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Total Synthesis of (+)-Desoxoprosopinine via the Intramolecular Reaction of γ-Aminoallylstannane

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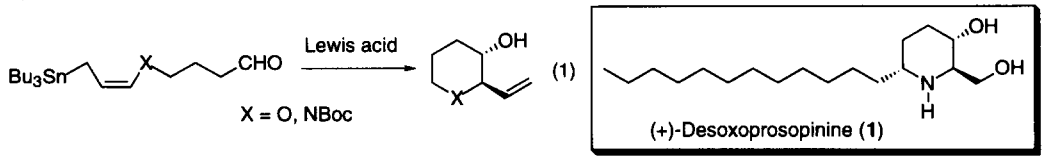
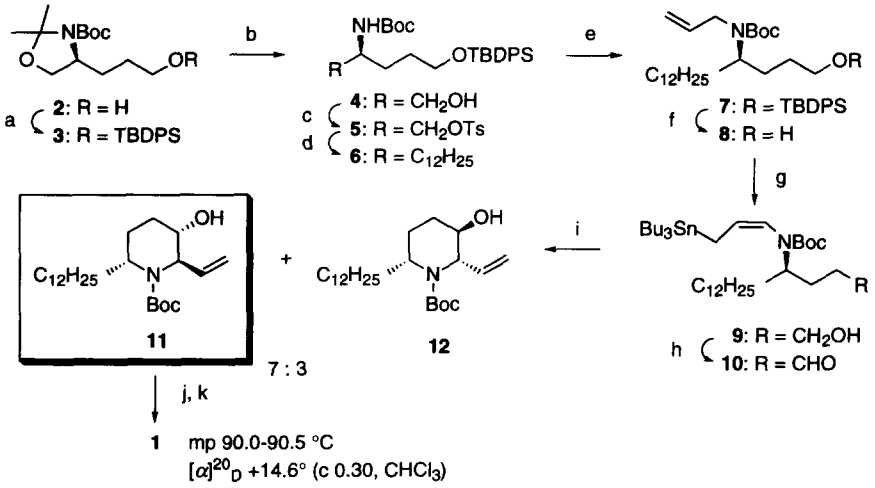
Abstract: A stereoselective total synthesis of (+)-desoxoprosopinine starting from L-glutamic acid as a chiral source was accomplished, in which the intramolecular reaction of γ-aminoallylstannane with aldehyde was used as a key step. © 1997 Elsevier Science Ltd.

During the past several years we have been investigating the stereocontrolled synthesis of polycyclic ethers via the intramolecular reaction of γ-alkoxyallylstannane with aldehyde (eq 1, X = O).[1] More recently, the methodology has been applied successfully to the synthesis of hydroxylated nitrogen heterocycles by using γ-aminoallylstannane derivatives (eq 1, X = NBoc).[2] We were interested in the applicability of the methodology to a natural product synthesis, and now we report that the stereoselective synthesis of (+)-desoxoprosopinine (**1**), [3,4] the reduction product of prosopinine, has been achieved via the γ-nitrogen containing allyltin method.



The L-glutamic acid derived starting material **2**[5] was quantitively converted to the silyl ether **3** by usual method (Scheme 1). Selective cleavage of the *N,O*-acetal protection of **3** was performed with $PdCl_2(CH_3CN)_2$ in refluxing acetonitrile[6] to give the alcohol **4** in 98% yield. Tosylation of **4** with $TsCl/Et_3N/DMAP$ followed by alkylation with $C_{11}H_{23}Li/CuI$ furnished, in 80% overall yield, the compound **6** via the tosylate **5**. Allylation of **6** with allyl bromide/KH gave **7** (92%), which upon desilylation with TBAF led to **8** (74%). Treatment of **8** with *sec*-BuLi/TMEDA followed by trapping of the corresponding allylic anion with *n*-Bu_3SnCl afforded the allylstannane derivative **9** in 62% yield. Oxidation of **9** with SO_3·py/DMSO/Et_3N produced the cyclization precursor **10** in 92% yield. Cyclization of **10** with $BF_3 \cdot OEt_2$ procceded smoothly to give a 7:3 mixture of **11** and **12** in 98% yield. The use of other Lewis acids such as $TiCl_4$, $SnCl_4$, and $MgBr_2$ gave unsatisfactory results. Ozonolysis of **11** followed by reductive treatment gave the corresponding diol in 80% yield. The *N*-protected (+)-desoxoprosopinine obtained was treated with 6N HCl in refluxing dioxane gave **1**, mp 90.0-90.5 ℃; $[\alpha]^{20}_D$ +14.6° (c 0.30, $CHCl_3$) {lit.[4b] mp 90.7-91 ℃; $[\alpha]^{18}_D$ +13° (c 0.31, $CHCl_3$)}, in 66% yield. The ^1H NMR spectrum of the synthetic **1** was in good agreement with the literature data.[4b]

Scheme 1[a]



[a](a) TBDPSCl, imidazole, CH_2Cl_2, rt, 100%; (b) $PdCl_2(CH_3CN)_2$, CH_3CN, reflux, 98%; (c) TsCl, Et_3N, DMAP, CH_2Cl_2, rt, 97%; (d) $C_{11}H_{23}Li$, CuI, Et_2O, -35 °C, 85%; (e) allyl bromide, KH, THF, 0 °C to rt, 92%; (f) TBAF, THF, rt, 74%; (g) *sec*-BuLi, TMEDA, THF, -78 °C, then *n*-Bu_3SnCl, -78 °C to rt, 62%; (h) SO_3·py, DMSO, Et_3N, CH_2Cl_2, 0 °C, 92%; (I) BF_3·OEt_2, CH_2Cl_2, -78 °C, 98%; (j) O_3, MeOH, -78 °C, then $NaBH_4$, -78 °C to rt, 80%; (k) 6N HCl, dioxane, reflux, 66%.

In summary, a new synthesis of (+)-desoxoprosopinine (**1**) was accomplished by using the intramolecular reaction of γ-aminoallylstannane with aldehyde as a key step. We believe that the strategy developed here is widely applicable to the stereoselective synthesis of naturally occuring nitrogen heterocycles

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