RACEMIC AND CHIRAL SYNTHESES OF THE ALANGIUM ALKALOID ALANCINE

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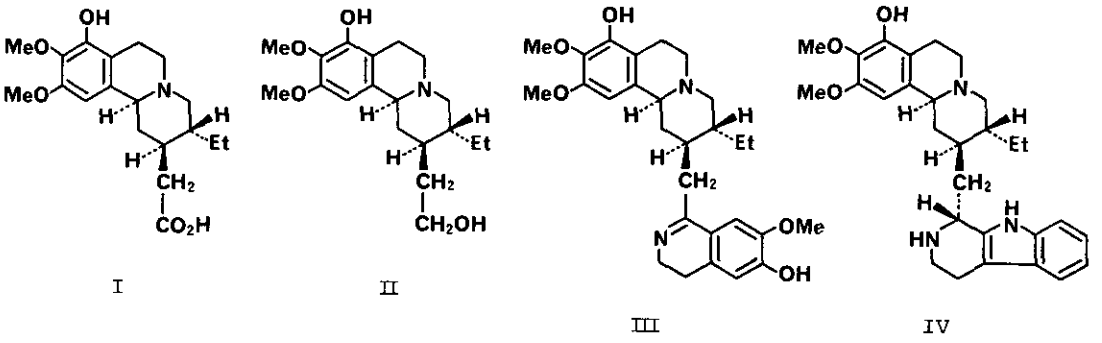
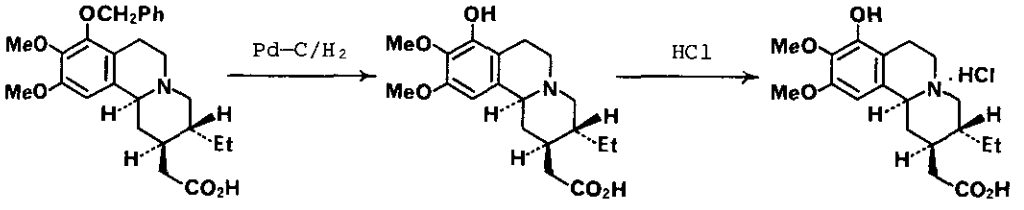
Abstract —— (±)-Alancine [(±)-I] has been synthesized in good yield from the tricyclic amino acid (±)-V by catalytic hydrogenolysis. Treatment of (±)-I with aqueous HCl gave the hydrochloride salt (±)-I·HCl. A parallel synthesis starting with (−)-V produced (−)-alancine [(−)-I] as well as its hydrochloride (−)-I·HCl in good yields. The synthetic (−)-I·HCl was found to be identical with a sample isolated from Alangium lamarckii Thw.

(−)-Alancine (I)[1] is a phenolic benzo[a]quinolizidine alkaloid isolated quite recently from the stem bark of Alangium lamarckii Thw. (Alangiaceae) by Schiff and co-workers.[2] Its tricyclic amino acid structure, unique in all the known benzo[a]quinolizidine-type alkaloids,[3] has been determined[2] by spectral evidence and chemical correlation with (−)-ankorine (II),[4] another Alangium alkaloid with established absolute stereochemistry. In the present work, we have achieved the racemic and chiral syntheses of alancine from the (±)- and (−)-tricyclic amino acids V,[5] which were key intermediates in the previous racemic and chiral syntheses of alangicine (III)[5] and alangimarckine (IV),[6] two other Alangium alkaloids. Catalytic hydrogenolysis of (±)-V using hydrogen and 10% Pd–C catalyst in EtOH at 24°C for 3 h produced racemic alancine [(±)-I] [mp 217–218°C (dec.)][7] in 82% yield. Treatment of (±)-I with aqueous HCl afforded the corresponding hydrochloride salt



I II III IV



(±)-V (±)-I (±)-I·HCl
(−)-V (−)-I (−)-I·HCl

(±)-I·HCl [mp 241.5–245°C (dec.)] in quantitative yield. A parallel transformation of (−)-V gave (−)-alancine [(−)-I] [82% yield; mp 216–220.5°C (dec.); $[\alpha]_D^{20}$ −29.3° (c 0.097, MeOH); cd (c 2.66 × 10^{-4} M, MeOH) $[\theta]_{280}^{18}$ −1000 (neg. max.); uv λ_{max}^{MeOH} nm (log ε) 230 (shoulder) (3.97), 273 (3.01), 280 (shoulder) (2.99); $\lambda_{max}^{H_2O}$ (pH 13) 287 (3.43); $\lambda_{max}^{H_2O}$ (pH 1) 273 (3.02), 279 (shoulder) (3.01); ir ν_{max}^{KBr} cm^{-1} 3430 (broad, OH), 2530 (broad, N^+H), 1707 (weak, broad, CO_2H), 1566 (CO_2^-)][7] as well as its hydrochloride (−)-I·HCl [85% yield; mp 247.5–248.5°C (dec.); $[\alpha]_D^{22}$ −27.9° (c 0.101, MeOH); cd (c 4.72 × 10^{-4} M, MeOH) $[\theta]_{280}^{22}$ −1080 (neg. max.); uv λ_{max}^{MeOH} 230 (shoulder) (3.98), 273 (3.04), 280 (shoulder) (3.01); $\lambda_{max}^{H_2O}$ (pH 13) 287 (3.42); $\lambda_{max}^{H_2O}$ (pH 1) 273 (3.02), 279 (shoulder) (3.01); ir ν_{max}^{KBr} cm^{-1} 3325 (broad, OH), 2710–2620 (N^+H), 1725 (CO_2H)]. The spectral identity of (−)-I with (±)-I and that of (−)-I·HCl with (±)-I·HCl were confirmed by comparison of their ^1H nmr (CD_3OD), ^{13}C nmr (CD_3OD or CD_3OD–D_2O), and mass spectra. To our surprise, the previously reported ir (KBr), ^1H nmr (CD_3OD), and ^{13}C nmr (CD_3OD) spectra of "natural alancine"[2] did not match those of the synthetic (−)-I, but matched those of its hydrochloride salt [(−)-I·HCl] instead. Thus, the physical, chemical, and spectral data reported for "natural alancine" in the previous communication[2] are in reality those for the hy-

drochloride salt [(−)-I·HCl] of alancine. Since the "natural alancine" had been isolated from the plant by a procedure utilizing the Mayer's complex formation and subsequent treatment with anion-exchange resin (Cl^-),[2] it is not unreasonable to consider that the alkaloid had actually been obtained in the form of the hydrochloride salt.

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