ISSN 1070-4272, Russian Journal of Applied Chemistry, 2009, Vol. 82, No. 6, pp. 1025–1028. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © Yu.E. Klimko, S.D. Isaev, D.A. Pisanenko, 2009, published in Zhurnal Prikladnoi Khimii, 2009, Vol. 82, No. 6, pp. 968–971.

ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Vinylnorbornene in the Ritter Reaction

Yu. E. Klimko, S. D. Isaev, and D. A. Pisanenko

National Technical University of Ukraine, Kiev, Ukraine

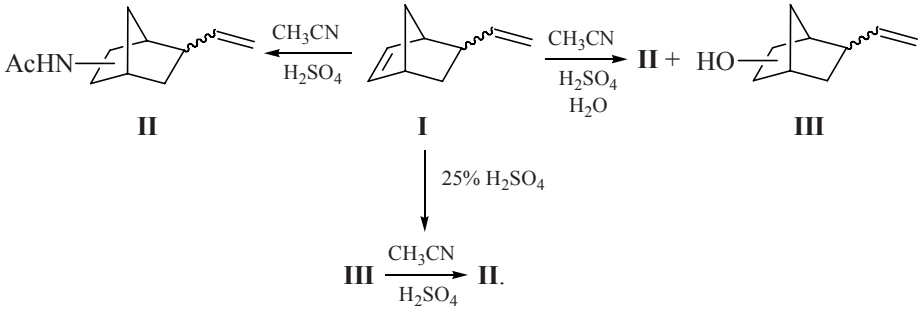
Received December 6, 2007

Abstract—Reaction of vinylnorbornen with acetonitrile in the presence of H_2SO_4 at 20°C and 50°C was investigated.

DOI: 10.1134/S1070427209060184

Amino derivatives of carcass hydrocarbons containing norbornane structural fragment are known to possess high physiological activity [1]. One of the simplest methods of synthesis of this group compounds, for example, acylated amines, is Ritter reaction; however, for bicyclic dienes it is studied on a limited number of examples [2, 3]. In this connection it is interesting to investigate the influence of the reaction conditions on its direction for vinylnorbornen a which is highly reactive in the addition reactions [4] and is sufficiently accessible [5].

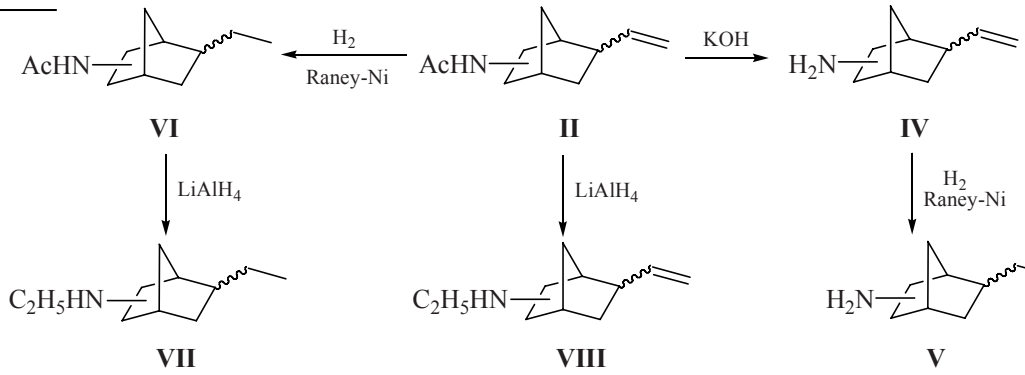
In this communication are presented the results of investigation of vinylnorbornene (**I**) reaction with acetonitrile in the presence of sulfuric acid proceeding, as experiments showed, with the formation of the following products:



The reaction was carried out with different mole ratios of reagents, sulfuric acid and water, varied duration and temperature of experiments (see the table). For the experiments was used H_2SO_4 conc. and excess of acetonitrile, since it was used as a reagent and a solvent simultaneously. The application of H_2SO_4 conc. makes it possible to increase the fraction of the protonated nitrile and respectively to decrease the solvation of the carbcations formed at the protonation of vinylnorbornene and thus to increase their reactivity [2]. In some experiments to the reaction medium water was added water in order to prevent various rearrangements of these carbcations [2, 6]. However, it turned out that this leads not only to the formation of the final reaction product 5-vinyl-2(3)-acetylaminonorbornane **II**, but also to 5-vinyl-2(3)-norbornanol (**III**) in a significant amount. The formation of alcohol **III** was confirmed by an experiment in which at the addition of olefin **I** to 25% H_2SO_4 at 95°C within only 2 h the alcohol **III** is obtained in 83% yield. As can be seen from data of the table, a noticeable increase in the quantity of basic product **II**, even in the presence of water, is promoted by the increase in the reaction temperature with the simultaneous decrease in duration. Probably in this case main role in directing the process to the formation of acetamino derivative **II** plays the increase in the temperature, since alcohol **III** itself at the reaction with acetonitrile in the

presence of H_2SO_4 conc. and water at 50–60°C in 1 h was converted into compound **II** only in 33% yield only.

Study of both the composition of the reaction products and their individuality after the isolation from the mixture was carried out by the methods of analytical and capillary GLC. At the analysis on the capillary column of the preparatively isolated acetyl derivative **II** and alcohol **III,** on the chromatograms were revealed two peaks in approximate ratio 1:1. In the IR spectra of these compounds there are the absorption bands at 890, 1640 and 2900 cm^{-1} characteristic of the terminal vinyl group, whose presence is confirmed by signals of protons at 4.75 (=CH_2) and 5.5 ppm. (–CH=) in the ^1H NMR spectra. The stretching vibrations of the NH group of compound **II** are characterized by absorption band in the IR spectrum at 3300 cm^{-1}, the absorption of OH group of alcohol **III** occurs at 3100, 3310 cm^{-1}. In the ^1H NMR spectra of these substances appear broad singlets of the proton of NH group at 7.95 ppm, the signal of hydroxyl proton at 3.5 ppm. Among the multiplet signals of the protons of norbornane fragment it is possible to isolate the multiplets of methine protons at C^2, C^3 atoms with the centers at 3.45 ppm for acetylamine **II** and at 3.1 ppm for alcohol **III**. The regions of the chemical shifts of remaining protons correspond to published data on ^1H NMR spectroscopy [7, 8]. It follows from the given spectral data and results of GLC analysis that under the studied conditions the reaction occurs at the endocyclic double bond with the formation of 2- and 3-substituted isomers of 5-vinylnorbornane. The possible transformations of the synthesized acetylamine **II** into other amines of norbornane series are shown in the scheme:



By alkaline hydrolysis of compound **II** 5-vinyl-2(3)-aminonorbornane (**IV**) was obtained by hydrogenation on Raney-Ni 5-ethyl-2(3)-aminobornane (**V**) was prepared. By reduction with hydrogen on Raney-Ni and with $LiAlH_4$ are synthesized 5-ethyl-2(3)-acetylaminonorbornane (**VI**) and 5-ethyl-2(3)-*N*-ethylaminononorbornane (**VII**). By the action of lithium aluminum hydride, from compound **II** 5-vinyl-2(3)-ethylaminononorbornane (**VIII**) was obtained.

Composition of the reaction product formed in the reaction of vinylnorbornene **I** with acetonitrile (by the data of GLC)

Exp. no.	Mole ratio **I**:MeCN:H_2O:H_2SO_4	τ, h	*T*, °C	Yield, %
1	1:90:12:5	26	20	15(**II**), 82(**III**)
2	1:90:12:5	8	50	59(**II**), 41(**III**)
3	1:90:0:5	26	20	86 (**II**)

EXPERIMENTAL

The IR spectra were registered on a Specord 75-JR instrument, ^1H NMR spectra on a TESLA BS-487 spectrometer (80 MHz), internal reference HMDS, chemical shifts were measured in δ scale. Chromatographic analysis was carried out on a Tsvet-102 instrument with a glass column 1000×3 mm (5% of Apiezon L on the carrier inerton N-AW-HMDS) and capillary column 50 m length filled with Apiezon L, carrier gas helium. The separation of the mixtures of the reaction products was carried out by the method of the adsorption chromatography on the sorbent Silicagel 40/100 and TLC on Silufol plates. Freshly distilled technical vinylnorbornene was used for the experiments.

Reaction of vinylnorbornene (I) with acetonitrile. *a*. To a solution of 5 g (0.042 mole) of diene **I** in 193.5 ml (3.78 mol) of acetonitrile was added at stirring and cooling by ice 11.5 ml (0.21 mol) of H_2SO_4 conc. and

9 ml (0.5 mol) of water. Cooling bath was removed, and the mixture was maintained at 20°C for 24 h. Then the solution of sodium carbonate was added till alkaline reaction of the reaction mixture, the organic layer was separated, the precipitate was washed with acetonitrile. The combined organic extracts were dried over anhydrous $MgSO_4$, acetonitrile was removed in a ,vacuum and the residue was analyzed by GLC. Yield of the mixture of compounds 6.1 g.

b. Experiment was carried out by analogy with *a*. The reaction mixture was maintained for 8 h at 50°C. Yield of products 6.4 g.

c. To a solution of 5 g (0.042 mole) of diene **I** in 193.5 ml (3.78 mole) of acetonitrile was added dropwise for 10 min at stirring and cooling by ice 11.5 ml (0.21 mole) of H_2SO_4 conc., the solution was left at 20°C for 26 h, then the reaction mixture was processed as in *a*. Yield of compound **II** was 6.44 g.

5-Vinyl-2(3)-acetylaminonorbornane (II). Separated by column chromatography from the mixture of the compounds, obtained according to *a*; eluent ether–hexane (10: 1). R_f 0.5. Yield 0.9 g, mp 81–88°C. IR spectrum, ν, cm^{-1}: 890, 1640, 2900, 3090, 3300. ^1H NMR spectrum, δ, ppm: 7.95 br.s (NH, 1H), 5.5 m (–CH=, 1H), 4.75 m (=CH_2, 2H), 3.45 m (AcNH–CH=, 1H), 1.2–1.25 (skeleton H). Found, %: C 73.65, H 9.59, N 7.79. $C_{11}H_{17}NO$. Calculated, %: C 73.74, H 9.49, N 7.82.

5-Vinyl-2(3)-norbornanol (III). *a*. Separated as compound **II**, R_f 0.80. Yield 5 g, bp 75–80°C (1.5 mm Hg) [6]. IR spectrum, ν, cm^{-1}: 890, 1640, 2900, 3100, 3310. ^1H NMR spectrum, δ, ppm: 5.5 m (–CH=, 1H), 4.75 m (=CH_2, 2H), 3.5 br.s (OH, 1H), 3.1 m (=CH–OH, 1H), 1.2–2.0 m (skeleton H). Found, %: C 78.19, H 10.25. $C_9H_{14}O$. Calculated, %: C 78.26, H 10.14.

b. 12 g (0.1 mol) of diene **I** was added to 38 ml of 25% H_2SO_4 at stirring and cooling by ice, the mixture was heated to 95°C and kept for 2 h. After cooling 20 ml of ether was added, the organic layer was separated, washed with a solution of sodium carbonate, and dried over anhyrous Na_2SO_4. After evaporation of ether was obtained 13.1 g of residue containing 83% of alcohol **III** (according to the data of GLC). The mixture was distilled in a vacuum, the fraction with bp 85–90°C (1.7 mm Hg) [7] was collected, yield of alcohol 9.9 g (71.1%). IR spectrum, ν, cm^{-1}: 890, 1640, 2900, 3090, 3305. ^1H NMR spectrum, δ, ppm: 5.5 m (–CH=, 1H), 4.75 m (=CH_2, 2H), 3.5 br.s (OH, 1H), 3.0 m (=CH–OH, 1H), 1.2–2.0 m (skeleton H).

Reaction of 5-vinyl-2(3)-norbornanol (III) with acetonitrile. To a solution of 0.15 g of alcohol **III** obtained by Ritter reaction from diene **II** in 5.8 ml of acetonitrile was added 0.35 ml of H_2SO_4 conc. and 0.25 ml of water. The reaction mixture was maintained for 1 h at 50–60°C and then treated with a solution of sodium carbonate, and the organic layer was separated. The sodium sulfate precipitate was washed with acetonitrile and combined extracts were dried over Na_2SO_4. After distilling off the solvent 0.2 g of a mixture was obtained containing 67% of alcohol **III** and 33% of acetamino derivative **II** (by GLC).

5-Vinyl-2(3)-aminonorbornane (IV). To a solution of 3 g of acetamine **II** in 35 ml of diethylene glycol was added 4.68 g of KOH, and the mixture was refluxed for 6 h. After cooling, the mixture was poured into 200 ml of 10% KOH, extracted with ether, the extract was dried over KOH. Ether solution was saturated with gaseous HCl, and the precipitate formed was filtered off. Yield of the hydrochloride in the form of hygroscopic crystals was 2.19 g (76%). By the action of 10% solution of KOH free amine **IV** was separated in the form of viscous dark liquid. ^1H NMR spectrum, δ, ppm: 5.5 m (–CH=, 1H), 4.75 m (=CH_2, 2H), 2.75 m (–CH–NH_2, 1H), 1.2–2.0 (skeleton H). Found, %: C 78.73, H 11.05, N 10.19. $C_9H_{15}N$. Calculated, %: C 78.83, H 10.95, N 10.22.

5-Ethyl-2(3)-aminonorbornane (V). To a solution of 0.5 g of the amine **IV** hydrochloride in 30 ml of methanol was added a suspension of Raney Ni in methanol. The mixture was stirred for 6 h at 20°C in a hydrogen atmosphere, methanol and catalyst were removed. 0.5 g of hygroscopic amine **V** hydrochloride was obtained. ^1H NMR spectrum, δ, ppm: 8.0 (–NH_3^+, 3H), 3.0 (CH–NH_3^+, 1H), 1.5–2.5 (skeleton H). Amine **V** was separated like amine **IV** in the form of oily liquid, n_D^{20} 1.4677 [9].

5-Ethyl-2(3)-acetaminorbornane (VI). To a solution of 1.0 g of compound **II** in 30 ml of methanol was added a suspension of Raney Ni in methanol, the mixture was stirred for 6 h at 20°C in the atmosphere of hydrogen, catalyst and methanol were removed. The yield of compound **VI** in the form of viscous fluid was 1.0 g. ^1H NMR spectrum, δ, ppm: 5.75 (NH, 1H), 3.5 (–CH–NH–$COCH_3$, 1H), 1.6 (–$COCH_3$, 3H), 0.6–2.1 (skeleton H). Found, %: C 72.86, H 10.50, N 7.75. $C_{11}H_{19}NO$. Calculated, %: C 72.93, H 10.50, N 7.73.

5-Ethyl-2(3)-N-ethylaminonorbornane (VII). To a suspension of 0.4 g of $LiAlH_4$ in 50 ml of ether was

added 0.9 g of compound **VI**, and the mixture was heated to boiling and stirred for 4 h. After cooling were added consecutively 1.6 ml of water and 0.4 ml of 15% NaOH, the inorganic salts precipitate was filtered off. The filtrate was dried over KOH and ether saturated with gaseous HCl was added; the precipitate formed was filtered off. The yield of amine **VII** hydrochloride 0.9 g (91%), mp 190–193°C. Amine **VII** was separated like amine **IV**, n_D^{20} 1.4820 [9]. Found, %: C 78.93, H 12.67, N 8.83. $C_{11}H_{21}N$. Calculated, %: C 79.04, H 12.57, N 8.38.

5-Vinyl-2(3)-N-ethylaminonorbornane (VIII). To the suspension of 0.4 g of $LiAlH_4$ in 50 ml of ether was added 1.0 g of acetamine **II** and the mixture was stirred for 8 h at reflux till the disappearance of solid. The mixture was worked up as in the case of compound **VII**, yield of hygroscopic precipitate of the amine **VIII** hydrochloride was 1.05 g (93%). Amine **VIII** in the form of viscous liquid was isolated like the amine **IV**. Found, %: C 79.91, H 11.63, N 8.45. $C_{11}H_{19}N$. Calculated, %: C 80.00, H 11.52, N 8.48.

CONCLUSIONS

(1) Ritter reaction of vinylnorbornene with the acetonitrile in the presence of concentrated H_2SO_4 proceeds only at the double bond of the cycle and leads to 5-vinyl-2(3)-acetylaminonorbornane, and in the presence of water in the system affords a significant amount of by-product 5-vinyl-2(3)-norbornanol.

(2) Synthesized by the method of alkaline hydrolysis and reduction with hydrogen on Raney Ni and by lithium aluminum hydride 5-vinyl-2(3)-acetylaminonorbornane can be converted into amines both with the double bond in the side chain and without it.

REFERENCES

1. US Patent no. 3444302 US, US Cl. 424–325. *Method of Preventing Influenza Viral Infections*.
2. Nigmatova, V.B., Andreev, V.A., Pekhk, T.I., et al., *Zh. Org. Khim*., 1990, vol. 26, no.12, p. 2552.
3. Samaniego, W.N., Baldessari, A., Ponce, M.A., et al., *Tetr. Lett*., 1994, vol 35, no. 38, p. 6967.
4. Kozina, M.P., Mastryukov, V.S., Mil'vitskaya, E.M., *Usp. Khim*., 1982, vol. 51, no. 8, p. 1337.
5. Fel'dblyum, V.Sh., *Sintez i primenenie nepredel'nykh tsiklicheskikh uglevodorodov* (Synthesis and Application of Unsaturated Technical Hydrocarbons), Moscow: Khimiya, 1982.
6. Betel, D. and Gold, V., *Karbonievye iony* (Carbonium Ions), Moscow: Mir, 1970.
7. Inoue, Y., Tamimoto, F., and Kitano, H., *Bull. Chem. Soc. Japan*., 1984, vol. 57, no. 9, p. 2468.
8. Shields, T.C., *Canad. J. Chem*., 1971, vol. 49, no. 7, p. 1142.
9. Kozlov, N.G., Kalechits, G.V., Belikova, N.A., et al., *Zh. Org. Khim*., 1985, vol. 21, no. 3, p. 535.