LITERATURE CITED

1. N. I. Belousov, V. A. Khan, and T. P. Berezevskaya, Khim. Prir. Soedin., 472 (1990).
2. F. W. Wehrli and T. Nishida, "The use of carbon-13 NMR spectroscopy in natural products chemistry," Fortschr. Chem. Org. Naturst., (1979).
3. A. V. Tkachev, O. P. Toropov, G. E. Sal'nikov, Yu. V. Gatilov, and I. Yu. Bagryanskaya, Zh. Org. Khim., 25, No. 2, 249 (1989).
4. N. P. Kir'yalov, Zh. Obshch. Khim., 19, 2123 (1949).
5. L. Dolejs and F. Šorm, Tetrahedron Lett., No. 17, 1 (1959).
6. G. V. Pigulevskii and N. V. Belova, Zh. Obshch. Khim., 34, No. 4, 1345 (1964).
7. Y. Naya, Y. Nagahama, and M. Kotake, Heterocycles, 10, 29 (1978).
8. E. Talman, P. E. J. Verwiel, and A. C. Lakwijk, Adv. Mass Spectrom. Biochem. Med., 2, 215 (1977).
9. U. Buckert and N. L. Allinger, Molecular Mechanisms, ACS Monograph No. 177, Am. Chem. Soc., Washington, D.C. (1982).

BECKMANN REARRANGEMENT OF THE E ISOMER OF CIS-4,6,6-TRIMETHYLBICYCLO[3.1.1]-HEPTAN-2-ONE OXIME

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The individual E isomer of 4,6,6-trimethylbicyclo[3.1.1]heptan-2-one oxime has been obtained, and its transformations under the conditions of acid catalysis have been studied. The action of sulfuric acid on a solution of the oxime in acetonitrile leads to the selective formation of 5,7,7-trimethyl-2-azabicyclo[4.1.1]octan-3-one, while the action of hydrochloric acid with heating gives 4-isopropyl-3-methylaniline.

The interest of research workers in the Beckmann rearrangement is due to the fact that the amides formed as a result of this reaction are used as intermediates for obtaining pharmacologically active azacyclic compounds [1, 2]. However, in the majority of cases the rearrangement of terpene bicyclic oximes forms a mixture of unsaturated nitriles [3, 4]. This circumstance is obviously connected with the high degree of strain of the carbon skeleton of the derivatives of a number of bicyclo[2.2.1]- and -[3.1.1]heptanes, leading to rupture of a carbon–carbon bond and to dehydration. Thus, under the conditions of the Beckmann rearrangement, oximes of ketones of the pinane series are mainly converted into mixtures of unsaturated nitriles, and only in some cases have the corresponding lactams been obtained, in low yield. Only from nopinone oxime by the action of benzenesulfonyl chloride in the presence of sodium hydroxide has 7,7-dimethyl-2-azabicyclo[4.1.1]octan-3-one been obtained, with a yield of 43% [5]. When pinocamphone and isopinocamphone oximes were treated with p-toluenesulfonyl chloride in the presence of NaOH [6] or with polyphosphoric acid [2] the corresponding lactams were again obtained, but only in trace amounts. The action of sulfuric acid on verbanone oxime (I) formed nitriles exclusively [1], and only under the action of p-toluenesulfonyl chloride in pyridine on verbanone oxime, in the form of a mixture of the E and Z isomers in a ratio of 3:1 was a multicomponent mixture obtained from which it was possible to isolate a 2-azalactam [7].

The aim of the present work was to study the behavior of the oxime of verbanone (cis-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one) (I) under the conditions of the Beckmann rearrangement.

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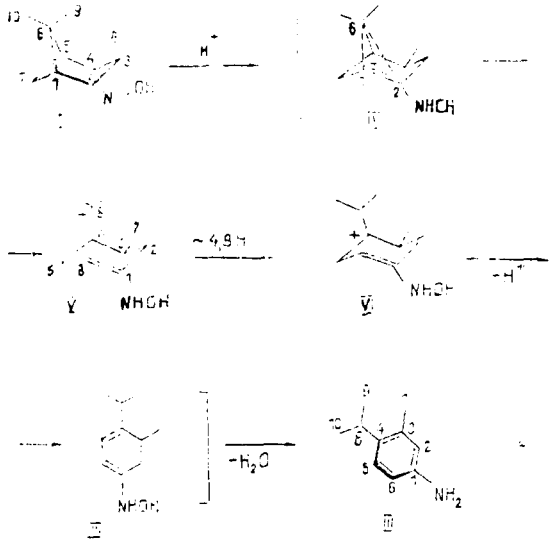
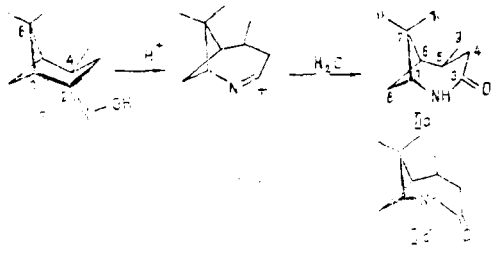
The oxime (I) was obtained by a known procedure [4] from cis-verbanone. By repeated recrystallization from ethanol of the reaction product we succeeded for the first time in separating and characterizing the individual E isomer of the oxime (I). It is known from the literature [8, 9] that the signal of a proton in the α position to a hydroxyimino group undergoes a downfield displacement by ~0.4 ppm with a change in the orientation of the hydroxy group from anti to syn, and in the Z and E isomers of verbanone oxime the signals of the 1-H protons are found at 3.28 and 2.86 ppm, respectively [7]. In the spectrum of the oxime isomer that we had isolated the shift of the 1-H proton was 2.85 ppm and that of the 3-H_e proton 3.02 ppm (d, ^2J = 12.0 Hz). The closeness of the values of the chemical shifts in the ^{13}C NMR spectrum of the C-1 and C-5 carbon atoms (33.1 and 33.2 ppm) was also evidence in favor of the E configuration of the oxime (I).

The performance of the Beckmann rearrangement by the procedure of [10] under the action of concentrated hydrochloric acid with the boiling of the reaction mixture unexpectedly led to the selective transformation of the oxime (I) into an aromatic amine. On the basis of an analysis of the results of IR, mass, and ^1H and ^{13}C NMR spectroscopies (see the Experimental section) the amine (III) was ascribed the structure of 4-isopropyl-3-methylaniline.



The "nonclassical" cation (IV) probably gave the intermediate (V) as a consequence of a redistribution of charges leading to the rupture of the C-1—C-6 bond. This intermediate, as the result of a 4,8-hydride shift and the ejection of a proton by the cation (VI), was converted into compound (VII) the dehydration of which led to the formation of the aromatic amine (III).

It was considered previously that the action of sulfuric acid on verbanone oxime (I) formed a mixture of unsaturated nitriles exclusively [1]. However, the procedure for obtaining lactams that we have developed, consisting in the slow addition of concentrated sulfuric acid to a solution of the oxime in acetonitrile at room temperature, usually permits bicyclic lactams to be obtained with good yields. In the case of verbanone oxime the yield of 5,7,7-trimethyl-2-azabicyclo[4.1.1]octan-3-one after purification by vacuum distillation amounted to 60%.



The results of IR, mass, and ^1H spectroscopies unambiguously confirmed the structure of the product as the 2-azalactam (II). Thus, the IR spectrum of this compound contained bands at 3270 and 3200 cm^{-1}, characteristic for the vibrations of a N–N bond, and a band at 1650 cm^{-1}, characteristic for the vibrations of a lactam C=O bond. The mass spectrum of this compound contained the peak of the molecular ion, M^+ 167, with an intensity of 13% of the maximum in spectrum. In the ^1H NMR spectrum the signal of the 1-H proton, present in the α-position to the NH group, appeared in the form of a doublet of triplets with a chemical shift of 3.13 ppm. A spin-spin coupling constant (SSCC) of 7.2 Hz corresponds to the interaction of the 1-H proton with the 8-H-syn and the N–H protons and a SSCC of 3.6 Hz to interaction with the 8-H-anti proton. The signal of the 4-H_e pseudoequatorial proton appeared in the form of a doublet of doublets with a chemical shift of 2.57 ppm. The geminal SSCC had a value of 18.2 Hz, which is characteristic for the protons of methylene group in the α position to a carbonyl group. A SSCC value of 5.4 Hz corresponded to the interaction of the 4-H_e proton with the 5-H proton. The signal of the pseudoequatorial proton at the C-4 atom also had the form of a doublet of doublets, with a chemical shift of 3.01 ppm; the constant of its coupling with the 5-H proton was 9.0 Hz and corresponded to an axial-axial interaction of these protons. Thus, it was possible to conclude that the azalactam (II) existed predominantly in the conformation with the pseudoequatorial orientation of the C_5–CH_3 methyl group (IIa), and not in the conformation (IIb) with the axial orientation of the methyl at C-5.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were taken on a Bruker WM-360 instrument with a resonance frequency of 360.134 MHz for ^1H nuclei and 90.56 MHz for ^{13}C. The concentration of the solutions was ~10%. The chemical shifts were determined relative to the internal standard HMDS. IR spectra were taken on a UR-20 instrument. Mass spectra were recorded on a MKh-1320 instrument.

The course of the reaction was followed and the purity of the products synthesized was checked by GLC on a Chrom-5 chromatograph with a glass column (2 × 2000 mm) filled with the support Chromaton-N-AW-DMCS (0.16-0.20) impregnated with Apiezon L.

Verbanone oxime (I), obtained by the procedure of [4], had bp 125-126°C (5 mm Hg). The individual E isomer, with mp 66-67°C, was isolated by three recrystallizations of the reaction product from ethanol. According to the literature, the melting point of a mixture of the E and Z isomers in a ratio of 3:1 was 64-69°C [7]. IR spectrum (λ_{max}^{KBr}, cm^{-1}): 3280 (OH), 1670 (C=N), 970 (NOH). Mass spectrum (m/z): 167 (M^+, 27%), 152, 150, 123, 110, 83 (100%), 55.41. PMR spectrum (δ, ppm, CCl_4): 0.98 (s, 3H, 7-CH_3-syn), 1.14 (d, 3H, 4-CH_3), 1.32 (s, 3H, 7-CH_3-anti), 1.95 (m, 1H, 4-H), 2.24 (m, 1H, 5-H), 2.46 (dd, 1H, 3-H_a, ^2J = 12.0 Hz, ^3J_a = 9.6 Hz), 2.60 (m, 2H, 7-H_2), 2.85 (m, 1H, 1-H), 3.02 (d, 1H, 3-H_e, ^2J = 12.0 Hz). ^{13}C NMR spectrum (δ, ppm, CD_3OD): 22.0 q (C-8), 25.0 q (C-9 and C-10), 27.4 d (C-4), 28.5 t (C-7), 31.6 t (C-3), 33.1 d and 33.2 d (C-1 and C-5), 48.6 s (C-6), 165.4 s (C-2).

4-Isopropyl-3-methylaniline (III). A mixture of 1.5 g of the oxime (I) and 10 ml of concentrated HCl was boiled under reflux for 48 h. The precipitate that deposited from the reaction mixture after its cooling was separated off and was purified by recrystallization from ethanol. This gave 0.7 g of the pure hydrochloride of the amine (III) (42%). mp 195-196°C. IR spectrum (λ_{max}^{KBr}, cm^{-1}): 3000 (NH), 1620, 1580 (aromatic C=C). PMR spectrum (δ, ppm, CD_3OD): 1.24 (d, 6H, $CH(CH_3)_2$), 2.40 (s, 3H, 3-CH_3), 3.28 (m, 1H, $CH(CH_3)_2$), 7.25 (m, 2H), 7.39 (d, 1H). ^{13}C NMR spectrum (δ, ppm, CD_3OD): 19.2 q (C-7), 23.5 q (C-9 + C-10), 30.3 d (C-8), 121.7 d (C-5), 124.9 s (C-1), 125.4 d (C-6), 127.2 s (C-3), 127.5 d (C-2), 128.9 s (C-4).

5,7,7-Trimethyl-2-azabicyclo[4.1.1]octan-3-one (II). With constant stirring, 5.2 ml of concentrated H_2SO_4 was added slowly, dropwise, to a solution of 2.7 g of the oxime (I) in 5 ml of acetonitrile, which led to vigorous heating of the reaction mixture. Stirring was continued at room temperature for another three days and then the mixture was carefully poured into an excess of cooled aqueous ammonia and was extracted with ether, and the extract was dried with $MgSO_4$. The product obtained after the ether had been distilled off was purified by vacuum distillation. This gave 1.6 g (60%) of the pure lactam (II), bp 140°C (4 mm Hg). mp 91°C. IR spectrum (λ_{max}^{KBr}, cm^{-1}): 3270, 3200 (NH), 1650 (C=O). Mass spectrum (m/z): 167 (M^+, 13%), 152, 139, 136, 124, 109, 96, 85, 83 (100%),

71, 69, 67, 59, 55. PMR spectrum (δ, ppm, $CDCl_4$): 1.04 (s, 3H, 7-CH_3-syn), 1.09 (d, 3H, 5-CH_3, J = 6.6 Hz), 1.26 (s, 3H, 7-CH_3-anti), 1.56 (dt, 1H, 8-H-anti, ^2J = 12.0 Hz, $^3J_{8\text{-H-anti};1\text{-H}} = {}^3J_{8\text{-H-anti},6\text{-H}}$ = 3.6 Hz), 2.10 (dt, 1H, 6-H, $^3J_{8\text{-H-syn},6\text{-H}}$ = 7.2 Hz, $^3J_{6\text{-H},8\text{-H-anti}} = {}^3J_{6\text{-H},5\text{-H}}$ = 3.6 Hz), 2.22 (m, 1H, 5-H), 2.57 (dd, 1H, 4-H, ^2J = 18.2 Hz, $^3J_{4\text{-H}_e,5\text{-H}a}$ = 5.4 Hz), 2.70 (dt, 1H, 8-H-syn, ^2J = 12.0 Hz, $^3J_{8\text{-H-syn},1\text{-H}} = {}^3J_{8\text{-H-syn},6\text{-H}}$ = 7.2 Hz), 3.01 (dd, 1H, 4-H , ^2J = 18.2 Hz, $^3J_{4\text{-H}a,5\text{-H}a}$ = 9.0 Hz), 3.13 (dt, 1H, 1-H, $^3J_{1\text{-H,NH}} = {}^3J_{1\text{-H},8\text{-H-syn}}$ = 7.2 Hz, $^3J_{1\text{-H},8\text{-H-anti}}$ = 3.6 Hz). According to the literature [7]: mp 88-90°C. PMR spectrum (100 MHz, $CDCl_3$, TMS): 1.09, 1.31 (s, 6H, gem-CH_3), 1.14 (d, (3H, 5-CH_3, J = 7 Hz), 1.58 (dt, 1H, J = 12 Hz, J = 4 Hz, 8-H), 1.99-2.41 (m, 2H, 5-H and 6-H), 2.58 (dd, 1H, J = 18 Hz, J = 5 Hz, 4-H), 2.72 (dt, 1H, J = 12 Hz, J = 7 Hz, 8-H), 3.03 (dd, 1H, J = 18 Hz, J = 9 Hz, 3-H), 3.15 (triplet of broadened doublets, 1H, J = 7 Hz, J = 4 Hz, J = 1 Hz, 1-H).

LITERATURE CITED

1. G. R. Krow, Tetrahedron, 37, No. 7, 1283 (1981).
2. P. Brun, R. Furstoss, P. Teissier, W. Tubiana, and B. Waegell, C.R. Acad. Sci., Paris, 269, No. 6, 427 (1969).
3. R. W. Gottingham, J. Org. Chem., 25, 1473 (1960).
4. J. Soloducho and A. Zabza, Pol. J. Chem., 53, No. 5, 1497 (1979).
5. H. K. Hall, J. Org. Chem., 28, 3213 (1963).
6. A. Zabza, C. Wawrzenczyk, and H. Kuchynski, Bull. Acad. Pol. Sci., Ser. Sci. Chem., No. 22, 855 (1974).
7. H. Erdtman and S. Thoren, Acta Chem. Scand., 24, No. 1, p. 87 (1970).
8. A. Daniel and A. A. Pavia, Tetrahedron Lett., 1145 (1967).
9. H. Paulsen, K. Todt, and H. Ripperger, Chem. Ber., 101, 1145 (1968).
10. N. G. Kozlov and T. I. Pekhk, Zh. Org. Khim., 18, No. 5, 1118 (1982).

REACTIONS AT THE DOUBLE BOND IN THE EPOXY GROUP OF ARGLABIN

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The interaction of arglabin, a sesquiterpene lactone of the guaiane type, with peracetic acid and hydrogen chloride has been investigated. This led to the synthesis of nine compounds the structure of which have been established in the basis of spectral characteristics (IR, PMR, and mass spectra). The structures and absolute configurations of the molecules of 3α,10α-dichloro-1β,4β-dihydroxy- and 10α-chloro-1β-hydroxy-3β,4β-epoxyarglabins have been determined as 3R,10R-dichloro-1R,4R-dihydroxy-5S,6S,7S-trans-trans-guai-11(13)-en-6,12-olide and 10R-chloro-1R-hydroxy-3S,4R-epoxy-5S,6S,7S-trans-trans-guai-11(13)-en-6,12-olide, respectively.

Arglabin (I) is a sesquiterpene lactone of the guaiane type which is characteristic for the epigeal part of Artemisia glabella Kar. et Kir. (~ smooth wormwood) [1, 2]. The presence in the structure of (I) of a exomethylene group conjugated with a γ-lactone

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