A Novel Method for the Transformation of Acyclic α,ω-Diamino Acids to Cyclic Unsaturated α-Amino Acids using Anodic Oxidation

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The acyclic α,ω-diamino acids, L-ornithine and L-lysine, were transformed to optically pure cyclic α′,β′-unsaturated α-amino acids using anodic oxidation as the key step.

This report describes a new practical method for the cyclization of L-ornithine (**1a**) and L-lysine (**1b**) derivatives to the olefinic α-amino acid derivatives (**12**) and the optically pure olefinic L-amino acid derivatives (**8**), which have basic skeletons which are isomeric with those of Δ^1-pyrroline-5-carboxylic acid (**2a**) and Δ^1-piperideine-6-carboxylic acid (**2b**), suggested as intermediates[1-3] in the biosynthesis of pyrrolidine and piperidine alkaloids [equation (1)].

We have already reported that carbamates (**3**) of primary and secondary amines are methoxylated at the position α to nitrogen by direct anodic oxidation in methanol containing tetraethylammonium toluene-*p*-sulphonate (Et_4NOTs) as the supporting electrolyte [equation (2)].[4] However, the anodic methoxylation of *N*-methoxycarbonyl-α-amino acid esters (**4**) at the position α to the ester group proceeds only when halonium ions are used as mediators [equation (3)].[5]

These two types of anodic methoxylation were utilized in the cyclization of the *N*,*N*′-dimethoxycarbonylated L-ornithine and L-lysine methyl esters, (**5a**) and (**5b**), respectively (Scheme 1).

Thus, the methoxylated compounds (**6**) prepared by the anodic oxidation of (**5**) in methanol containing Et_4NOTs gave

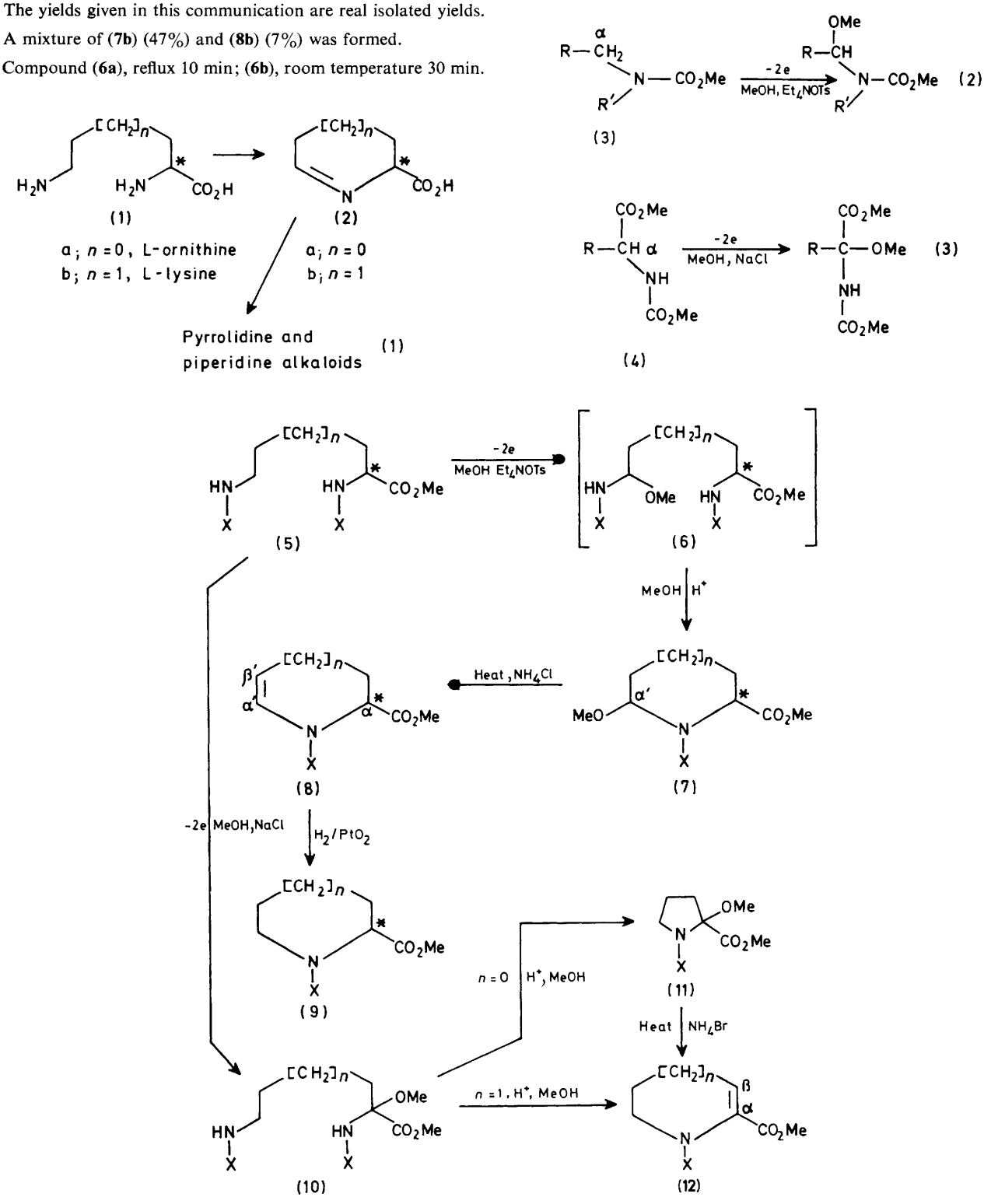
α′-methoxylated cyclic carbamates (**7**) [(**7a**), 51%† from (**5a**); (**7b**), 47%‡ from (**5b**)] upon treatment§ with methanol containing 5% conc. H_2SO_4. Heating (**7**) in the presence of a catalytic amount of NH_4Cl[6] gave the α′,β′-unsaturated carbamates (**8**) [(**8a**), 70%; (**8b**), 93%]. The hydrogenation of (**8**) in methanol to the saturated cyclic α-amino acids (**9**) was almost quantitative. The complete retention of chirality in these procedures was confirmed by comparing the specific rotation of (**9a**) with that of an authentic sample prepared from L-proline.

In contrast with the direct oxidation of (**5**) to yield (**6**), anodic oxidation of (**5**) using the mediator MeOH–NaCl gave

† The yields given in this communication are real isolated yields.

‡ A mixture of (**7b**) (47%) and (**8b**) (7%) was formed.

§ Compound (**6a**), reflux 10 min; (**6b**), room temperature 30 min.



Scheme 1. X = CO_2Me. a; $n = 0$ b; $n = 1$

α-methoxylated α-amino acid esters, (**10**) [(**10a**), *ca.* 100%; (**10b**), 70%], which were subsequently converted into the α,β-unsaturated cyclic carbamates (**12**). Thus, heating (**10a**) in methanol containing 5% H_2SO_4 for 1 h yielded racemic (**11a**) (60%), which was then converted into (**12a**) (86%) by heating with NH_4Br. On the other hand, (**12b**) was obtained directly from (**10b**) in 62% yield by treatment with acidic methanol at room temperature.

The products (**8**) and (**12**) are useful intermediates in organic synthesis as exemplified by the synthesis of a β-hydroxyproline ester from (**8a**).[7]

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