CHIRAL SYNTHESES OF THE BENZO[a]QUINOLIZIDINE-TYPE ALANGIUM ALKALOIDS BY THE "LACTIM ETHER METHOD"

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The optical resolution of trans-1-benzyl-5-ethyl-2-oxo-4-piperidineacetic acid [(±)-1], the key intermediate for the syntheses of the racemic modifications of benzo[a]quinolizidine alkaloids, was effected by the use of (R)-(+)-α-phenylethylamine. The conversion of (+)-1 into (4R,5R)-(+)-5-ethyl-1-(2-hydroxy-3,4-dimethoxyphenethyl)-2-oxo-4-piperidineacetic acid ethyl ester [(+)-2] by our "lactim ether method," i.e., debenzylation with Na/NH_3, O-alkylation with triethyloxonium fluoroborate, N-alkylation with 2-benzyloxy-3,4-dimethoxyphenacyl bromide (3), $NaBH_4$ reduction, and catalytic hydrogenolysis, constitutes a formal but new synthesis of the three Alangium alkaloids, (−)-ankorine, (+)-alangicine, and (−)-alangimarckine, which have already been synthesized by us via (+)-2 according to the "cincholoipon-incorporating method."

Another new synthetic route to the above benzo[a]quinolizidine-type Alangium alkaloids was also exploited in terms of the synthesis of (4R,5S)-(−)-5-ethyl-1-(2-hydroxy-3,4-dimethoxyphenethyl)-2-oxo-4-piperidineacetic acid ethyl ester from cincholoipon ethyl ester [(+)-4], a degradation product of the Cinchona alkaloid cinchonine. The steps involved are acetylation of (+)-4, RuO_4 oxidation, deacetylation, lactim ether formation, N-alkylation with 3, $NaBH_4$ reduction, and catalytic hydrogenolysis.

On the other hand, the unnatural enantiomer (+)-ankorine was prepared from (−)-1 through steps similar to those described above for (+)-2, followed by benzylation, Bischler-Napieralski cyclization, catalytic reduction, $LiAlH_4$ reduction, and debenzylation.