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Mn(III)-Mediated Reactions of Cyclopropanols with Vinyl Azides: Synthesis of Pyridine and 2-Azabicyclo[3.3.1]non-2-en-1-ol Derivatives
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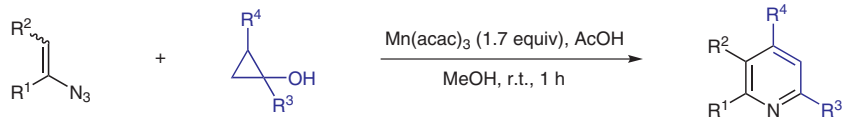
Category

Synthesis of Heterocycles

Key words

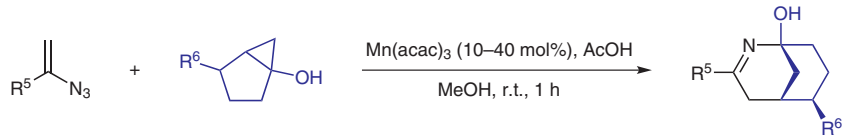
pyridines
vinyl azides
cyclopropanols
manganese

Mn(III)-Mediated Synthesis of Pyridines



1 **2** **3**
30–84% yield
24 examples

R^1 = Ph, 2-$MeOC_6H_4$, 4-$MeOC_6H_4$, 4-$MeO_2CC_6H_4$, 2-Naph, *N*-Ts-pyrrol-2-yl, *N*-Ts-indol-2-yl, CO_2Et
R^2 = H, Me, Ph
R^1–R^2 = –$(CH_2)_6$–
R^3 = *c*-Pr, *c*-Bu, CH_2Bn, *N*-Bn-piperidin-2-yl, (*E*)-CH=CHPh, C≡CPh, Ph, 2-BrC_6H_4, 4-BrC_6H_4, 4-PhC_6H_4, CO_2Me, $SiMe_2Ph$
R^4 = H, Me, Ph



4 **5** **6**
28–91% yield
6 examples

R^5 = Ph, *N*-Ts-pyrrol-2-yl, *N*-Ts-indol-2-yl
R^6 = H, vinyl, Ph, CH_2OMOM

Significance: Reported here is the Mn(III)-mediated synthesis of pyridines **3** from vinyl azides **1** and cyclopropanols **2**. Sub-stoichiometric amounts of $Mn(acac)_3$ may be used in the reaction, although an oxidant such as DDQ or molecular O_2 must be added. Ultimately, the use of excess $Mn(acac)_3$ led to higher yields and increased operational simplicity. Alkyl-, aryl-, heteroaryl-, alkenyl- and alkynyl-substituted pyridines may all be prepared using this methodology. When bicyclic cyclopropanols **5** were used as substrates under catalytic Mn(III) conditions, 2-azabicyclo[3.3.1]non-2-en-1-ols **6** were formed in excellent yields in most cases. A radical cyclization mechanism is proposed without experimental evidence.

Comment: Nitrogen-containing heterocycles are prevalent in a wide variety of natural products and drug molecules. The pyridine ring is particularly evident in bioactive molecules (see Book below), including alkaloids (nicotine) and herbicidal (paraquat dichloride), pesticidal (Densil S) and therapeutic agents (isoniazid). The current divergent method allows for the rapid and versatile synthesis of polysubstituted pyridines or azabicycles from readily available starting materials. The use of stoichiometric amounts of $Mn(acac)_3$ and the potentially explosive azides may, however, limit the utility of this methodology in large-scale applications.

Book: D. Spitzner, In *Science of Synthesis*, Vol. 15; D. Black, Ed.; Georg Thieme Verlag: Stuttgart, **2004**, 11-284.

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