SYNTHETIC STUDIES ON $\beta$-LACTAM ANTIBIOTICS:
CONVERSION OF 2-PYRIDONE INTO AZETIDIN-2-ONE

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Abstract—Azetidin-2-one (4), bearing a functionalized carbon atom at the $C_4$-position, was efficiently synthesized from 2-pyridone (1) by photolysis, followed by ozonolysis.

The 1-carbapenem antibiotics, such as thienamycin and PS-5, have been an interesting class of naturally occurring $\beta$-lactam antibiotics from biological and synethetical point of view. In connection with the synthesis of these antibiotics, we have been interested in the facile construction of an azetidin-2-one ring system which bears a functionalized carbon atom at the $C_4$-position. Although the number of papers concerning with the synthesis of azetidin-2-one ring system have been appeared, the conversion of 2-pyridone to it has not yet been reported up to date. Kaneko and his co-workers3, however, have recently published the synthesis of 5-alkoxy-3-oxo-2-azabicyclo-[2.2.0]hex-5-enes from the corresponding pyridones, whose fact prompted us to investigate a conversion of 2-pyridone to an azetidin-2-one derivative.

A solution of 4-methoxy-2-pyridone (1) in tetrahydrofuran was irradiated with high-pressure mercury lamp equipped with a Pyrex filter at 20~30°C for 32 h to furnish the 5-methoxy-3-oxo-2-azabicyclo-[2.2.0]hex-5-one (2)4, whose silylation with tert-butyldimethylsilyle chloride in the presence of lithium diisopropylamide in dry tetrahydrofuran gave the silylated compound (3)5. Ozonolysis of 3 in methanol at -78°C, followed by reduction with dimethyl sulfide, yielded the desired azetidin-2-one (4)6, with the trans-relationship between $C_3$ and $C_4$, in 85 % yield. The stereochemistry of 4 was easily deduced by its nmr spectral data. Reduction of 4 with an excess of sodium borohydride afforded the alcohol (6) and the diol (5) in a ratio of 1 : 4.5 in 80 % yield.

Thus, the conversion of 2-pyridone (1) into azetidin-2-one (4), which may serve as an important start-int material for the synthesis of carbapenem antibiotics, has been achieved by photolysis, followed by ozonolysis7.
REFERENCES AND FOOTNOTES


4 Although our synthetic bicyclo-compound (2) showed the same melting point with that of literature³, the chemical shift for C₁⁻ and C₄⁻H was quite different, δ(CDCl₃): 3.65 (3H, s, Me), 4.03 (2H, s, C₁⁻H and C₄⁻H), 5.03 (1H, s, C₆⁻H), 6.36 (1H, br s, NH).

5 \[ \text{v}_{\text{max}} (\text{CHCl}_3) \] 1720 and 1618 cm⁻¹; δ(CDCl₃) 0.12 (3H, s, Me), 0.16 (3H, s, Me), 0.87 (9H, s, Bu), 3.58 (3H, s, OMe), 4.01 – 4.15 (2H, m, C₁⁻H and C₄⁻H), 4.98 (1H, s, C₆⁻H); m/e 182 (M⁺ -57), 82 (base peak, cyclobutadiene cation).

6 \[ \text{v}_{\text{max}} (\text{CHCl}_3) \] 1760 and 1735 cm⁻¹; δ(CDCl₃) 0.17 (3H, s, Me), 0.33 (3H, s, Me), 0.97 (9H, s, Bu), 3.76 (3H, s, OMe), 4.01 (1H, d, J = 2 Hz, C₃⁻H), 4.28 (1H, dd, J = 2 and 3 Hz, C₄⁻H), 9.59 (1H, d, J = 3 Hz, CHO).

7 In the course of this study, the similar conversion of 4-methyl-2-pyridone into functionalized β-lactam has been published (J. Brennan, J. C. S. Chem. Comm., 1981, 880).

Received, 18th September, 1981