STEREOISOMERIC CARBOXAMIDES OF THE BICYCLO[2,2,1]HEPTENE SERIES IN THE EPOXIDATION REACTION

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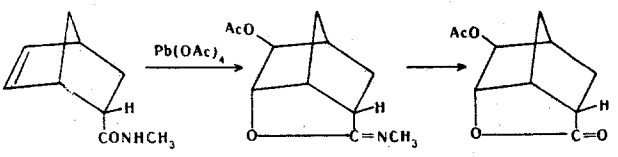
The epoxidation of isomeric carboxamides of the bicyclo[2,2,1]heptene series has been studied; in the case of exo-carboxamides it leads to expoxides, and in the case of endo-carboxamides to tricyclic lactones.

The influence of the spatial factor on the direction of the epoxidation reaction in a number of stereoisomeric derivatives of norbornene has been the subject of several investigations. With the exo arrangement of the functional groups, the sole reaction product was an epoxide [1, 2].

The endo configuration of carboxy [1, 3], hydroxymethyl [2, 4], and methoxycarbonyl [5] groups led completely or partially to the formation of tricyclic structures containing heteroatoms.

A similar pattern was observed in the oxidation of endo amides of the norbornene system with lead tetraacetate and with thallium triacetate [6, 7].



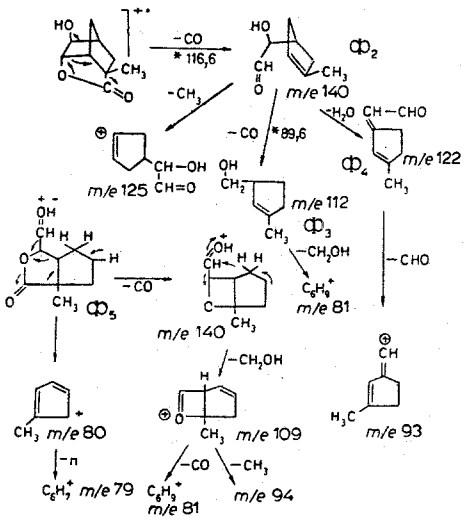
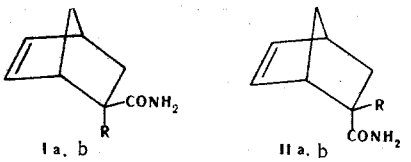


Fig. 1. Fragmentation pathways for the lactone of exo-5-endo-6-dihydroxy-exo-2-methylbicyclo[2,2,1]heptane-endo-2-carboxylic acid.

The epoxidation of the endo amides of the bicyclo[2,2,1]-heptene series has not been described in the literature. Bicyclo[2,2,1]hept-5-ene-2-carboxamide and 2-methylbicyclo-[2,2,1]hept-5-ene-2-carboxamide (the exo and endo stereoisomers of (I) and (II)) have been synthesized from the bicyclic unsaturated acids through the acid chlorides [8, 9].



I, II a R=H, b R=CH3

The oxidation of the exo-carboxamides (Ia, b) containing a strained double bond takes place readily with the formation of the corresponding epoxides. The reaction apparently proceeds in stereochemically homogeneous fashion with the formation of an oxirane having the exo configuration of the oxirane ring.

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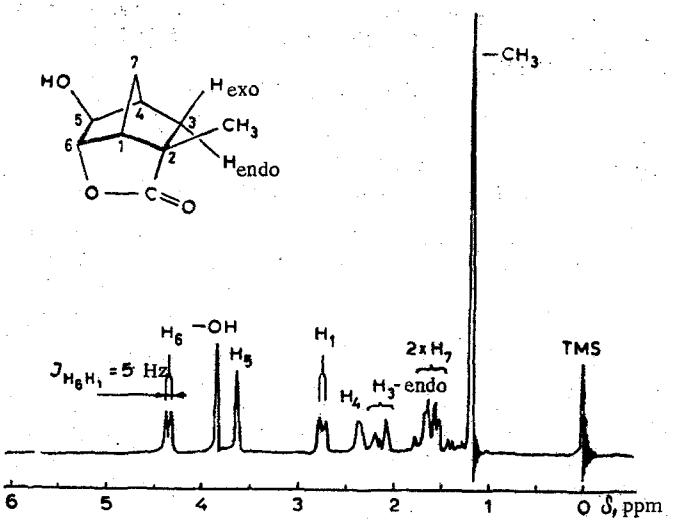
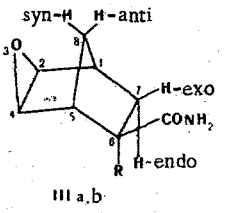


Fig. 2. PMR spectrum of the lactone of exo-5-endo-6-dihydroxy-exo-2-methylbicyclo[2,2,1]heptane-2-carboxylic acid.

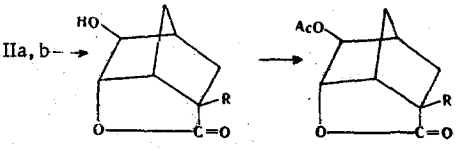
This is shown by the PMR spectrum of endo-6-methyl-3-oxatricyclo[3,2,1,$O^{2,4}$]-octane-exo-6-carboxamide (IIIb) recorded at a frequency of 100 MHz.

In favor of the exo configuration of the oxirane ring is the considerable nonequivalence of the 8-syn and 8-anti protons, which resonate in the form of an AB quadruplet with a geminal constant J = 11 Hz. The assignment of the resonance lines of the protons was based on the magnetic anisotropic influence of the oxirane ring and of the orbitals of the unshared pair of electrons of the oxygen atom in it, which leads to a shift in the resonance signal of the syn-proton in the downfield direction [10].



III a,b

The exo configuration of the amide grouping is shown by the small ($\Delta\delta$ 0.06 ppm) nonequivalence of the protons attached to the oxirane ring and the considerable nonequivalence of the protons of the 7-CH_2 group ($\Delta\delta$ 1.5 ppm), which resonate in the form of a AB quadruplet each component of which is split into a doublet under the action of the 1-H proton.



IVa, b Va, b

The epoxidation of the stereoisomeric endo-carboxamides (IIa, b) leads to the formation of lactones, thanks to the nucleophilic attack of the carbon atom of the carbonyl group in the direction of the carbon atom bearing the positive charge in the intermediate complex formed by the electrophilic attack of a peracid on the double bond of the bicycloheptene.

The lactones (IVa, b) give a positive test for a vicinal diol with periodic acid, which shows the absence of a Wagner–Meerwein rearrangement.

The structure of the lactone (IVb) was confirmed by its mass spectrum. The primary process of decomposition of the molecular ion, which is fairly intensive, was the loss of the carbonyl group, confirmed

by a metastable transition. In addition to the typical lactone nature of the decomposition, the molecular ion underwent the fragmentation characteristic for alicyclic alcohols, with the cleavage of the α,β carbon–carbon bond with respect to the hydroxy group. The results of this investigation are given in Fig. 1.

A definitive proof of the structure of the lactone became possible after an analysis of the PMR spectrum recorded at a frequency of 60 MHz at different temperatures and at a frequency of 100 MHz (Fig. 2). The assignment of the lines was made on the basis of literature information and the temperature dependence of the spectrum. With a rise in the temperature of the sample, the broadened singlet line at δ 3.85 ppm shifted upfield (at 50°C, δ 3.40 ppm), which shows that it was due to a OH group participating in an intramolecular bond. The singlet line at δ 3.65 ppm must be ascribed to the endo-5-H proton, in agreement with literature information for a homolog of the lactone under consideration [11, 12]. The 1-H and 6-H protons form a AB spin system with a constant $J_{AB} = 5$ Hz, while δ for 1-H is 2.75 ppm, and δ for 6-H is 4.37 ppm. The components of the AB quadruplet undergo successive spin–spin splitting with a small constant because of interaction with the endo-5-H and the 7-H. The doublet of the proton of the endo-3-H has a shift of δ = 2.14 ppm, and the complex multiplet of the exo-3-H is at the bottom of the sharp singlet line of the CH_3 group. The multiplet of the methylene group at 7-C has a shift of $\delta = 1.59$ ppm.

The acylation of the hydroxy lactones (IVa, b) led to the corresponding acetates (Va, b).

EXPERIMENTAL

To estimate the individuality of the substances obtained we used thin-layer chromatography on a nonfixed layer of alumina of activity grade II [ether; ether–ethanol (50:1); chromatograms revealed in iodine vapor].

The mass spectra of the substances obtained were taken on a IKS-14 instrument in paraffin oil.

The mass spectrum of the lactone of exo-5-endo-6-dihydroxy-exo-2-methylbicyclo[2,2,1]heptane-endo-2-carboxylic acid (IVb) was taken on a MKh-1303 instrument with a modified system for introduction into the ion source and oscillographic recording at an energy of the ionizing electrons of 20 eV, an emission current of 150 mA, and an accelerating voltage of 2 kV.

The NMR spectra of the lactone (IVb) were taken on JNM-C-60HL and JNM-4H-100 instruments (of the Japanese firm of JEOL).

3-Oxatricyclo[3,2,1,$0^{2,4}$]octane-exo-6-carboxamide (IIIa) was obtained from phthalic anhydride, concentrated H_2O_2, and bicyclo[2,2,1]hept-5-ene-exo-2-carboxamide (Ia) [8] as described by Malinovskii et al. [13]. Yield 55.5%, mp 164–165°C (benzene), R_f 0.2 [ether–ethanol (50:1)]. Found %: C 63.2; H 7.0; N 8.9. $C_8H_{11}NO_2$. Calculated %: C 62.7; H 7.2; N 9.1. IR spectrum, cm^{-1}: 1656, 1626, 850.

endo-6-Methyl-3-oxatricyclo[3,2,1,$0^{2,4}$]octane-exo-6-carboxamide (IIIb) was obtained from phthalic anhydride, concentrated hydrogen peroxide, and endo-2-methylbicyclo[2,2,1]hept-5-ene-2-carboxamide (Ib) [8] by the method for the synthesis of substituted epoxy carboxamides [13]. Yield 39%, mp 169–170°C (benzene), R_f 0.2 [ether–ethanol (50:1)]. Found %: C 64.5; H 8.0; N 8.1. $C_9H_{13}NO_2$. Calculated %: C 64.6; H 7.8; N 8.4. IR spectrum, cm^{-1}: 1632, 1598, 850.

Lactone of exo-5-endo-6-Dihydroxybicyclo[2,2,1]heptane-endo-2-carboxylic Acid (IVa). A mixture of 5.92 g (0.04 mole) of phthalic anhydride, 1.6 g (0.04 mole, 1.2 ml) of 85% hydrogen peroxide, and 0.6 g (0.01 mole) of urea in 10 ml of absolute ether was stirred at 20–25°C for 5 h, and then 1.51 g (0.01 mole) of bicyclo[2,2,1]hept-5-ene-endo-2-carboxamide (IIa) [8] was added in portions at 20°C. After the end of oxidation (as shown by TLC), the reaction mixture was treated with chloroform and with a saturated solution of sodium bicarbonate, and the aqueous solution was extracted with chloroform. The chloroform solution was dried and the solvent was evaporated off. Yield 19.5%, mp 157–158°C (hexane–benzene) [2], R_f 0.1 (ether). Found %: C 62.4; H 6.7. $C_8H_{10}O_3$. Calculated %: C 62.3; H 6.5. IR spectrum, cm^{-1}: 3300, 1760.

Lactone of exo-5-endo-6-Dihydroxy-exo-2-methylbicyclo[2,2,1]heptane-endo-2-carbonic Acid (IVb). This was obtained from exo-2-methylbicyclo[2,2,1]hept-5-ene-endo-2-carboxamide (IIb) in the same way as the preceding lactone. Yield 89%, mp 106–107°C (hexane–chloroform), R_f 0.4 (ether). Found %: C 64.6; H 7.2. $C_9H_{12}O_3$. Calculated %: C 64.3; H 7.1. IR spectrum, cm^{-1}: 3420, 1752.

Lactone of exo-5-Acetoxy-endo-6-hydroxybicyclo[2,2,1]heptane-endo-2-carboxylic Acid (Va). A mixture of 0.77 g (0.005 mole) of the lactone (IVa), 0.5 ml of acetic acid, and 0.6 ml of pyridine was boiled in 10 ml of chloroform on the water bath for 2 h. After the usual working up, the yield was 74.7%, mp 96°C (hexane) [2], R_f 0.5 (ether). Found %: C 60.3; H 6.2. $C_{10}H_{12}O_4$. Calculated %: C 61.22; H 6.2. IR spectrum, cm^{-1}: 1769, 1713.

The lactone of exo-5-acetoxy-endo-6-hydroxy-exo-2-methylbicyclo[2,2,1]heptane-endo-2-carboxylic acid (Vb) was obtained in the same way as the preceding lactone (Va). Yield 67.6%, mp 70-70.5°C (hexane), R_f 0.8 (ether). Found %: C 63.2; H 6.6. $C_{11}H_{14}O_4$. Calculated %: C 62.8; H 6.7. IR spectrum, cm^{-1}: 1773, 1734.

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