The Synthesis of Anti-smoking Nicotine Analogue

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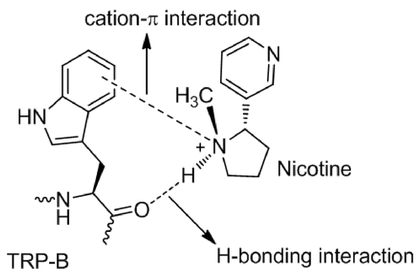
Abstract

The focus of the research is the synthesis of a nicotine analogue which has anti-smoking property. The proposed scheme is a seven-step process. In the first step, an imine is prepared by the condensation of an aldehyde and a primary amine. The product from the first step will be allylated to produce an amine, then be *N*-vinylated to provide the diene. The desired cyclic product will result from: the ring closing metathesis followed by nitrogen deprotection, reduction of the double bond and finally methylation.
In the poster, our effort in synthesizing nicotine in racemic form is shown. The next aim of the research is to conduct allylation on imines enantioselectively, which will be incorparorated in the achieved racemic scheme in order to synthesize the nicotine analogues enantioselctively. The success of this research will lead to the finding of an effective and safe agent that contain anti-smoking properties and significantly reduces the occurrence of relapses.

Introduction

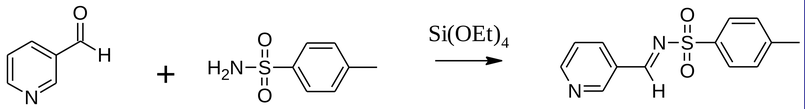
- The success of this research will provide a method to synthesize amines which can act as either antagonist or agonist to nicotine by:
  - Mimicking the two interactions between nicotine and α4β2 nicotinic acetylcholine receptor



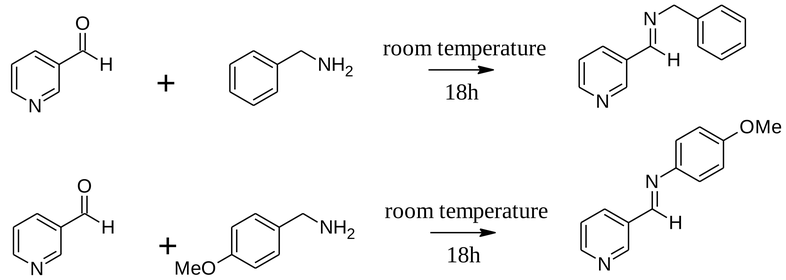
  - Providing a geometric space structure similar to nicotine which can reduce α4β2-nAChR binding ability of nicotine

Results

- **Condensation of aldehyde and amine**

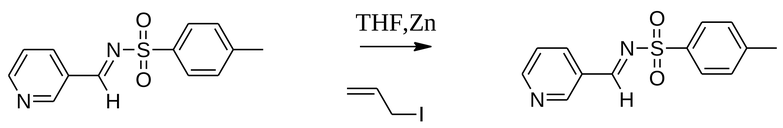


Percent yield: 23%



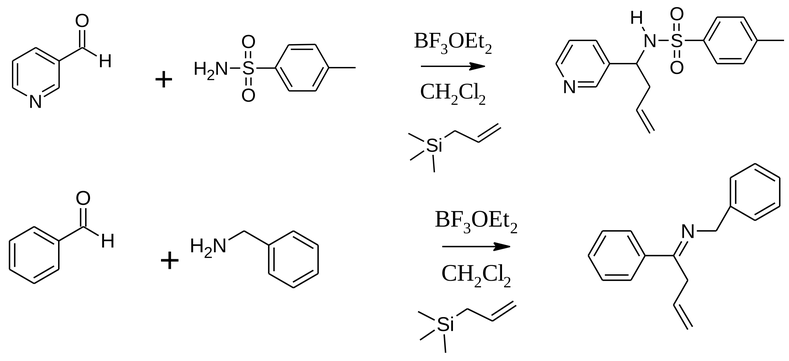
Protecting Group	Solvent	Reaction condition	Time	Percent Yield
Benzyl	None	Room temperature	18 h	56%
Methoxyphenyl	None	Room temperature	18 h	65%

- **Allylation of imine**:



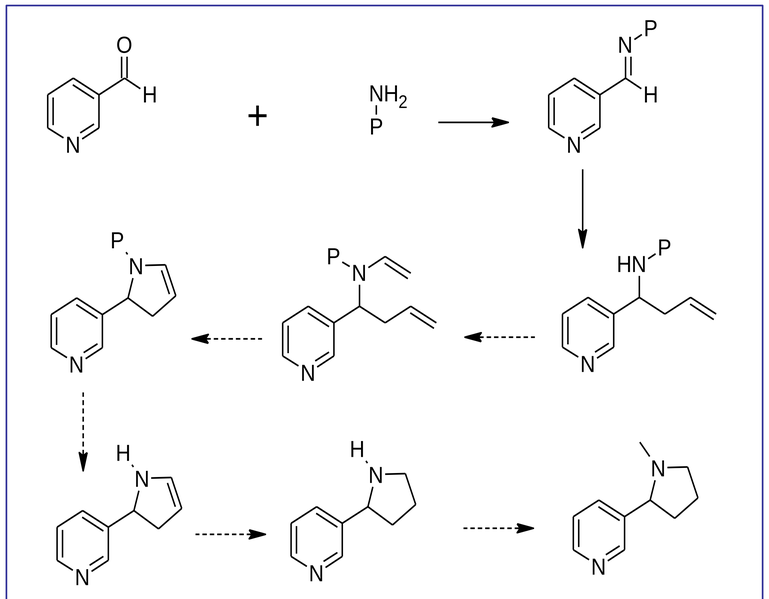
Percent yield: 47% yield

- **Attempts at direct allylation**



Negligible yields

Proposed Scheme



Conclusions

1. Benzyl and methoxyphenyl are found to produce a sufficient yield to be carried out in the next step.
2. Protecting groups will be screened to find imines that could be easily purified by crystalization.

Future Directions

- Prepare other imines with electron withdrawing and electron donating groups.
- Complete the racemic synthesis.
- Perform pharmacological studies of the end products.
- Perform eantioselective synthesis.

Acknowledgements

- CSURP
- TURC
- The University of Tulsa Department of Chemistry and Biochemistry