HETEROCYCLES, Vol 19, No 1, 1982

SYNTHETIC STUDIES ON β-LACTAM ANTIBIOTICS: CONVERSION OF 2-PYRIDONE INTO AZETIDIN-2-ONE

Tetsuji Kametani*, Tomoko Mochizuki, and Toshio Honda
Hoshi College of Pharmacy, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

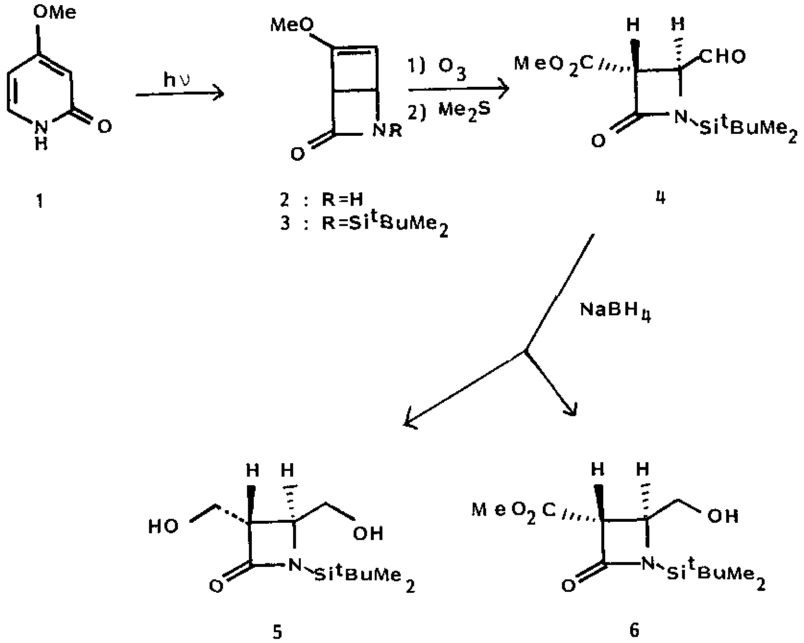
Abstract——Azetidin-2-one (4), bearing a functionalized carbon atom at the C_4-position, was efficiently synthesized from 2-pyridone (1) by photolysis, followed by ozonolysis.

The 1-carbapenem antibiotics, such as thienamycin and PS-5, have been an interesting class of naturally occurring β-lactam antibiotics from biological and synthetical 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[1,2] concerned 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-workers[3], however, have recently published the synthesis of 5-alkoxy-3-oxo-2-azabicyclo-[2.2.0]hex-5-enes from the coresponding 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-butyldimethylsilyl 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 startint material for the synthesis of carbapenem antibiotics, has been achieved by photolysis, followed by ozonolysis[7].



REFERENCES AND FOOTNOTES

1 A. K. Mukerjee and A. K. Singh, Synthesis, 1975, 547; Tetrahedron, 1978, 34, 1731.

2 K. Hirai, J. Syn. Org. Chem. Japan, 1980, 38, 97, and references cited therein.

3 C. Kaneko, K. Shiba, H. Fujii, and Y. Momose, J. C. S. Chem. Comm., 1980, 1177.

4 Although our synthetic bicyclo-compound (2) showed the same melting point with that of literature[3], the chemical shift for C_1- and C_4-H was quite different, $\delta(CDCl_3)$: 3.65 (3H, s, Me), 4.03 (2H, s, C_1-H and C_4-H), 5.03 (1H, s, C_6-H), 6.36 (1H, br s, NH).

5 $\nu_{max.}(CHCl_3)$ 1720 and 1618 cm^{-1} ; $\delta(CDCl_3)$ 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, C_1-H and C_4-H), 4.98 (1H, s, C_6-H); m/e 182 (M^+ -57), 82 (base peak, cyclobutadiene cation).

6 $\nu_{max.}(CHCl_3)$ 1760 and 1735 cm^{-1} ; $\delta(CDCl_3)$ 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, C_3-H), 4.28 (1H, dd, *J* = 2 and 3 Hz, C_4-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