Epoxidation of 2-Azabicyclo[2.2.1]hept-5-en-3-one

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Epoxidation of 2-azabicyclo[2.2.1]hept-5-en-3-one has been performed in high yield with potassium hydrogen persulfate at *p*H 6, ^{1}H nmr data indicate an exo stereoconfiguration of the epoxide.

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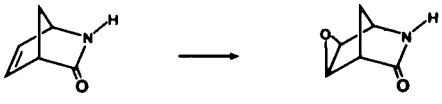
2-Azabicyclo[2.2.1]hept-5-en-3-one (**1**) [1,2] has been used as a starting material for the synthesis of a variety of carbocyclic ribo-lyxo-xylo- and arabino-furanosyl amines that in turn led to the corresponding carbocyclic nucleosides [3-5]. But the lactam **1** has not been used to obtain the cyclopentyl precursors of the 2'- or 3'-deoxycarbocyclic nucleosides which have been obtained from 5-norbornen-2-yl acetate [6-8]. We have envisaged the synthesis of the carbocyclic analogs of 2'- or 3'-deoxyribofuranosylamines from the epoxide derivative of **1** but the difficulties to epoxidize **1** with peracids like *m*-chloroperbenzoic acid (MCPBA) may explain that this epoxide was never reported.



1 **2**

Thus, the epoxidation of **1** with MCPBA in methylene chloride at 0° followed by usual work-up always led, in our hands, to mixtures from which **2** was at most isolated in low yield (< 15%). In contrast, potassium hydrogen persulfate (oxone) was able to perform cleanly the epoxidation of **1** in high yield under *p*H-controled conditions [9].

The ^{1}H nmr spectra of the two epoxide isomers of **1** are expected to be quite different. Thus exo protons (in the endo epoxide) should resonate downfield relative to the endo protons (in an exo epoxide) as observed in norbornenediol [10]. Hence the ^{1}H nmr data indicated that only one isomer was obtained. Proof of the exo configuration of **2** was completed by spin-decoupling experiments which showed that H-5 had a coupling constant of 1.5 Hz to H-4. This value is in full agreement with a dihedral angle formed by H-5 and H-4 near 90° according to the Karplus equation and therefore in favor of the exo epoxide **2**.

The results reported in this communication emphasize the interest of alkene epoxidation with potassium hydrogen persulfate around neutral *p*H in view of the instability of similar epoxides under acidic conditions [11].

Further epoxide **2** should lead after its selective reduction to the monoalcohol, to a new intermediate for the synthesis of cyclopentyl analogs of 2'- or 3'-deoxyribofuranosylamines *via* the synthetic sequence already described by Daluge and Vince [2].

EXPERIMENTAL

The melting point was taken on a Kofler hot stage apparatus and is uncorrected. Nuclear magnetic resonance (^{1}H nmr) spectra were obtained with a Varian XL100 at 100 MHz. The chemical shift values are expressed in δ values (parts per million) relative to tetramethylsilane. Elemental analyses were performed by the "Service de Microanalyses", CNRS-ICSN, 91190 Gif sur Yvette, France.

2-Azabicyclo[2.2.1]hept-5-en-3-one Epoxide (2).

A solution of the olefin **1** (1.09 g, 10 mmoles) in methanol (30 ml) was added in one portion to oxone (40 mmoles) in water (100 ml). The *p*H was adjusted to 6 during the entire reaction by dropwise addition of potassium hydroxide (1*M* in water). The reaction mixture was stirred for 5 hours at room temperature and extracted with methylene chloride. Crystallization from diethyl ether yielded an analytical sample of 2-azabicyclo[2.2.1]hept-5-en-3-one epoxide (**2**) (1 g, 80%), mp 146°; ^{1}H nmr (deuteriochloroform): 6.26 (1H, NH), 3.90 (m, 1H, H1), 3.68 (doublet of triplets, 1H, H6, J_{5-6} = 3.6 Hz), 3.58 (doublet of doublets, 1H, H5, J_{5-4} = 1.5 Hz), 2.90 (m, 1H, H4), 1.88 (doublet of quartets, 1H, H7b), 1.67 (doublet of quartets, 1H, H7a, J_{7a-b} = 9.8 Hz, J_{7a-H4} = 1.5 Hz = J_{7a-H1}).

Anal. Calcd. for $C_6H_7NO_2$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.37; H, 5.55; N, 11.24.

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