EFFECTIVE ROUTE TO AZETIDINES FROM AZETIDIN-2-ONES WITH THE USE OF HYDROALANES AS SPECIFIC REDUCING AGENTS

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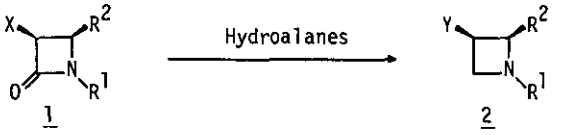
Although the chemistry and biochemistry of azetidin-2-ones have been extensively studied with regard to various β-lactam antibiotics, less attention has been drawn to those of azetidines. However, azetidines are an interesting class of four membered heterocyclic compounds, and it has been shown that a variety of azetidines exhibit various biological activities.

We would like to report here an effective route to azetidines (2) from azetidin-2-ones (1) with the use of hydroalanes as specific reducing agents. We examined various commonly used metal hydride reducing agents for the reaction, which, however, almost resulted in the recovery of starting materials or cleavage of the 1,2-bond to give the corresponding γ-amino alcohols (3). As an exception, $^{i}Bu_2AlH$ was found to undergo the desired reduction successfully to give 2 in 54-85% yields although small amounts (0-27%) of 3 were also produced. Next, we employed AlH_2Cl and $AlHCl_2$ in situ generated from $LiAlH_4$ and $AlCl_3$, which converted 1 into 2 in high yields (79-100%) without being accompanied by 3. Consequently, it can be said that the use of hydroalanes is highly recommended for the specific conversion of azetidin-2-ones into azetidines. Optically active azetidin-2-ones can be transformed to the corresponding azetidines without loss of optical activities. Possible mechanisms for the reaction will be discussed.

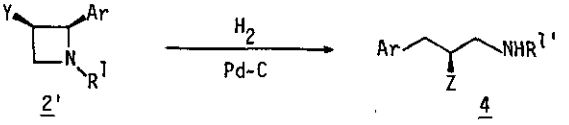


1 X = $PhCH_2O$, N_3

2 Y = $PhCH_2O$, NH_2

R^1 = Ph, $PhCH_2$, Ph(Me)CH, ^{t}Bu, $PhCH_2OCH_2(^{i}Bu)CH$; R^2 = Ph, p-FC_6H_4, 3,4-$(MeO)_2C_6H_3$, 2-C_4H_3O, 2-C_4H_3S

Among the azetidines thus obtained, 2-arylazetidines (2') were found to undergo reductive 1,2-bond fission through hydrogenolysis on Pd catalyst or Raney-nickel to give 2-hydroxy- or 2-amino-3-arylpropylamine derivatives (4) in high yields (81-100%), which may serve as versatile building blocks for organic syntheses.



2' Y = $PhCH_2O$, AcNH, NH_2

4 Z = HO, AcNH, NH_2