HETEROCYCLES, Vol 19, No 7, 1982

THERMAL REARRANGEMENT OF CYCLOHEXANONE OXIME O-BENZYL ETHER

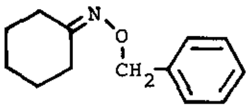
Junko Koyama, Teruyo Sugita, and Yukio Suzuta
Kobe Women's College of Pharmacy, Kobe 658, Japan
Hiroshi Irie
Faculty of Pharmaceutical Sciences, Nagasaki University,
Nagasaki 852, Japan

Abstract ——Thermal rearrangement of cyclohexanone oxime O-benzyl ether under air gave 1,2,3,4,7,8,9,10-octahydro-6-phenylphenanthridine in 35% isolated yield, which yielded 6-phenylphenanthridine by dehydrogenation reaction with palladium carbon. The structure of the latter was confirmed by direct comparison with the authentic sample. The mechanism for the reaction was briefly discussed.

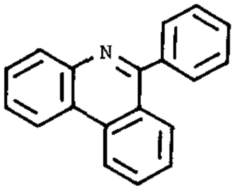
As a continuation of our synthetic work1) for constructing pyridine ring by oxidative thermal rearrangement of cycloalkanone oxime O-allyl ethers, we report here the result of the rearrangement of cyclohexanone oxime O-benzyl ether (1) having O-benzyl group in place of O-allyl group.

Treatment of cyclohexanone with O-benzylhydroxylamine2) in ethanol in the presence of sodium acetate gave cyclohexanone oxime O-benzyl ether (1) as an oil in 92% yield. Thermolysis of the ether (1) in a sealed tube under air at 175-180 °C (bath temperature) for 45 h gave a mixture which exhibited several spots on thin layer chromatography. The major product, mp 81.5-83 °C, was isolated from the mixture by preparative thin layer chromatography in 35% yield, which formed crystalline picrate, mp 161-162 °C.3) The molecular ion peak at m/z 263 in its mass spectrum and elemental analysis confirmed the molecular formula $C_{19}H_{21}N$. Its ^{1}H-NMR spectrum

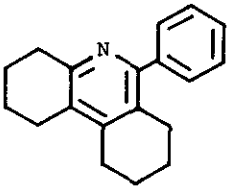
($CDCl_3$) exhibited the signals corresponding to sixteen protons in methylene region (δ 1.52-3.10) and the signals corresponding to five aromatic protons as multiplet (δ 7.23-7.52), and its ^{13}C-NMR spectrum ($CDCl_3$) showed seven signals corresponding to eight methylenes at 22.6, 22.7, 23.0(two methylenes), 25.5, 26.3, 28.1, and 33.1 ppm and eight signals corresponding to aromatic carbons at 127.4(d), 127.6(s), 128.0(d, two carbons), 129.0(d, two carbons), 141.4(s), 144.9(s), 153.1(s), and 155.9(s) ppm. Dehydrogenation of the product with 5% palladium carbon under argon gave 6-phenylphenanthridine (2) in 50% yield, which was identical with the authentic sample of 6-phenylphenanthridine (2) synthesized on the route reported by Bartram, Harrison, and Short.[4] Based on the above results, we assigned the structure (3) to the major product produced by the thermolysis of cyclohexanone oxime O-benzyl ether (1).



(1)

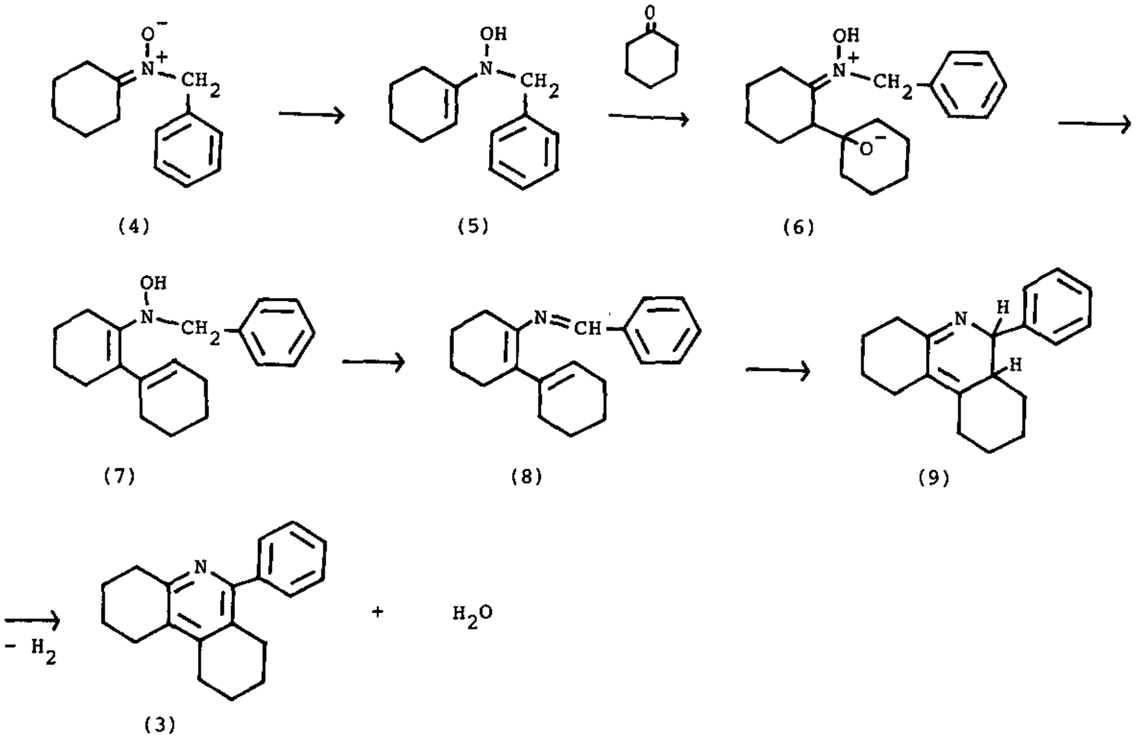


(2)



(3)

Though the mechanism for this reaction has not been clear at present, it is suggested from the molecular formula of the product (3) that cyclohexanone or its equivalent should be produced from the oxime (1) by hydrolysis of the oxime moiety, which would be caused by moisture existing in air. When a 1,2-shift of benzyl group in the starting material (1) was allowed as the first stage, the nitrone (4) would be formed and tautomerized to the hydroxylamine (5). Condensation of (5) with cyclohexanone followed by elimination of water would give the triene (8), which was subjected to 6π electrocyclic reaction to (9) as depicted in Chart. Dehydrogenation of (9) with oxygen in air furnished (3) and water, the latter of which would trigger further hydrolysis of the oxime (1) yielding cyclohexanone.



Chart

Experimental

Cyclohexanone oxime O-benzyl ether (1) :

A solution of cyclohexanone (5g), O-benzylhydroxylamine hydrochloride (8.5g), and anhydrous sodium acetate (4.2g) in ethanol (100ml) was refluxed for 3 h. After evaporation of the solvent, the residue was extracted with chloroform. The chloroform extract was washed with water, dried with magnesium sulfate, and evaporated to dryness to give cyclohexanone oxime O-benzyl ether as an oil. Yield ; 9.5g (92%). bp 130 °C/5mm.. IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 1645. ^{1}H-NMR ($CDCl_3$) δ : 5.06 (2H, s, CH_2), 7.33 (5H, s, aromatic-H). MS m/z : 203.1311 (calcd. 203.1310)

Thermolysis of the ether (1) :

Cyclohexanone oxime O-benzyl ether (1) (400mg) in a sealed tube was heated at 175-180 °C (bath temperature) for 45 h to give a tarry product which was taken up in chloroform. The chloroform solution was washed with water, dried, and concentrated to dryness to leave an oily residue which exhibited several spots on thin layer chromatography with a silica gel plate [Silica Gel F_{254}(Merck), $CHCl_3$: MeOH = 20 : 1]. Separation of the mixture by repeated preparative thin layer chromatography afforded 1,2,3,4,7,8,9,10-octahydro-6-phenylphenanthridine (3) (180mg, 35% yield) as colorless crystals, mp 81.5-83 °C (from ether-petroleum ether), [the picrate, mp 161-162 °C (from ethanol)]. IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 1560. ^{1}H-NMR ($CDCl_3$) δ : 1.52-3.10 (16H, CH_2x8), 7.23-7.52 (5H, aromatic-H). ^{13}C-NMR ($CDCl_3$) ppm : 22.6 (t), 22.7 (t), 23.0 (t, x2), 25.5 (t), 26.3 (t), 28.1 (t), 33.1 (t), 127.4 (d), 127.6 (s), 128.0 (d, x2), 129.0 (d, x2), 141.4 (s), 144.9 (s), 153.1 (s), 155.9 (s). UV λ_{max}^{MeOH} nm (logε) : 282 (3.79), 236 (3.83). MS m/z : 263. Anal. Calcd for $C_{19}H_{21}N$: C, 86.64 ; H, 8.04 ; N, 5.32. Found : C, 86.63 ; H, 8.21 ; N, 5.33

Dehydrogenation of (3) :

A mixture of (3) (40mg) and 5% Pd-C (50mg) was heated at 220 °C (bath temperature) under argon for 24 h. The product was chromatographed on silica gel. Elution with chloroform gave 6-phenylphenanthridine (2) (20mg) as colorless crystals, mp 103 °C (from petroleum ether), the picrate, mp 252-254 °C (from acetone-ethanol). ^{1}H-NMR ($CDCl_3$) δ : 7.42-8.75 (13H, m, aromatic-H). MS m/z : 255.1048 (calcd. 255.1048)

REFERENCES

1. H. Irie, I. Katayama, Y. Mizuno, J. Koyama, and Y. Suzuta, Heterocycles, 1979, **12**, 771.
2. T. Fujii, C.C. Wu, and S. Yamada, Chem. Pharm. Bull., 1967, **15**, 345.
3. Chemical Abstracts, 1968, **68**, 29621t and 1969, **70**, 19950b.
   Since the mp 137-139 °C of the octahydro-6-phenylphenanthridine (3) picrate reported in the literatures[3)] was different from ours, mp 161-162 °C, we carried out the synthesis of 6-phenylphenanthridine (2) for confirmation of the structure (3).
4. C.A. Bartram, D. Harrison, and W.F. Short, J. Chem. Soc., 1958, 1158.

Received, 24th February, 1982