Synthesis of anabaseine and anabasine derivatives: Structural modifications of possible nicotinic agonists

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Coupling nicotinoyl chloride with 3,4-dimetoxyphenethylamine under Bischler-Napieralski cyclization afforded the isoquinoline (4) in good yield. This latter was used as starting material to obtain with only hydrobromic acid a product with demethylation at the position 7 (5). In addition, treatment of (4) with NaBH4/MeOH gave 6,7-dimetoxy-1-(pyridin-3-yl)-1,2,3,4- tetrahydroisoquinoline (6) and unexpectedly, under mild reduction of the pyridine moiety with H2/PtO2/AcOH/, gave 6,7-dimetoxy-1-(piperidin-3-yl)-1,2,3, 4-tetrahydroisoquinoline (7) as the title compound. The unusual chemical reactivity of 4 onto acidic conditions and catalytic hydrogenation allowed us to obtain anabaseine and anabasine derivatives under mild conditions.