SO_4. Removal of the solvent *in vacuo* yielded a colorless oil, which was crystallized from hexane containing a small amount of EtOH to give (±)-**12** (542 mg, 91%) as colorless prisms. Recrystallization from the same solvent afforded an analytical sample, mp 98.5—99.5 °C; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3640 (OH), 2815, 2760 (*trans*-quinolizidine ring);[27] ^1H-NMR ($CDCl_3$) δ: 0.90 (3H, t, J=6.5 Hz, $CCH_2\underline{Me}$), 1.43 (1H, s, OH), 3.69 (2H, br, $C\underline{H}_2OH$), 3.84 (3H, s, OMe), 5.10 (2H, s, $OC\underline{H}_2Ph$), 6.59 (1H, s, $H_{(8)}$ or $H_{(11)}$), 6.69 (1H, s, $H_{(11)}$ or $H_{(8)}$), 7.2—7.5 (5H, m, Ph). *Anal.* Calcd for $C_{25}H_{33}NO_3$: C, 75.92; H, 8.41; N, 3.54. Found: C, 76.01; H, 8.63; N, 3.64.

(2*R*,3*R*,11b*S*)-10-Benzyloxy-3-ethyl-1,3,4,6,7,11b-hexahydro-9-methoxy-2*H*-benzo[*a*]quinolizine-2-ethanol [(−)-12]——According to the procedure described above for (±)-**10**, except that the reaction time was prolonged to 2 h, (−)-**9**[2] (1.09 g, 2.5 mmol) was reduced with $LiAlH_4$ (190 mg, 5 mmol) in dry ether (60 ml) to give (−)-**12** (910 mg, 92%). Recrystallization of crude (−)-**12** from hexane–AcOEt (3 : 1, v/v) furnished an analytical sample as almost colorless prisms, mp 85—86 °C; $[\alpha]_D^{16}$ −50.6° (c=0.50, EtOH). *Anal.* Calcd for $C_{25}H_{33}NO_3$: C, 75.92; H, 8.41; N, 3.54. Found: C, 76.14; H, 8.44; N, 3.66. The IR ($CHCl_3$) and ^1H-NMR ($CDCl_3$) spectra and TLC mobility of this sample were identical with those of the racemic modification [(±)-**12**] described above.

(±)-3α-Ethyl-1,3,4,6,7,11bα-hexahydro-9-hydroxy-10-methoxy-2*H*-benzo[*a*]quinolizine-2β-ethanol [(±)-9-Demethylprotoemetinol] [(±)-3d]——A solution of (±)-**10** (1.19 g, 3 mmol) in EtOH (40 ml) was hydrogenated over 10% Pd–C (400 mg) at atmospheric pressure and 30 °C for 1 h. Removal of the catalyst by filtration and concentration of the filtrate under reduced pressure gave (±)-**3d** (852 mg, 93%) as a pale brown solid, mp 166.5—168 °C. Recrystallization of the solid from acetone yielded an analytical sample as colorless prisms, mp 171—171.5 °C; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3630, 3560 (OH's), 2810, 2750 (*trans*-quinolizidine ring);[27] ^1H-NMR ($CDCl_3$) δ: 0.91 (3H, t, J=6.5 Hz, $CCH_2\underline{Me}$), 3.77 (2H, m, $C\underline{H}_2OH$), 3.85 (3H, s, OMe), 6.63 and 6.66 (1H each, s, aromatic protons). *Anal.* Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.66; H, 9.11; N, 4.75.

(2*R*,3*R*,11b*S*)-3-Ethyl-1,3,4,6,7,11b-hexahydro-9-hydroxy-10-methoxy-2*H*-benzo[*a*]quinolizine-2-ethanol [(−)-9-Demethylprotoemetinol] [(−)-3d]——This was obtained in 97% yield from (−)-**10** (990 mg, 2.5 mmol) by catalytic hydrogenolysis [10% Pd–C (400 mg), EtOH (40 ml), 1 atm, 24 °C, 1 h] similar to that described above for (±)-**3d**. Purification by means of recrystallization from acetone gave (−)-**3d** as slightly yellowish prisms, mp 157—158.5 °C; $[\alpha]_D^{25}$ −61.0° (c=0.50, EtOH); MS m/z (relative intensity): 306 (12), 305 (M^+) (66), 304 (100), 260 (11), 233 (10), 232 (49), 191 (47), 178 (12), 177 (50), 176 (13); UV λ_{max} (EtOH) 225 nm (sh) (log ε 3.87), 285 (3.60), 288 (3.60); λ_{max} (0.1 N aq. NaOH) 242 (3.91), 299 (3.70); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3630, 3560, 3005, 2930, 2810, 2750, 1508, 1467, 1448, 1361, 1336, 1254, 1148, 1133, 1034, 1018; ^1H-NMR ($CDCl_3$) δ: 0.90 (3H, t, J=6.5 Hz, $CCH_2\underline{Me}$), 1.0—3.2 (unresolved m), 3.74 (2H, m, $C\underline{H}_2OH$), 3.84 (3H, s, OMe), 6.60 and 6.65 (1H each, s, aromatic protons). *Anal.* Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.59; H, 8.91; N, 4.56. The IR and ^1H-NMR spectra and TLC mobility of this sample were identical with those of the racemic sample [(±)-**3d**] described above.

(±)-3α-Ethyl-1,3,4,6,7,11bα-hexahydro-10-hydroxy-9-methoxy-2*H*-benzo[*a*]quinolizine-2β-ethanol [(±)-10-Demethylprotoemetinol] [(±)-4d]——Catalytic hydrogenolysis of (±)-**12** was carried out as described above for (±)-**3d** except that the reaction time was extended to 2 h. The crude product (96% yield) that resulted was recrystallized from hexane–$CHCl_3$ to provide (±)-**4d** as colorless prisms, mp 151—152 °C; MS m/z (relative intensity): 306 (11), 305 (M^+) (62), 304 (100), 290 (13), 260 (12), 248 (12), 233 (11), 232 (56), 191 (46), 178 (13), 177 (62), 176 (11); UV λ_{max} (EtOH) 225 nm (sh) (log ε 3.87), 285 (sh) (3.61), 288 (3.61); λ_{max} (0.1 N aq. NaOH) 243 (3.87), 300 (3.73); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3635, 3560 (OH's), 2810, 2755 (*trans*-quinolizidine ring);[27] ^1H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.5 Hz, $CCH_2\underline{Me}$), 3.70 (2H, m, $C\underline{H}_2OH$), 3.81 (3H, s, OMe), 6.53 and 6.74 (1H each, s, aromatic protons). *Anal.* Calcd for

$C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.79; H, 8.83; N, 4.63.

(2*R*,3*R*,11b*S*)-3-Ethyl-1,3,4,6,7,11b-hexahydro-10-hydroxy-9-methoxy-2*H*-benzo[*a*]quinolizine-2-ethanol [(−)-10-Demethylprotoemetinol] [(−)-4d]——Catalytic hydrogenolysis of (−)-**12** (870 mg, 2.2 mmol) was effected [10% Pd–C (350 mg), EtOH (40 ml), 1 atm, 17 °C, 2 h] as described above for (±)-**3d**. The crude glassy material (656 mg, 98%) that resulted was purified on an alumina column [$CHCl_3$–EtOH (20 : 1, v/v)] to give (−)-**4d** as a pale yellow glass, $[\alpha]_D^{17}$ −35.2° (*c*=0.50, EtOH); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3635, 3560, 3005, 2930, 2810, 2755, 1508, 1465, 1448, 1370, 1266, 1147, 1131, 1032, 1018; ^1H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.5 Hz, $CCH_2\underline{Me}$), 1.0—3.2 (unresolved m), 3.68 (2H, m, $\underline{CH_2}OH$), 3.81 (3H, s, OMe), 6.53 and 6.73 (1H each, s, aromatic protons). Apart from the chiroptical property, this sample was identical with (±)-**4d** by direct comparison of the mass, UV (EtOH or 0.1 N aq. NaOH), IR ($CHCl_3$), and ^1H-NMR ($CDCl_3$) spectra and TLC mobility.

(±)-9-Acetyloxy-3α-ethyl-1,3,4,6,7,11bα-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizine-2β-ethanol Acetic Ester [(±)-11]——A stirred mixture of (±)-**3d** (92 mg, 0.3 mmol), pyridine (0.5 ml), and acetic anhydride (0.3 ml) was heated at 60 °C for 30 min. After cooling, the reaction mixture was concentrated *in vacuo*. The resulting oil was purified by column chromatography [silica gel, AcOEt–$CHCl_3$ (2 : 1, v/v)] to afford (±)-**11** (109 mg, 93%) as a yellow oil; MS *m/z* (relative intensity): 390 (14), 389 (M^+) (66), 388 (84), 347 (13), 346 (54), 332 (13), 330 (29), 300 (15), 274 (41), 260 (15), 233 (47), 232 (33), 191 (21), 178 (15), 177 (100); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2810, 2760 (*trans*-quinolizidine ring),27) 1754, 1730 (ester CO's); ^1H-NMR ($CDCl_3$) δ: 0.92 (3H, t, *J*=6.5 Hz, $CCH_2\underline{Me}$), 2.06 (3H, s, $CH_2OCO\underline{Me}$), 2.29 (3H, s, $ArOCO\underline{Me}$), 3.81 (3H, s, OMe), 4.19 (2H, t, *J*=6.5 Hz, $\underline{CH_2}OAc$), 6.76 (2H, s, aromatic protons).

(2*R*,3*R*,11b*S*)-9-Acetyloxy-3-ethyl-1,3,4,6,7,11b-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizine-2-ethanol Acetic Ester [(−)-11]——Acetylation of (−)-**3d** (92 mg, 0.3 mmol) was carried out [pyridine (0.5 ml), Ac_2O (0.3 ml), 60 °C, 30 min] as described above for (±)-**11**, giving (−)-**11** (110 mg, 94%) as an unstable yellow oil, $[\alpha]_D^{25}$ −34.3° (*c*=0.40, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 2810, 2760, 1754, 1730, 1508, 1466, 1366, 1136, 1030; ^1H-NMR ($CDCl_3$) δ: 0.91 (3H, t, *J*=6.5 Hz, $CCH_2\underline{Me}$), 1.0—3.2 (unresolved m), 2.06 (3H, s, $CH_2OCO\underline{Me}$), 2.29 (3H, s, $ArOCO\underline{Me}$), 3.81 (3H, s, OMe), 4.18 (2H, t, *J*=6.5 Hz, $\underline{CH_2}OAc$), 6.75 (2H, s, aromatic protons). The mass, IR, and ^1H-NMR spectra of this specimen were superimposable on those of the racemic modification [(±)-**11**] described above.

(±)-10-Acetyloxy-3α-ethyl-1,3,4,6,7,11bα-hexahydro-9-methoxy-2*H*-benzo[*a*]quinolizine-2β-ethanol Acetic Ester [(±)-13]——Acetylation of (±)-**4d** was effected as described above for (±)-**11**, and the resulting crude oil was crystallized from hexane to afford (±)-**13** in 85% yield. Recrystallization from hexane–$CHCl_3$ yielded an analytical sample as colorless prisms, mp 97—98 °C; MS *m/z* (relative intensity): 390 (15), 389 (M^+) (69), 388 (100), 346 (21), 332 (17), 330 (15), 302 (11), 300 (13), 275 (15), 274 (64), 260 (10), 234 (12), 233 (61), 178 (12), 177 (84); UV λ_{max} (EtOH) 222 nm (sh) (log ε 4.00), 277 (3.43), 281 (3.44), 286 (3.42); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2815, 2760 (*trans*-quinolizidine ring),27) 1755, 1730 (ester CO's); ^1H-NMR ($CDCl_3$) δ: 0.91 (3H, t, *J*=6.5 Hz, $CCH_2\underline{Me}$), 2.06 (3H, s, $CH_2OCO\underline{Me}$), 2.31 (3H, s, $ArOCO\underline{Me}$), 3.79 (3H, s, OMe), 4.17 (2H, t, *J*=6.4 Hz, $\underline{CH_2}OAc$), 6.66 and 6.86 (1H each, s, aromatic protons). *Anal.* Calcd for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02; N, 3.60. Found: C, 68.11; H, 8.05; N, 3.66. The mass, UV, IR, and ^1H-NMR spectra and TLC mobility of this sample were identical with those of the diacetate derived from natural 10-demethylprotoemetinol26) as well as with those of synthetic (−)-**13** described below.

(2*R*,3*R*,11b*S*)-10-Acetyloxy-3-ethyl-1,3,4,6,7,11b-hexahydro-9-methoxy-2*H*-benzo[*a*]quinolizine-2-ethanol Acetic Ester [(−)-13]——Treatment of (−)-**4d** (92 mg, 0.3 mmol) with acetic anhydride (0.3 ml) and pyridine (0.5 ml) in a manner similar to that described above for (±)-**11** and purification of the crude oily product by column chromatography [silica gel, $CHCl_3$–EtOH (20 : 1, v/v)] gave (−)-**13** (102 mg, 87%) as a pale orange oil, $[\alpha]_D^{25}$ −29.7° (*c*=0.38, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3015, 2950, 2815, 2760, 1755, 1730, 1508, 1465, 1366, 1145, 1030; ^1H-NMR ($CDCl_3$) δ: 0.90 (3H, t, *J*=6.5 Hz, $CCH_2\underline{Me}$), 1.0—3.2 (unresolved m), 2.06 (3H, s, $CH_2OCO\underline{Me}$), 2.31 (3H, s, $ArOCO\underline{Me}$), 3.79 (3H, s, OMe), 4.17 (2H, t, *J*=6.2 Hz, $\underline{CH_2}OAc$), 6.65 and 6.86 (1H each, s, aromatic protons). This sample was identical [by comparison of mass, IR ($CHCl_3$), and ^1H-NMR ($CDCl_3$) spectra, TLC behavior, and specific rotation] with the diacetate [lit.26) $[\alpha]_D$ −15.8° ($CHCl_3$)] of an *Alangium* alkaloid inferred to be 10-demethylprotoemetinol.26)

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