Russian Journal of Organic Chemistry, Vol. 39, No. 2, 2003, pp. 183–189. Translated from Zhurnal Organicheskoi Khimii, Vol. 39, No. 2, 2003, pp. 206–212.

Sterical Hindrances as a Driving Force of Skeleton Rearrangements of Fenchone and Its Oxime in Ritter Reaction

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Received March 18, 2002

Abstract—Fenchone (1,3,3-trimethylbicyclo[2.2.1]heptan-2-one) in reaction with acetonitrile in the presence of sulfuric acid (Ritter reaction) due to steric hindrances preventing geminal addition of two nucleophile molecules gives rise to a mixture of 1,2-*exo*-diacetamido-6-*endo*,7,7-trimethylbicyclo[2.2.1]heptane, 2-*endo*,6-*exo*-diacetamido-3,3,6-trimethylbicyclo[2.2.1]heptane, and 2-*exo*,6-*exo*-diacetamido-1,3,3-trimethylbicyclo[2.2.1]heptane in the ratio of ~6 : 4 : 1. Fenchone oxime under condition of this reaction affords a mixture of stereoisomeric cis- and trans-acetamido-1-methyl-3-(α-cyanoisopropyl)cyclopentanes in 2 : 3 ratio.

We have shown previously that terpene ketones of the bicyclo[2.2.1]heptane series, namely, camphor [1], isocamphanone [2], 3-bromoisocamphanone [3], and isofenchone [4], unlike the other alicyclic ketones can be brought into Ritter reaction as substrates. As a result form the corresponding geminal diamides originating from the successive addition of two nucleophile (nitrile) molecules to the carbonyl carbon atom. Therewith in no case we observed skeletal rearrangements. We were first to establish that oximes of terpene ketones, among them those from the series of bicyclo[2.2.1]heptane, also might serve as substrates for this reaction. In the first stage of transformations arose bicyclic N-acylamidines as products of nucleophilic stabilization of the corresponding azabicyclic carbocations [5]. If a methyl group is attached to the C^1 atom of the bicyclo[2.2.1]-heptane skeleton then the forming 3-(*N*-acylamino)-2-azabicyclo[3.2.1]heptanes do not transform further under the reaction conditions. In the absence of nucleophile the acid catalysis results in the rupture of the C^1–C^2 bond, and instead of expected products of Beckmann rearrangement (lactams) arise unsaturated monocyclic nitriles.

In this study we investigated transformations under conditions of Ritter reaction of fenchone (1,3,3-trimethylbicyclo[2.2.1]heptan-2-one) (**I**) and its oxime (**II**). We found that due to significant sterical shielding of the reaction sites in these compounds their behavior was quite unlike that observed in the other bicyclic ketones and oximes under conditions of this reaction.

As a result of Ritter reaction fenchone furnished a mixture of three compounds neither of which was a geminal diamide. The major component (53% of the mixture) was isolated by fractional crystallization from ethanol. Basing on IR, ^{1}H NMR, and mass spectra it was assigned a structure of 1,2-*exo*-diacetamido-6-*endo*,7,7-trimethylbicyclo[2.2.1]heptane (**III**). Its IR spectrum contained absorption bands characteristic of carbonyl (1660 cm^{-1}) and NH (3480 and 1540 cm^{-1}) groups in substituted amides. The presence in the mass spectrum of the compound of the molecular ion M^+ 252 (19% relative to the most abundant peak) indicated addition of two acetonitrile molecules to the initial ketone. The presence in the ^{1}H NMR spectrum of a downfield signal at 4.28 ppm characteristic of a proton neighboring to amido group evidences that this compound is not a geminal diamide. The multiplicity and values of coupling constants corresponding to this signal (d.t, $^3J_{NH} \approx {}^3J_{endo,endo}$ 9.0 Hz, $^3J_{endo,exo}$ 4.6 Hz) indicate, firstly, that the said proton has *endo*-orientation and consequently the acetylamino group has *exo*-orientation; secondly, that two coupling constants beside the coupling with a proton attached to nitrogen show the presence of a methylene group in the α-position to the amide one. Three signals in the spectrum belong to the methylene groups of the skeleton: two singlets at δ 1.27 and 1.32 ppm, and a doublet at δ 1.09 ppm, ^3J 7.2 Hz. In the spectrum is also observed a signal of multiplicity characteristic of a bridgehead proton (δ 1.71 ppm, triplet, two ^3J 4.2 Hz each). These two vicinal coupling constants correspond to the presence

1070-4280/03/3902-0183$25.00

of two *exo*-directed protons in the α,α'-positions at the bridgehead. A pair of geminal protons was also identified in the spectrum with the chemical shifts 1.39 and 1.62 ppm (^2J 12.4 Hz) the multiplicity of whose signals (see EXPERIMENTAL) indicated the neighboring position to the unsubstituted bridgehead (δ 1.71 ppm), and also the presence in the α-position to this methylene group of a single proton with *exo*-orientation. Obviously this methylene group is linked to a methyl appearing in the spectrum as a doublet; taking into account the corresponding coupling constants values this methyl group was assigned an *endo*-orientation. These data permitted assignment to the reaction product the structure 1,2-*exo*-diacetamido-6-*endo*,7,7-trimethylbicyclo[2.2.1]heptane (**III**). The chemical shifts and multiplicity of signals from the other protons (see EXPERIMENTAL) also are well consistent with the assigned structure. The bonding of the second amido group to C^1 atom is additionally supported by the absence in the 4 ppm region of any signals but that mentioned above, by the larger than in the other amides downfield shift of signals from protons attached to nitrogen (6.82 and 7.36 ppm) indicating their partial chelating and closeness in space of the two acetylamino groups, and also by the value of the chemical shift of the proton adjacent to a methyl group (δ 2.12 ppm) characteristic of a proton in the α-position to an amido group.

The second compound (38% in the mixture) was separated by fractional crystallization from acetonitrile of the residue after isolation of diamide **III**. Proceeding from the spectral data this compound was assigned a structure 2-*endo*,6-*exo*-diacetamido-3,3,6-trimethylbicyclo[2.2.1]heptane (**IV**). In the IR spectrum of the compound are present the same characteristic absorption bonds as in the spectrum of diamide **III**. In the mass spectrum also appeared the molecular ion peak of 252 mass (17%) corresponding to a diamide. In the ^{1}H NMR spectrum of compound **IV** was observed a downfield signal characteristic of a proton adjoining to an amide group (δ 3.38 ppm). Alongside the coupling with the proton bonded to the nitrogen (9 Hz) the above proton is also coupled with another one (4.4 Hz). This coupling constant value indicates contiguity of an unsubstituted bridgehead (δ 2.58 ppm, doublet, ^3J 4.4 Hz); another neighboring atom is a quaternary carbon bonded to methyl groups (singlets at 1.07 and 1.27 ppm). The coupling with the bridgehead proton indicates the *exo*-orientation of the proton appearing as a signal at 3.38 ppm; consequently, the adjacent amido group is in the *endo*-orientation. The second $NHCOCH_3$ group of the compound is apparently adjacent to the methyl group whose signal appears at 1.55 ppm. The chemical shift of the latter indicates its spatial nearness to both acetylamido groups. In the spectrum are registered also a signal of proton at the second bridgehead (δ 1.73 ppm, doublet, ^3J 4.2 Hz), and signals from a pair of geminal protons neighboring to this bridgehead (2.37 ppm, doublet of doublets, H_{exo}, ^2J 14.0, $^3J_{5,4}$ 4.2 Hz; δ 2.17 ppm, doublet of doublets, H_{endo} ^2J 14.0, ^WJ 2.4 Hz). The chemical shifts of these geminal protons show the contiguity of an amido group. The second pair of geminal protons (δ 1.82 ppm, doublet of doublets, ^2J 10.2, ^WJ 2.4 Hz; δ 2.09 ppm doublet, ^2J 10.2 Hz) corresponds to the bridging methylene group C^7H_2. To the second amido group of this compound we ascribed the *exo*-orientation from the following reasons. Firstly, the signal of the *exo*-oriented proton from the adjoining methylene group appears in the weaker field. Secondly, just at this orientation of amido group attached to C^6 the neighboring methyl group occurs in the shielding field of both amido groups (a shielding from a single amido group would have resulted in methyl singlet at ~1.3 ppm). Besides the reaction mechanism proper suggests *exo*-addition of a nucleophile to nonclassical carbocations of the bicyclo[2.2.1]heptane series [6], and it will be demonstrated below in discussion on the reaction mechanism that this amido group adds in the last stage of reaction and therefore its orientation cannot change, e.g., due to rearrangement.

The isolation of the minor component of the mixture was the most difficult task, for its content was small (9%), and the residue after evaporation of the mother liquor left by separation of diamides **III** and **IV** contained all three components. We succeeded in separation of small quantities of this compound of sufficient purity for spectral measurements by utilizing its somewhat better solubility in ether compared to the other two products (see EXPERIMENTAL). The data of IR, ^{1}H NMR, and mass spectroscopy suggested for this compound a structure 2-*exo*,6-*exo*-diacetamido-1,3,3-trimethylbicyclo[2.2.1]heptane (**V**). IR and mass spectra of this compound are similar to those of substances **III** and **IV**. Unlike ^{1}H NMR spectra of compounds **III** and **IV**, that of compound **V** contains two downfield signals of protons in the α-position to amido groups (δ 3.85 and 3.96 ppm). First of these signals is a doublet of doublets where the coupling constant of 9 Hz corresponds to its coupling with the proton attached to nitrogen (this signal disappears at recording the spectrum in deuteromethanol). The constant of 2.2 Hz corresponds to *W*-coupling with a proton at C^7

atom indicating the *endo*-orientation of this proton and *exo*-orientation of the adjacent amide group. Since no more couplings with this proton are observed, obviously it has in α-positions the gem-dimethyl fragment (singlets at 1.03 and 1.24 ppm) and the substituted bridgehead atom. The second downfield signal has on the contrary a complex multiplicity (see EXPERIMENTAL) corresponding to the presence in α-position to the second amide group of a methylene fragment. Multiplicity of signals from the latter (δ 2.33 ppm, doublet of triplets H_{exo}, ^2J 14.2, $^3J_{5,4}$ and $^3J_{exo,endo}$ 4.2 Hz; δ 2.18 ppm, double doublet of doublets, H_{endo}, ^2J 14.2, $^3J_{endo,end}$ 9.0, ^WJ 2.4 Hz) indicates the contiguity of the unsubstituted bridgehead (δ 1.72 ppm, doublet, ^3J 4.2 Hz). In the spectrum was also identified a pair of geminal protons with the multiplicity of signals characteristic of the bridging methylene group C^7H_2 (see EXPERIMENTAL). Apparently the third methylene group (singlet at 1.27 ppm) of this compound is linked to the bridgehead carbon, and the structure of the minor component **V** of the reaction products corresponds to the least rearranged skeleton of the original hydrocarbon.

Apparently the following transformations of fenchone in the course of Ritter reaction result in this mixture of compounds. The addition of acetonitrile molecule to the protonated carbonyl of fenchone followed by migration of a hydroxy group to the iminium cation center gives rise to acetamido-substituted cation **VIII**, similarly to the reactions of all the ketones from the bicyclo[2.2.1]heptane series previously investigated by us. However the significant sterical screening of the C^2 atom of the ion prevents the addition of the second nucleophile molecule to the same carbon atom and excludes the formation of geminal diamide **IX**. Apparently cation **VIII** suffers a Wagner-Meerwein (WM) rearrangement; therewith at the rupture of C^1–C^6 bond arises cation **X** with an amido group at the bridgehead position. The second acetonitrile molecule adds thereto at the C^2 atom in the *exo*-position characteristic of the cationic reactions of bicyclo[2.2.1]heptane derivatives [6]. The subsequent hydration furnishes the main reaction product, 1,2-diamide **III**. If the Wagner-Meerwein rearrangement involves the cleavage of C^1–C^2 bond, then cation **XI** forms that undergoes similar transformations resulting in the second product, 2,6-diamide **IV**. Therewith the first amide group primarily added in 2-*exo*-position by the Wagner–Meerwein rearrangement acquires the *endo*-orientation. It should be noted that cations **X** and **XI**, precursors respectively of amides **III** and **IV**, under the reaction conditions can undergo interconversions through the same Wagner–Meerwein rearrangement. Consequently the prevailing formation of a certain reaction product is governed mostly by thermodynamic reasons.

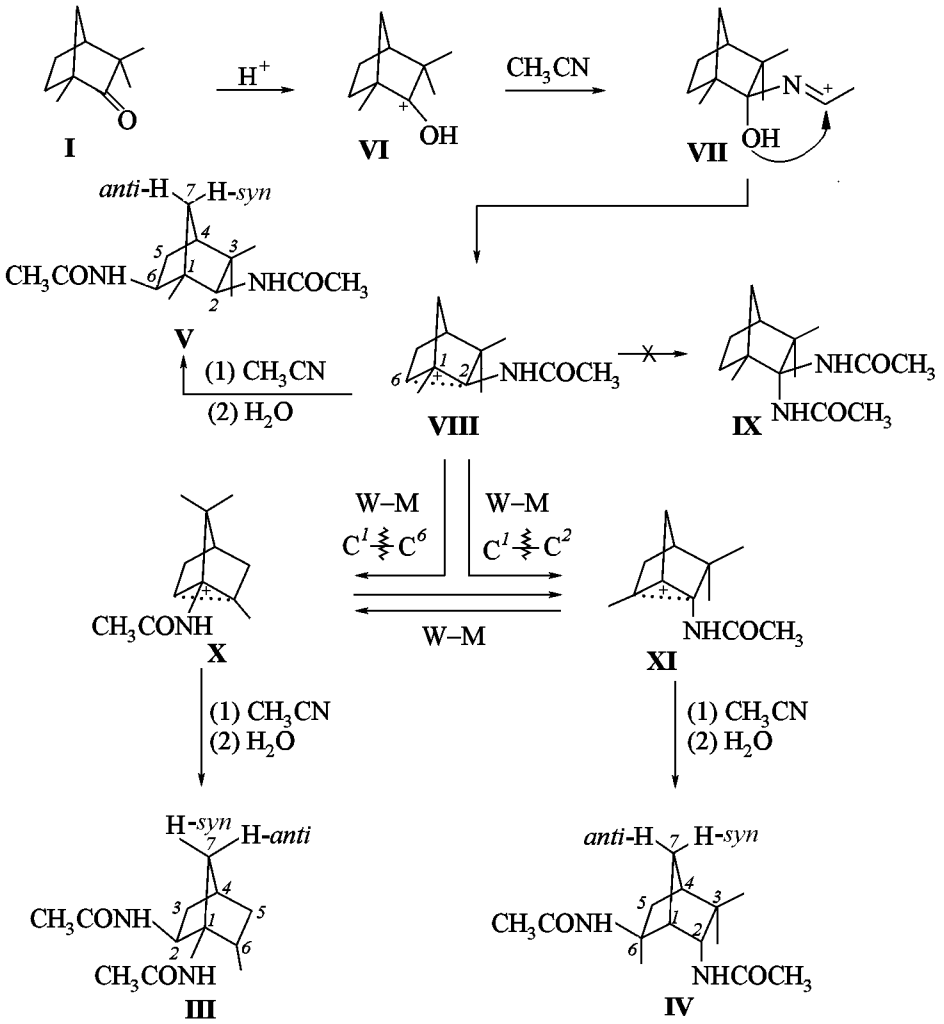
Note that similar rearrangements of the fenchane skeleton involving rupture both of C^1–C^2 and C^1–C^6 bonds occur at acid-catalyzed fenchol dehydration [7]. Thus forming the α- and β-fenchenes, 2-methylene-7,7-dimethylbicyclo[2.2.1]heptane and 2-methylene-5,5-dimethylbicyclo[2.2.1]heptane respectively, have hydrocarbon skeletons analogous to those of diamides **III** and **IV**.

The minor component of the reaction mixture, 2-*exo*,6-*exo*-diacetamido-1,3,3-trimethylbicyclo-[2.2.1]heptane (**V**), results apparently from addition of the nucleophile to C atom of cation **VIII** that does not undergo a rearrangement. It would have been expected that just this compound arising without rearrangement of the original hydrocarbon skeleton would prevail among the products. But the fraction of this compound is only 9%. It probably is due to the arrangement in succession of four of the five substituents of compound **V**, both amido and two methyl groups, which also are located virtually in the same plane. The steric interactions between them should increase the skeleton strain in the molecule and consequently make the product of such structure thermodynamically unfeasible notwithstanding the obvious kinetic advantages (Scheme 1).

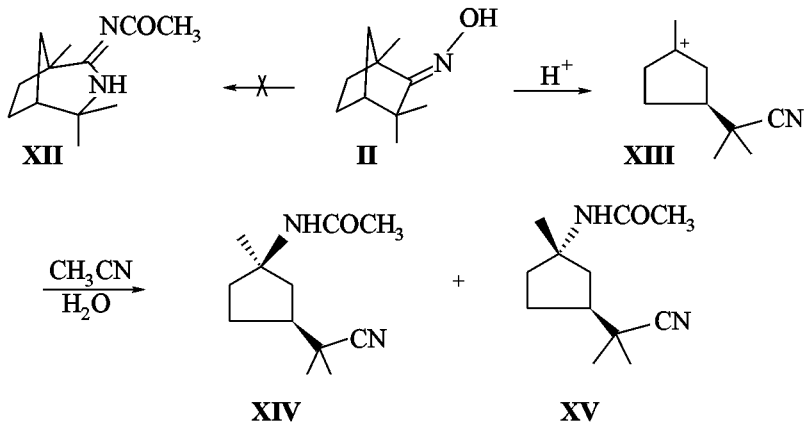
Thus fenchone transformations under conditions of Ritter reaction in contrast to the other ketones from the bicyclo[2.2.1]heptane series are accompanied by rearrangement ot the original hydrocarbon skeleton due to considerable steric shielding of the reaction site of this compound preventing addition of both nucleophile molecules to the carbonyl carbon.

Fenchone oxime (**II**) that we prepared by known procedure [8] was an individual stereoisomer as shown by ^{1}H NMR spectrum. Note that the published data do not indicate whether *E*- or *Z*-isomer arises on oximation of ketone **I**. By the following reasons we assigned the oxime obtained the *Z*-structure. The proton signals or those of methyl groups spatially close to the hydroxyl of the oximine substitutent are known [9] to suffer downfield shift as compared to the spectrum of the initial ketone. Consequently at the *E*-configuration of the oxime obtained (hydroxy group turned in the direction of the gem-dimethyl fragment) the strongest downfield shift should be observed for the signal of 3-Me-*exo* methyl group,

Scheme 1.



Scheme 2.



and the methyl group at the bridgehead should suffer the least shift. In the spectrum of the initial ketone the signals of the methyl groups appear at δ 1.00 (1-CH_3), 1.02 (3-*endo*-CH_3) and 1.11 ppm (3-*exo*-CH_3). In keeping with the above stated, in case of *E*-isomer formation the difference in chemical shifts of methyl groups attached to C^1 and C^3 should have increased to ~0.3 ppm. However the chemical shifts of methyl signals in the oxime are rather close and are equal to 1.20, 1.28, and 1.30 ppm. Thus the oxime has *Z*-configuration, and the most downfield is the signals of 1-CH_3 group (Δ +0.30 ppm compared with the spectrum of the original ketone), and two other signals belong to the groups 3-*endo*-CH_3 (Δ +0.18 ppm) and 3-*exo*-CH_3 (Δ +0.17 ppm).

Therefore if the fenchone oxime behave in Ritter reaction as a common bicyclic terpene ketone the expected product should have a structure of *N*-acetylamidine with a 3-azabicyclo[3.2.1]octane skeleton (**XII**) (Scheme 2).

However the considerable sterical shielding of the reaction site in this compound prevents addition of nucleophile (acetonitrile) molecule to the oximine carbon atom. Therefore follows cleavage of the C^1–C^2 bond with formation of a monocyclic carbocation **XIII** as it is observed when the fenchone oxime is treated with acids in the absence of nucleophiles [10].

The formation of stereoisomeric *cis*-(**XIV**) and *trans*-(**XV**) 1-acetamido-1-methyl-3-(α-cyanoisopropyl)cyclopentanes apparently occurs by acetonitrile addition to the cationic center of ion **XIII** from α- or β-site of the molecule followed by stabilization with water.

The separation of the mixture (~2 : 3) of stereoisomeric amidonitriles **XIV** and **XV** was performed by crystallization from ethanol (see EXPERIMENTAL). Their structure was established from the IR, ^{1}H NMR, and mass spectra. In the IR spectra of both compounds appear absorption bands characteristic of cyano (2230 cm^{-1}) and amide [3290 (*trans*-isomer) or 3400 (*cis*-isomer), 3080, 1640 and 1560 cm^{-1}] groups. In the mass spectra are present molecular ion peaks M^+ 208 with integral intensity of 1–2% relative to the most abundant peaks. In the ^{1}H NMR spectra of both isomers appear singlets from three methyl and one acetyl group, multiplets from three methylene groups, and a quintet from the methine proton attached to C^3. The assignment of spatial structure to stereoisomeric amidonitriles **XIV** and **XV** was done basing on comparison of the chemical shift of the signals from H^3 proton in the spectra of these compounds. It was established that the proton signal belonging to the prevailing isomer appeared in a weaker field (δ 2.31 ppm) than that of the other isomer (2.01 ppm). This fact demonstrates the presence of a 1,3-nonbonded interaction of this proton with a polar substituent, amide group at C^1, that reveals the *trans*-configuration of the prevailing isomer. Somewhat more favorable formation of a *trans*-isomer is caused by a moderate steric hindrance of the approach to one side of the molecule by the cyanoisopropyl substituent.

Thus fenchone oxime (**II**) in contrast to the other oximes of the bicyclo[2.2.1]heptane series under conditions of Ritter reaction gives rise to products of nitrile addition to monocyclic carbocation **XIII** and not to azabicyclic cation. Cation **XIII** forms under acid catalysis also in the absence of nucleophile [10]. In the latter case the stabilization of ion **XIII** occurs by ejection of a proton resulting in a mixture of α- and β-fencholene nitriles.

EXPERIMENTAL

IR spectra were measured on Fourier spectrophotometer Nicolet Protege-460. ^{1}H NMR spectra were registered on spectrometers Tesla BS-567 (100 MHz) and Bruker DRX-500 (500 MHz) from solutions in $CDCl_3$, internal reference HMDS. Mass spectra were taken on MS-GC instrument Hewlett Packard 5890/5972, column 5MS (70 eV). The course of reaction was monitored and the purity of products synthesized was checked by GLC on chromatograph Chrom-5 equipped with a glass column (2000 × 2 mm), stationary phase Apieson L on the carrier Chromaton-N-AW-DMCS (0.16–0.20).

Ritter reaction with fenchone (I) was carried out by common procedure [1–3]. To 5.0 g of fenchone dissolved in 10 ml of acetonitrile was cautiously added at room temperature 6.5 ml of sulfuric acid. The reaction mixture was stirred for 5 days and then poured into excess aqueous ammonia. The reaction products were extracted into chloroform, the extract was dried with $CaCl_2$. On removing the solvent an oily mixture was obtained consisting of diamides **III**–**V** and unreacted fenchone (**I**). Increased reaction time and acid amount resulted in higher conversion of the original ketone, but in this case formed significantly more polymerization products that hampered isolation of amides **III**–**V** to a greater extent than unreacted fenchone. The latter was easily separated by adding hexane to the products mixture. The amides poorly soluble in hexane precipitated as colorless semicrystalline solid. We obtained 2.68 g (32%) of a mixture of diamines **III**, **IV**, and **V** in 53 : 38 : 9 ratio.

The separation of this mixture turned out to be a labor-consuming procedure for the compounds possess similar solubility in all available solvents. In order to prepare small quantities of each pure compound required for spectral measurements the mixture of compounds **III**–**V** first was dissolved in methanol, and the solution was slowly evaporated at room temperature. First 200–300 mg of precipitate formed contained predominantly 1,2-diamide **III** with impurity of compound **IV**. The repeated crystallization of this precipitate from ethanol afforded virtually pure 1,2-diacetamido-6-*endo*,7,7-trimethylbicyclo-[2.2.1]heptane (**III**), mp 196–198°C. IR spectrum, cm^{-1}: 3480 (NH), 2960, 2930, 2870 (C–H), 1660 (C=O), 1540 (NH). Mass spectrum, *m/z*: 252 (19%, M^+), 237 (M^+ – CH_3), 209 (M^+ – $COCH_3$), 194 (M^+ – $NHCOCH_3$), 179 (M^+ – $NHCOCH_3$ – CH_3), 165, 151, 140, 122 (100%), 108, 98, 81, 60, 57, 43. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.09 d (3H, 6-CH_3, ^3J 7.2 Hz), 1.27 s (3H, 7-*anti*-CH_3), 1.32 s (3H, 7-*syn*- CH_3), 1.39 d.d.d. (1H, H^5_{exo} , ^2J 12.4, $^3J_{5exo,}$ $^3J_{6exo}$ *10.5*, $^3J_{5exo,4}$ 4.2 Hz), 1.62 d.d. (1H, H^5_{endo}, ^2J 12.4, $^3J_{6exo,\ 5endo}$, 4.5 Hz), 1.71 t (1H, H^4, $^3J_{4,5exo}$, and $^3J_{3exo,4}$ 4.2 Hz,), 1.98 s (3H, $COCH_3$), 2.07 s (3H, $COCH_3$), 2.12 m (2H, H^6 + H^3_{endo}), 2.62 d.t. (1H, H_{3exo}, ^2J 14.0, $^3J_{3exo,}$ $^3J_{2endo}$ 4.5, $^3J_{3exo,4}$ 4.2 Hz,), 4.28 d.t (1H, H^2, $^3J_{2,\ NH}$ ≈ $^3J_{2endo,\ 3endo}$ 9.0, $^3J_{3exo}$ 4.5 Hz), 6.82 br.s and 7.36 br.s (2NH).

2-*endo*,6-*exo*-Diacetamido-3,3,6-trimethylbicyclo[2.2.1]heptane (IV) (second component of the reaction products). The remaining ethanol solution was evaporated till the most part of compound **III** precipitated (till its content in the mother liquor according to GLC was less than 10%). Diamide **IV** also partly precipitated, but its fraction in the solution grew to 65–70%. This solution was evaporated to dryness, and the residue was dissolved in acetonitrile, and the solution was left to evaporate at room temperature. The first portion of separated crystals (200–300 mg) contained predominantly compound **IV**, and it was repeatedly crystallized from acetonitrile. mp 168–169°C. IR spectrum, cm^{-1}: 3450 (NH), 2980, 2950, 2860 (C–H), 1660 (C=O), 1550 (NH). Mass spectrum, *m/z*: 252 (17%, M^+), 237 (M^+ – CH_3), 209 (M^+ – $COCH_3$), 194 (M^+ – $NHCOCH_3$), 180, 166, 152, 141, 122, 121, 109 (100%), 98, 86, 81, 60, 57, 43. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.07 s (3H, 3-*exo*-CH_3), 1.23 s (3H, 3-*endo*-CH_3), 1.55 s (3H, 6-*endo*-CH_3), 1.73 d (1H, H^4, $^3J_{5exo,4}$ 4.2 Hz), 1.82 d.d. (1H, H^7_{syn}, ^2J 10.2, $^WJ_{7syn,\ 5endo}$ 2.4 Hz), 1.86 s (3H, $COCH_3$), 1.92 s (3H, $COCH_3$), 2.09 d (1H, H^7_{anti} ^2J 10.2), 2.17 d.d. (1H, H^5_{endo}, ^2J 14.0, $^WJ_{5endo,\ 7syn}$ 2.4 Hz), 2.37 d.d. (1H, $H_{5exo,}$ ^{2}J 14.0, $^3J_{3exo,}$ *4 4.2 Hz), 2.58 d (1H,* H^1, $^3J_{1,\ 2exo}$ 4.4 Hz), 3.38 d.d. (1H, H^2, $^3J_{2,NH}$ 8.8, $^3J_{1,\ 2exo}$ 4.4 Hz,), 5.60 br.s and 5.80 br.s (2NH).

2-*exo*,6-*exo*-Diacetamido-1,3,3-trimethylbicyclo-[2.2.1]heptane (V). In order to isolate the minor component the remaining acetonitrile solution was evaporated till the main part of compounds **III** and **IV** precipitated. Then from the residual solution acetonitrile was distilled off to dryness. The residue contained all three amides in comparable quantities. It was dissolved in a minimal volume of ethyl ether. As the solvent evaporated at room temperature most part of amides **III** and **IV** precipitated, and the solution was enriched with the minor component **V**. After the solution evaporated to a half of its initial volume it was decanted from the precipitate, the ether was distilled off, and the residue was crystallized from anhydrous acetone. After 3–4 recrystallizations we succeeded in isolating 30–40 mg of pure compound **V**, mp185–186°C. IR spectrum, cm^{-1}: 3430 (NH), 2980, 2940, 2870 (C–H), 1660 (C=O), 1560 (NH). Mass spectrum, *m/z*: 252 (9%, M^+), 237 (M^+ – CH_3), 209 (M^+ – $COCH_3$), 194 (M^+ – $NHCOCH_3$), 180, 167, 165, 151, 140, 122, 121, 108, 98 (100 %), 81, 70, 60, 59, 57, 43. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.03 s (3H, 3-*endo*-CH_3), 1.24 s (3H, 3-*exo*-CH_3), 1.27 s (3H, 1-CH_3), 1.72 d (1H, H^4, $^3J_{5exo,4}$ 4.2 Hz), 1.88 s (3H, $COCH_3$), 1.91 s (3H, $COCH_3$), 1.99 d.t. (1H, H^7_{syn}, ^{2}J 10.4, $^WJ_{7syn,\ 5endo}$ and $^WJ_{7syn,6endo}$ 2.2 Hz), 2.03 d.d. (1H, H^7_{anti}, ^2J 10.2, $^WJ_{7anti,2endo}$ 2.2 Hz), 2.18 d.d.d (1H, H_{5endo}, ^2J 14.2, $^3J_{5endo,6endo}$ 9.0, $^WJ_{5endo,\ 7syn}$ 2.2 Hz), 2.33 d.t. (1H, $H_{5exo,}$ ^2J14.0, $^3J_{6endo,\ 5exo}$ ≈ $^3J_{5exo,\ 4}$ 4.2 Hz), 3.85 d.d. (1H, H^2, $^3J_{2,NH}$ 9.0 Hz, $^WJ_{2endo,\ 7anti}$ 2.2 Hz), 3.96 m (1H, H^6, $^3J_{6,NH}$ ≈ $^3J_{6endo,\ 5endo}$ 9.0, $^3J_{6endo,\ 6exo}$ *4.2*, $^WJ_{6endo,\ 7syn}$ 2.2 Hz), 5.50 br.s and 5.70 br.s (2 NH).

Ritter reaction with fenchone oxime (II) was carried out in a similar way by adding 4 ml of sulfuric acid to a solution of 3.0 g of oxime in 7 ml of acetonitrile. We obtained 3.12 g (84%) of a mixture of amidonitriles **XIV** and **XV** in 2:3 ratio according to GLC. The isomer mixture was separated by crystallization from ethanol. After the first crystallization we obtained *cis*-isomer **XIV** containing ~7% of *trans*-isomer **XV**. The recrystallization from ethanol afforded pure *cis*-1-acetamido-1-methyl-3-(1-methyl-1-cyanoethyl)cyclopentane (**XIV**), mp 127–128°C. IR spectrum, cm^{-1}: 3400, 3080 (NH), 2980, 2960, 2940, 2860 (C–H), 2230 (C≡N), 1650 (C=O),

1550 (NH). Mass spectrum, *m/z*: 208 (M^+, 1%), 193 ($M^+ - CH_3$), 167 ($M^+ - CH_3 - CN$), 165 ($M^+ - COCH_3$), 151 ($M^+ - NCOCH_3$), 140, 128, 122, 112, 98, 81, 60 (100%), 57, 43. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.25 s, 1.27 s and 1.28 s [3H each, 1-CH_3 + C(CN)(CH_3)2], 1.59 m (2H, C^4H_2), 1.76 s (3H, $COCH_3$), 1.80 m (2H, C_5H_2), 1.90 m (2H, C^2H_2), 2.01 quintet (1H, 3-H, 4 ^3J 8.0 Hz), 7.52 br.s (NH).

***trans*-1-Acetamido-1-methyl-3-(1-methyl-1-cyanoethyl)cyclopentane (XV)** isolated from the mother liquor was purified by double recrystallization from anhydrous acetone. mp 114–115°C. IR spectrum, cm^{-1}: 3290, 3080 (NH), 2980, 2960, 2940, 2860 (C–H), 2230 (C≡N), 1640 (C=O), 1550 (NH). Mass spectrum, *m/z*: 208 (M^+, 2%), 193 ($M^+ - CH_3$), 167 ($M^+ - CH_3 - CN$), 165 ($M^+ - COCH_3$), 151 ($M^+ - NCOCH_3$), 140, 128, 122, 112, 98 (100%), 81, 60, 57, 43. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.27 s, 1.28 s and 1.35 s [each 3H, C(CN)$(CH_3)_2$ + 1-CH_3], 1.43 m (2H, C_4H_2), 1.78 s (3H, $COCH_3$), 1.98 m (2H, C_5H_2), 2.10 m (2H, C_2H_2), 2.31 quintet (1H, 3-H, 4 ^3J 8.0 Hz), 7.38 br.s (NH).

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