Russian Journal of Organic Chemistry, Vol. 41, No. 12, 2005, pp. 1836–1844. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 12, 2005, pp. 1869–1878.

Mannich Condensation of 3,3,5-Trimethylcyclohexanone and Its Oxime

S. S. Koval'skaya[1], N. G. Kozlov[1], and A. V. Tkachev[2]

[1] *Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, ul. Surganova 13, Minsk, 220072 Belarus*
e-mail: loc@ifoch.bas-net.by

[2] *Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia*

Received December 3, 2004

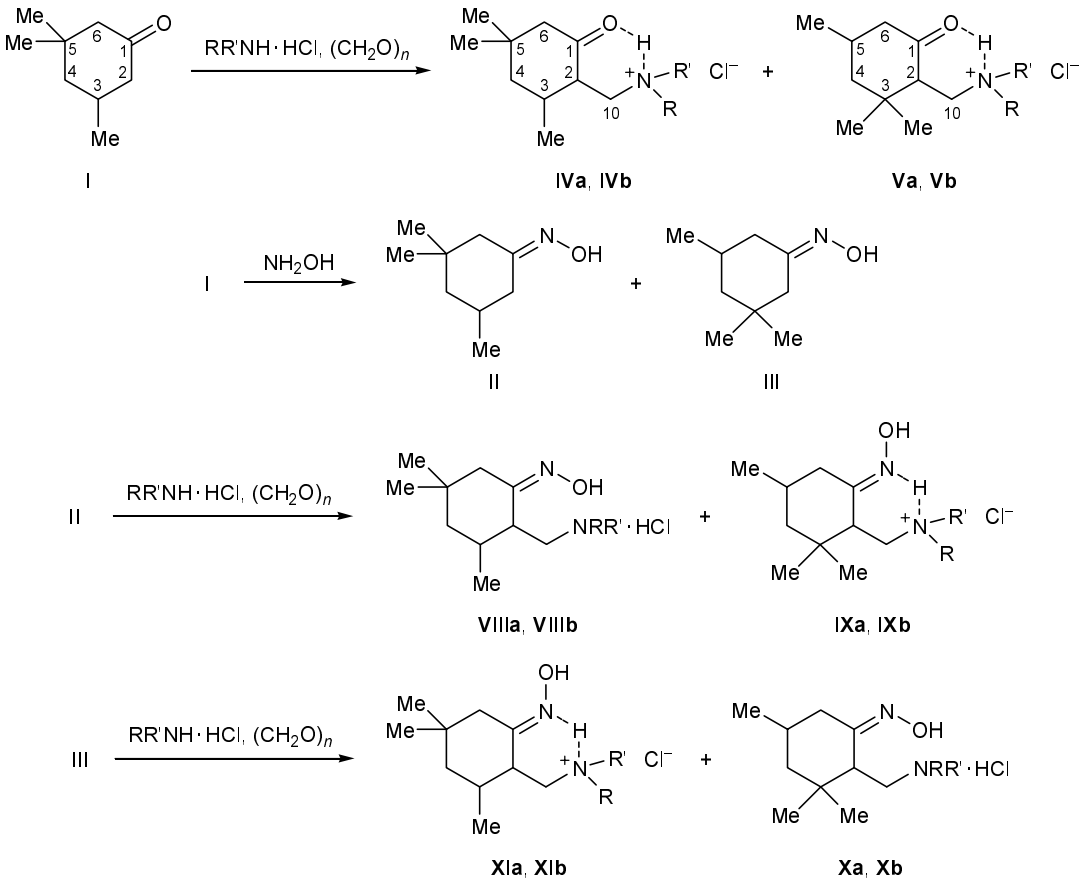
Abstract—Mannich condensation of 3,3,5-trimethylcyclohexanone with paraformaldehyde and dimethylamine or benzylamine hydrochloride involves both activated methylene group in the initial ketone to give compounds with equatorial aminomethyl substituent. The major isomer is that formed by addition at the less sterically hindered carbon atom. Likewise, Mannich condensation of the *E* and *Z* isomers of 3,3,5-trimethylcyclohexanone oxime react at both methylene groups, and the addition of aminomethyl fragment occurs preferentially at that methylene group which is located more closely to the oxime hydroxy group.

Trimethylcyclohexane moiety constitutes a structural fragment of many naturally occurring compounds, such as α- and β-ionones (fragrant substances) [1], vitamin A, and carotinoids [2]. Therefore, the synthesis of potential biologically active compounds incorporating a trimethylcyclohexane fragment seems to be reasonable. Mannich bases are widely used in organic synthesis as chemical precursors of the corresponding α,β-unsaturated compounds [3]. We previously demonstrated the possibility of using cyclic Mannich bases in the synthesis of prostaglandin analogs [4]. Taking the above stated into account, the accessibility of 3,3,5-trimethylcyclohexanone (**I**) makes this compound promising from the viewpoint of preparation of both biologically active substances and their precursors.

In the present work we examined Mannich condensation of 3,3,5-trimethylcyclohexanone (**I**), as well as of (*E*)- and (*Z*)-oximes **II** and **III** derived therefrom, with paraformaldehyde and dimethylamine and benzylamine hydrochlorides. We have found that the Mannich condensation of ketone **I** with the above amines involves both methylene groups in the α-position with respect to the carbonyl group in the substrate. Among the regioisomeric products, the major is that formed via addition of the aminomethyl fragment to spatially more accessible α-methylene carbon atom in ketone **I** (Scheme 1). The reaction with dimethylamine hydrochloride afforded a mixture of 2-dimethylaminomethyl-3,5,5-trimethylcyclohexanone hydrochloride (**IVa**) and 2-dimethylaminomethyl-3,3,5-trimethylcyclohexanone hydrochloride (**Va**) at a ratio of 2:1 (according to the ^{1}H NMR data). Both these products have fairly low melting points, and they were isolated from the reaction mixture as a thick oily material. We failed to separate isomeric hydrochlorides **IVa** and **Va** by crystallization from all available solvents or their mixtures. Vacuum distillation of a mixture of the corresponding free bases **VI** and **VII** was accompanied by deamination and was unsuccessful as well. We succeeded in isolating small amounts of amino ketones **VI** and **VII** by column chromatography on aluminum oxide (see Experimental); they were converted back to the corresponding hydrochlorides, for free Mannich bases are very unstable compounds, and they readily undergo tarring. Samples of **IVa** and **Va** obtained in such a way were subsequently used for spectral studies. *N*-Benzyl analogs **IVb** and **Vb** melted at higher temperatures, and we succeeded in isolating the major isomer (compound **IVb**) as individual substance; also, a sample enriched with the minor component (containing no less than 90% of hydrochloride **Vb**) was obtained. The structure of compounds **IV** and **V** was determined on the basis of their NMR, IR, and mass spectra. The IR spectra of both regioisomeric amino ketones **IVa** and **Va** contained an absorption band at 1720 cm^{-1}, corresponding to stretching vibra-

1070-4280/05/4112-1836

Scheme 1.

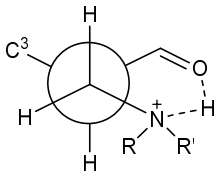


R = R' = Me (**a**), R = H, R' = $PhCH_2$ (**b**).

tions of the carbonyl group, and bands at ~3400, 2700, and 2650 cm^{-1}, which are typical of protonated amino group. Benzylamine derivatives **IVb** and **Vb**, apart from the above bands, showed in the IR spectra absorption at 1570 cm^{-1} due to vibrations of the aromatic ring. In the mass spectra of amino ketones **IVa**/**Va** and **IVb**/**Vb**, the molecular ions $[M]^+$ had *m*/*z* values of 198 and 260, respectively, which correspond to the hydrochlorides.

The steric structure of the isomeric amino ketones was established on the basis of the ^1H NMR data. The ^1H NMR spectra of benzylaminomethylcyclohexanones **IVb** and **Vb** were the most convenient to interpret. Unlike dimethylaminomethyl analogs **IVa** and **Va**, the key proton signals (2-H) in the spectra of **IVb** and **Vb** were not overlapped by signals of *N*-methyl groups. The signals were assigned using the COSY-45 technique which allowed direct determination of ^1H–^1H coupling constants. In the ^1H NMR spectrum of major isomer **IVb**, a doublet signal at 1.00 ppm (^3J = 7.0 Hz) from methyl protons was present. In the correlation spectrum we observed a response at δ 1.63 ppm (multiplet), corresponding to the 3-H proton neighboring to that methyl group. According to the correlation spectrum, 3-H is coupled with three protons which resonate at δ 2.85 (2-H) and 1.50 ppm (2H, 4-H). The presence of three protons in the α-position with respect to 3-H indicates that the aminomethyl group is attached to C^2; i.e., the addition occurred at the spatially more accessible α-methylene group in the initial ketone. The coupling constant between 2-H and 3-H is 10.5 Hz. This value suggests axial orientation of these protons and hence equatorial orientation of both methyl group on C^3 and aminomethyl fragment on C^2. The multiplicity of the 2-H_{ax} signal (a doublet of triplets, J = 10.5, 10.5, 3.5 Hz) shows that protons on C^{10} are not equivalent and that rotation about the C^2–C^{10} bond is restricted. Obviously, as in bicyclic Mannich bases described previously [5, 6], a strong intramolecular hydrogen bond is formed between the NH and carbonyl groups in **IVb**. This also follows from the fact that protons on the nitrogen atom appear

in the spectrum as two separate signals, one of which being displaced strongly downfield (δ 10.70 and 8.22 ppm). The formation of that hydrogen bond restricts conformational mobility of the aminomethyl fragment in **IVb**, so that one proton on C^{10} adopts an antiperiplanar (transoid) orientation with respect to 2-H (the corre-sponding vicinal coupling constant is 10.5 Hz), while the other proton on C^{10} is fixed in a synclinal *gauche* conformation (^3J = 3.5 Hz). The Newman projection of the cationic fragment of **IVb** along the C^2–C^{10} bond is shown below.



In the ^{1}H NMR spectrum of regioisomeric aminomethylcyclohexanone **Vb**, the doublet signal from methyl protons is located at δ 0.95 ppm. Irradiation at the corresponding resonance frequency gives a response in the correlation spectrum at δ 1.93 ppm (multiplet); the latter signal belongs to a proton neighboring to that methyl group. This protons is coupled with four protons resonating at δ, ppm: 2.35 d.d.d (6-H_{eq}, ^2J = 14.0, ^3J = 3.0, ^WJ = 1.6 Hz), 2.19 d.d (6-H_{ax}, ^2J = 14.0, ^3J = 10.0 Hz), and 1.49 m (2H, 4-H). The presence of four protons in the α-positions with respect to $CH(CH_3)$ suggests that the minor product is formed via aminomethylation at the spatially less accessible methylene group, i.e., that neighboring to the $C(CH_3)_2$ fragment. The coupling constant between the protons resonating at δ 1.93 and 2.19 ppm is equal to 10 Hz, indicating their axial orientation. Correspondingly, the methyl group on C^5 occupies equatorial position. The 2-H signal is a doublet of doublets located at δ 2.94 ppm. The axial orientation of 2-H (and hence equatorial orientation of the aminomethyl substituent) follows from its chemical shift which is similar to the chemical shift of 2-H in isomer **IVb**, as well as from the absence of *W*-coupling with equatorial protons on C^4 and C^6 (the latter are coupled with each other through a constant ^5J of 1.6 Hz). As noted above, the coupling constants with protons on C^{10} (J = 10.0, 3.5 Hz) indicate formation of intramolecular hydrogen bond which restricts rotation about the C^2–C^{10} bond. As in the spectrum of **IVb**, protons on the amino nitrogen atom give rise to two signals, for one of these is involved in hydrogen bonding. Regioisomer **Vb** characteristically showed an appreciable upfield shift of the signal from the axial methyl group on C^3 (δ 0.61 ppm). This means that the 3-Me group falls into the area shielded by the benzene ring, which may be regarded as an indirect support to the equatorial orientation of the benzylaminomethyl group. Otherwise, the benzyl fragment and the axial methyl group on C^3 would appear at different sides of the cyclohexane ring, and they could not be arranged close to each other. The shielding effect of the aromatic ring on the neighboring equatorial methyl group on C^3 is not strong: δ 1.00 and 1.03 ppm for benzylamines **IVb** and **Vb** and 1.04 and 1.12 ppm for dimethyl analogs **IVa** and **Va**.

Signals in the ^{1}H NMR spectra of regioisomeric amino ketones **IVa** and **Va** were assigned by analogy with the spectra of benzylamines **IVb** and **Vb**. On the whole, the spectra of the corresponding regioisomers are very consistent with each other; only a slight difference in the chemical shifts of some protons is observed due to different shielding effects of the dimethylamino and benzylamino groups.

The ^{13}C NMR spectra confirm the structure of compounds **IVb** and **Vb**, determined on the basis of the ^{1}H NMR data. The ^{13}C signals were assigned by analysis of their multiplicity (*J*-modulation), as well as by determination of direct ^{13}C–^{1}H couplings (COSY). The ^{13}C NMR spectrum of major isomer **IVb** contains three upfield (δ_C <55 ppm) signals from methyl groups (quartets), four triplets from methylene carbon atoms, two doublets from CH groups, and one singlet from quaternary carbon atom. In the downfield region, we observed three doublets and one singlet from aromatic carbon nuclei and a singlet from the carbonyl carbon atom (see Experimental). The chemical shifts of C^1–C^6 and C^{10} approach standard values, in keeping with the assumed structure. Signals from the methyl groups on C^5 in **IVb** are located at δ_C 31.6 and 25.6 ppm; according to the correlation spectrum, the upfield signal corresponds to the methyl groups whose protons resonate at δ 0.78 ppm in the ^{1}H NMR spectrum (axial 5-CH_3 group). Usually, methyl groups attached to cyclohexane ring give signals in a much stronger field, at δ_C ~22 (equatorial) and ~17 ppm (axial) [7]. Presumably, intramolecular hydrogen bond (see above) fixes such a conformation of the benzylaminomethyl fragment that both methyl groups on C^5 appear in the benzene ring plane; as a result of deshielding by the benzene ring, their signals are displaced downfield by about 8 ppm relative to the expected position.

The ^{13}C NMR spectrum of regioisomeric benzylaminomethylcyclohexanone **Vb** is characterized by

a set of signals with similar multiplicities (see Experimental). Some differences in the chemical shifts may be attributed to differences in steric environment. The signal from the equatorial 5-CH_3 group appears in an anomalously weak field (δ_C 29.3 ppm), which corresponds to the benzene ring orientation analogous to that noted above for isomer **IVb**. A slightly lesser downfield shift of the 5-CH_3 signal (by about 6 ppm) may be due to shielding effect of the "extra" methyl group on C^3.

Thus the structure of amino ketones formed by Mannich condensation of 3,3,5-trimethylcyclohexanone **I** is determined by both steric and thermodynamic factors: aminomethylation occurs preferentially at the spatially more accessible methylene group, the products are characterized exclusively by *trans* orientation of the methyl and aminomethyl groups, and both these substituents in the predominant conformation are equatorial.

We previously showed that, like ketones, oximes derived from bicyclic ketones of the terpene series, isocamphanone and verbanone, are also capable of reacting with amines and paraformaldehyde according to Mannich with formation of the corresponding amino oximes and that the reaction is regioselective and stereospecific [5, 6]. We have found no published data on Mannich reactions with oximes as substrates.

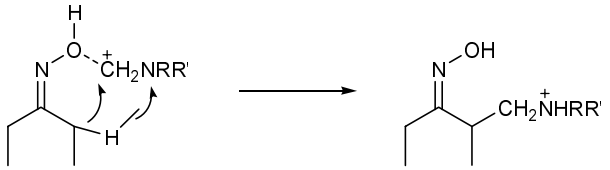
By treatment of 3,3,5-trimethylcyclohexanone (**I**) with hydroxylamine we obtained a mixture of the corresponding (*E*)- and (*Z*)-oximes **II** and **III**, the *E* isomer slightly prevailing (*E*/*Z* ratio ≈ 5:4, according to the ^{1}H NMR data). The isomers were separated by repeated crystallization from acetonitrile (see Experimental). We found that crystallization from anhydrous acetonitrile gives a mixture enriched in *E* isomer **II** and that crystallization from acetonitrile containing 2–3% of water afforded a mixture enriched in *Z* isomer **III**. These findings may seem to be surprising, but they can readily be rationalized on the basis of the following considerations. The hydroxy group in oxime **II** is less sterically shielded; therefore, it is better solvated with water molecules thus hindering crystallization of the *E* isomer from moist solvent.

Isomeric 3,3,5-trimethylcyclohexanone oximes **II** and **III** were also brought into Mannich condensation with the same amines. Unlike isocamphanone and verbanone oximes, the reactions with monocyclic oximes **II** and **III** were not so smooth and were accompanied by considerable tarring. Possible reasons are discussed below. Moreover, as in the condensation with parent ketone **I**, the reaction gave a mixture of regioisomeric Mannich bases; however, in this case the preferential formation of one or another isomer was determined by different factors. Taking into account that the C^2H_2 methylene group in (*E*)-oxime **II** is shielded by two methyl groups and that the C^6H_2 group in the same molecule is shielded by one methyl group and oxime hydroxy group, formation of comparable amounts of regioisomeric amino oximes **VIII** and **IX** might be expected. Nevertheless, the fraction of 2-(R,R'-amino)-methyl-3,5,5-trimethylcyclohexanone (*Z*)-oxime **VIIIa** or **VIIIb** (Scheme 1) was thrice as large as the fraction of the corresponding *E* isomer **IX**. The major isomers (compounds **VIIIa** and **VIIIb**) were isolated by fractional crystallization from acetone–diethyl ether or chloroform–diethyl ether (see Experimental). The structure with spatially close aminomethyl fragment and oxime hydroxy group (*Z* isomers) was assigned to **VIIIa** and **VIIIb** on the basis of the ^{1}H NMR data. Signals from the 2-H proton of oximes **VIIIa** and **VIIIb** are displaced downfield by more than 0.5 ppm relative to the corresponding signals of amino ketones **IVa** and **IVb**. It is known [8] that such shift is typical of protons located in the α-position with respect to *syn*-hydroxyimino group. By contrast, in the spectra of regioisomeric amino oximes **IXa** and **IXb** (which are products of aminomethylation at the other methylene group with *anti* orientation of the hydroxyimino group), signals from 2-H appears even in a stronger field, as compared to amino ketones **Va** and **Vb**. Different conformational mobilities of the aminomethyl substituents in regioisomeric amino oximes **VIII** and **IX** should also be noted. The signals from protons on C^2 and C^{10} in the spectra of *E* isomers **IX** are characterized by the same multiplicities as the corresponding signals of amino ketones **V**. This indicates (see above) formation of intramolecular hydrogen bond between the NH proton and lone electron pair on the oxime nitrogen atom. The same also follows from the presence of two NH signals (from chelated and free NH protons) in the spectrum of oxime **IXb**. The multiplicity of signals from protons on C^2 and C^{10} in the spectra of (*Z*)-oximes **VIIIa** and **VIIIb** differs from that observed for amino ketones **IVa** and **IVb**: the 2-H proton, apart from the axial–axial coupling with 3-H_{ax} (^3J = 10 Hz), is characterized by two additional coupling constants, each equal to 7 Hz; the latter correspond to vicinal interaction with protons of the conformationally labile methylene group. Obviously, mutual arrangement of the hydroxyimino and amino groups in the *Z* isomer is unfavorable for intramolecular hydrogen bonding.

The α-methylene group C^2H_2 in (*Z*)-3,3,5-trimethylcyclohexanone oxime (**III**) is even less accessible than in initial ketone **I**. Nevertheless, the Mannich condensation with oxime **III**, as well as with its *E* isomer, involves predominantly that methylene group which is spatially closer to the oxime hydroxy group. Despite considerable steric hindrances, the fraction of *Z* isomers **Xa** and **Xb** in the reaction mixture decreases only slightly (to ~65%) relative to the fraction of *E* isomers **VIII**. Like amino oximes **VIIIa** and **VIIIb**, compounds **Xa** and **Xb** showed in the ^{1}H NMR spectra an appreciable downfield shift of the 2-H signal. The NMR data also indicate conformational lability of the aminomethyl substituent in **Xa** and **Xb**. As follows from the multiplicity of the 2-H and 10-H signals of (*E*)-oximes **XIa** and **XIb** and from the presence of a signal from chelated NH proton at δ >10 ppm, strong intramolecular hydrogen bond =N···H–N is formed in their molecules (cf. **IXa** and **IXb**).

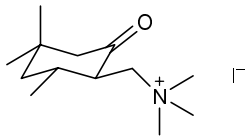
Preferential aminomethylation of 3,3,5-trimethylcyclohexanone oximes at the methylene group located closer to the oxime hydroxy group rather than at the more spatially accessible methylene group (as in the reaction with ketone **I**) suggests that the formation of Mannich bases from oximes involves association of the aminomethylating agent at the hydroxyimino group as shown in Scheme 2.

Scheme 2.



This assumption is supported by the fact that compounds having nucleophilic OH, NH, and SH groups are capable of undergoing aminomethylation at the heteroatom in the Mannich reaction [9]. However, taking into account that the Mannich condensation with monocyclic oximes is neither regioselective nor stereospecific, there are no reasons to believe that the above mechanism is the only possible.

We also made an attempt to obtain quaternary ammonium salts from amino ketones **IVa** and **Va** and amino oximes **VIIIa**–**XIa** by the action of methyl iodide on the corresponding free bases. However, the desired quaternary ammonium derivatives turned out to be unstable, and they underwent deamination and polymerization during the process. We succeeded in isolating only a small amount of trimethyl(2-oxo-4,4,6-



XII

trimethylcyclohexylmethyl)ammonium iodide (**XII**) as individual substance. Deamination of quaternary salts derived from amino oximes was especially fast: trimethylamine hydroiodide separated from the reaction mixture immediately after addition of methyl iodide to a solution of amino oxime in alcohol. Presumably, amino oxime hydrochlorides also undergo partial deamination under the Mannich conditions to give unstable α,β-unsaturated compounds which are responsible for strong tarring.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Nicolet Protégé-460 Fourier spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker DRX-500 spectrometer at 500.132 MHz for ^{1}H and 125.758 MHz for ^{13}C from solutions in $CDCl_3$ and DMSO-d_6 (*c* = 50–100 mg/ml) at 25–27°C. The chemical shifts were measured relative to the solvent signals: $CDCl_3$: δ 7.24, δ_C 76.90 ppm; DMSO-d_6: δ 2.50, δ_C 39.50. Signals were assigned using *J*-modulation technique (noise decoupling from protons, opposite phases for signals of carbon atoms with even and odd numbers of protons attached thereto, optimization for direct ^{1}H–^{13}C coupling constant J = 135 Hz) and two-dimensional techniques: homonuclear ^{1}H–^{1}H correlation and heteronuclear ^{13}C–^{1}H correlation by direct coupling constants (J = 135 Hz). The multiplicities of signals and coupling constants for protons on C^{10} and C^{11} (in benzylamino derivatives) were determined from the spectra recorded in DMSO-d_6; in the spectra recorded in $CDCl_3$, these signals showed a more complex coupling pattern due to splitting on protons at the nitrogen atom. The chemical shifts are given for the spectra recorded in $CDCl_3$. Dimethyl sulfoxide was less suitable for structure determination, for the key 2-H signals in the spectra of most compounds were overlapped by the solvent signals (the 2-H signals in DMSO-d_6 appeared in a weaker field than in $CDCl_3$). The mass spectra (electron impact, 70 eV) were obtained on a Hewlett–Packard 5890/5972 GC–MS system using an HP-5MS column. The progress of reactions and isomeric compositions of the products were monitored by GLC on a Chrom-5 chromatograph

(2000×2-mm glass column packed with Apiezon L on Chromaton-N-AW-DMCS, 0.16–0.20 mm).

3,3,5-Trimethylcyclohexanone oximes II and III were synthesized by standard procedure [10]. According to the ^{1}H NMR data, the ratio of isomeric (*E*)- and (*Z*)-oximes **II** and **III** was 5:4. The isomers were separated by repeated crystallization from acetonitrile. Recrystallization from anhydrous acetonitrile (distilled over calcined potassium carbonate) gave a mixture enriched in the *E* isomer, while the *Z* isomer precipitated mainly from moist acetonitrile.

(*E*)-3,3,5-Trimethylcyclohexanone oxime (II) with a purity of no less than 95% (according to the ^{1}H NMR data) was isolated after six recrystallizations. mp 78–79°C. IR spectrum, ν, cm^{-1}: 3450 (NOH); 2960, 2910, 2870, 2840 (CH); 1670 (C=N), 960 (NOH). ^{1}H NMR spectrum, δ, ppm: 8.70 br.s (NOH), 3.31 d.d.t (6-H$_{eq}$, ^2J = 14.0, $^3J_{ax,eq}$ = 4.0, ^WJ = 1.8 Hz), 2.08 d.t (2-H$_{eq}$, ^2J = 14.0, ^WJ = 1.8 Hz), 1.98 d (2-H$_{ax}$, ^2J = 14.0 Hz), 1.78 d.d (6-H$_{ax}$, ^2J = 14.0, $^3J_{ax,ax}$ = 10.0 Hz), 1.44 m (2H, 4-H), 0.98 s (3H, 3-CH$_3$-*eq*), 0.95 d (3H, 5-CH$_3$-*eq*, ^3J = 7.0 Hz), 0.83 s (3H, 3-CH$_3$-*ax*).

(*Z*)-3,3,5-Trimethylcyclohexanone oxime (III) with a purity of no less than 95% (according to the ^{1}H NMR data) was isolated after seven recrystallizations. mp 70–72°C. IR spectrum, ν, cm^{-1}: 3430 (NOH); 2960, 2910, 2870, 2840 (CH); 1660 (C=N); 950 (NOH). ^{1}H NMR spectrum, δ, ppm: 9.10 br.s (NOH), 3.07 d.t (2-H$_{eq}$, ^2J = 14.0, ^WJ = 1.8 Hz), 2.34 d.d.t (6-H$_{eq}$, ^2J = 14.0, $^3J_{ax,eq}$ = 4.0, ^WJ = 1.8 Hz), 1.98 d.d (6-H$_{ax}$, ^2J = 14.0, $^3J_{ax,ax}$ = 10.0 Hz), 1.65 d (2-H$_{ax}$, ^2J = 14.0 Hz), 1.40 m (2H, 4-H), 1.02 s (3H, 3-CH$_3$-*eq*), 0.97 s (3H, 3-CH$_3$-*ax*), 0.90 d (3H, 5-CH$_3$-*eq*, ^3J = 7.0 Hz).

Mannich condensation of 3,3,5-trimethylcyclohexanone (I) and its (*E*)- and (*Z*)-oximes II and III (*general procedure*). Dimethylamine hydrochloride, 4.5 g (55 mmol), or benzilamine hydrochloride, 7.2 g (50 mmol), and paraformaldehyde, 2 g (67 mmol), were added to a solution of 50 mmol of compound **I**–**III** in 30 ml of ethanol. The mixture was heated under reflux until the initial compound disappeared according to the GLC data. The solution was evaporated to 1/5 of the initial volume, and the resulting Mannich base was precipitated by adding excess anhydrous acetone.

Dimethylaminomethylcyclohexanones IVa and Va were isolated as a mixture of isomers in an overall yield of 58%; thick dark yellow oily substance. We failed to separate the isomers by crystallization from various solvents (such as acetone, chloroform, tetrahydrofuran, C$_1$–C$_4$ lower aliphatic alcohols, dioxane, DMF, and DMSO). From less polar solvents, an oily substance separated, whose isomer composition was the same as in the initial mixture, while no product separated from more polar solvents. Attempts to precipitate the product from the above solvents by adding diethyl ether resulted in either separation of the initial oily substance or division of the solution into layers without precipitation of Mannich base. Therefore, hydrochloride mixture **IVa**/**Va** was converted into a mixture of the corresponding bases **VI**/**VII** by adding a required amount of alcoholic alkali (NaOH) to a solution of **IVa**/**Va** in ethanol. The precipitate of NaCl was filtered off, and the solvent was distilled off. Vacuum distillation of the residue through an effective column was accompanied by tarring, presumably as a result of deamination and polymerization of enones thus formed. Small amounts of individual amino ketones **IVa** and **Va** were isolated by column chromatography on aluminum oxide (Chemapol L, 40–250 μm) using diethyl ether–chloroform (4:1) as eluent. The isolated aminoketones were converted back to their hydrochlorides by passing gaseous hydrogen chloride through a solution of **VI**/**VII** in diethyl ether.

2-Dimethylaminomethyl-3,5,5-trimethylcyclohexanone hydrochloride (IVa). mp 56–58°C. IR spectrum, ν, cm^{-1}: 3410 (NH); 2955, 2910, 2870, 2840 (CH); 2700, 2655, 2430, 2330 (NH$^+$); 1720 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.80 s (3H, 5-CH$_3$-*ax*), 1.04 d (3H, 3-CH$_3$, ^3J = 7.0 Hz), 1.06 s (3H, 5-CH$_3$-*eq*), 1.61 t (4-H$_{ax}$, ^2J = 10.0, $^3J_{ax,ax}$ = 10.0 Hz), 1.66 d.d.d (4-H$_{eq}$, ^2J = 10.0, $^3J_{eq,ax}$ = 3.6, ^WJ = 1.6 Hz), 1.78 m (3-H$_{ax}$), 2.13 d (6-H$_{ax}$, ^2J = 14.8 Hz), 2.45 d.d (6-H$_{eq}$, ^2J = 14.8, ^WJ = 1.6 Hz), 2.81 d.t (2-H$_{ax}$, $^3J_{ax,ax}$ = 10.0, $^3J_{2,10\text{-}trans}$ = 10.0, $^3J_{2,10\text{-}gauche}$ = 4.0 Hz), 2.88 s [6H, N(CH$_3$)$_2$], 2.96 d.d (*gauche*-10-H, ^2J = 10.0, $^3J_{10\text{-}gauche,2}$ = 4.0 Hz), 3.02 t (*trans*-10-H, ^2J = 10.0, $^3J_{10\text{-}trans,2}$ = 10.0 Hz), 10.65 br.s (NH). Mass spectrum, *m*/*z* (I_{rel}, %): 198 [*M*]$^+$ (1), 152 [*M* – Me$_2$NH$_2$]$^+$, 137, 119, 109, 97, 96, 83, 68 (100), 53, 43.

2-Dimethylaminomethyl-3,3,5-trimethylcyclohexanone hydrochloride (Va). mp 65–67°C. IR spectrum, ν, cm^{-1}: 3400 (NH); 2955, 2915, 2870, 2840 (CH); 2700, 2655, 2435, 2330 (NH$^+$); 1720 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.91 d (3H, 5-CH$_3$, ^3J = 7.0 Hz), 1.04 s (3H, 3-CH$_3$-*ax*), 1.12 s (3H, 3-CH$_3$-*eq*), 1.59 t (4-H$_{ax}$, ^2J = 10.0, $^3J_{ax,ax}$ = 10.0 Hz), 1.65 d.d.d (4-H$_{eq}$, ^2J = 10.0, $^3J_{eq,ax}$ = 3.2, ^WJ = 1.6 Hz), 1.93 m (5-H$_{ax}$), 2.18 d.d (6-H$_{ax}$, ^2J =

14.4, $^3J_{ax,ax}$ = 10.0 Hz), 2.40 d.d.d (6-H$_{eq}$, ^2J = 14.4, $^3J_{eq,ax}$ = 3.2, ^WJ = 1.6 Hz), 2.88 s [6H, N(CH$_3$)$_2$], 2.91 d.d (2-H$_{ax}$, $^3J_{2,10\text{-}trans}$ = 10.0, $^3J_{2,10\text{-}gauche}$ = 4.0 Hz), 2.94 d.d (*gauche*-10-H, ^2J = 10.0, $^3J_{10\text{-}gauche,2}$ = 4.0 Hz), 3.01 t (*trans*-10-H, ^2J = 10.0, $^3J_{10\text{-}trans,2}$ = 10.0 Hz), 10.60 br.s (NH). Mass spectrum, *m*/*z* (I_{rel}, %): 198 $[M]^+$ (1), 152 $[M - Me_2NH_2]^+$, 137, 119, 109, 91, 83, 69 (100), 53, 44.

Benzylamino ketone hydrochlorides IVb and Vb (a mixture of isomers) were isolated as a colorless finely crystalline material (yield 64%) by removal of the solvent. This material was dissolved in a new portion of ethanol, and anhydrous acetone was added. A mixture enriched in the major component (up to ~80%) was thus precipitated. The precipitate was filtered off, and the procedure was repeated four times to obtain isomer **IVb** with a purity of no less than 98%. The first mother liquor was evaporated, the residue was dissolved in a new portion of ethanol, and acetone was added to precipitate the major component. After 5–6 precipitations, the mother liquor contained a mixture enriched in the minor component (up to ~80%). By double crystallization from anhydrous *tert*-butyl alcohol we obtained a sample containing no less than 90% of the minor component; this sample was used for recording the NMR spectra. Two additional recrystallizations from *tert*-butyl alcohol gave 3 mg of a product containing no less than 98% of isomer **Vb**.

2-Benzylaminomethyl-3,5,5-trimethylcyclohexanone hydrochloride (IVb). mp 147–148°C. IR spectrum, ν, cm^{-1}: 3425 (NH); 2955, 2915, 2870, 2840 (CH); 2700, 2655, 2430, 2330 (NH$^+$); 1720 (C=O); 1570 (C–C$_{arom}$). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 0.78 s (3H, 5-CH$_3$-*ax*), 1.00 d (3H, 3-CH$_3$, ^3J = 7.0 Hz), 1.01 s (3H, 5-CH$_3$-*eq*), 1.50 m (2H, 4-H$_{ax}$, 4-H$_{eq}$), 1.63 m (3-H$_{ax}$), 2.09 d (6-H$_{ax}$, ^2J = 14.5 Hz), 2.50 d.d (6-H$_{eq}$, ^2J = 14.5, ^WJ = 1.6 Hz), 2.85 d.t (2-H$_{ax}$, $^3J_{ax,ax}$ = 10.5, $^3J_{2,10\text{-}trans}$ = 10.5, $^3J_{2,10\text{-}gauche}$ = 3.5 Hz), 3.01 m (2H, *gauche*-10-H, *trans*-10-H), 4.07 d and 4.22 d (PhC**H**$_2$, ^2J = 13.2 Hz), 7.38 m (3H) and 7.60 d (2H) (H$_{arom}$), 8.22 br.s (NH, free), 10.70 br.s (NH, chelated). ^{13}C NMR spectrum (CDCl$_3$), δ$_C$, ppm: 20.0 q (3-CH$_3$-*eq*), 25.6 q (5-CH$_3$-*ax*), 31.6 q (5-CH$_3$-*eq*), 33.1 d (C^3), 35.4 s (C^5), 44.1 t (C^{10}), 47.1 t (C^4), 51.6 t (C^{11}), 52.5 d (C^2), 54.0 t (C^6), 129.1 d (2C), 129.4 d (1C, C^p), 129.9 d (2C), 130.4 s (1C) (C$_{arom}$), 212.6 s (C^1). Mass spectrum, *m*/*z*, (I_{rel}, %): 260 $[M]^+$ (1), 152 $[M - PhCH_2NH_2]^+$, 137, 119, 109, 97, 96, 83, 68 (100), 53, 43.

2-Benzylaminomethyl-3,3,5-trimethylcyclohexanone hydrochloride (Vb). mp 168–169°C. IR spectrum, ν, cm^{-1}: 3420 (NH); 2955, 2910, 2870, 2840 (CH); 2700, 2655, 2435, 2330 (NH$^+$); 1720 (C=O); 1570 (C–C$_{arom}$). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 0.61 s (3H, 3-CH$_3$-*ax*), 0.95 d (3H, 5-CH$_3$, ^3J = 7.0 Hz), 1.03 s (3H, 3-CH$_3$-*eq*), 1.49 m (2H, 4-H$_{ax}$, 4-H$_{eq}$), 1.92 m (5-H$_{ax}$), 2.19 d.d (6-H$_{ax}$, ^2J = 14.0, $^3J_{ax,ax}$ = 10.0 Hz), 2.35 d.d.d (6-H$_{eq}$, ^2J = 14.0, $^3J_{eq,ax}$ = 3.0, ^WJ = 1.6 Hz), 2.94 d.d (2-H$_{ax}$, $^3J_{2,10\text{-}trans}$ = 10.0, $^3J_{2,10\text{-}gauche}$ = 3.5 Hz), 3.13 m (2H, *gauche*-10-H, *trans*-10-H), 4.06 d and 4.22 d (PhC**H**$_2$, ^2J = 13.2 Hz), 7.35 m (3H) and 7.58 d (2H) (H$_{arom}$), 8.64 br.s (NH, free), 10.70 br.s (NH, chelated). ^{13}C NMR spectrum (CDCl$_3$), δ$_C$, ppm: 21.4 q (3-CH$_3$-*ax*), 22.0 q (3-CH$_3$-*eq*), 29.3 q (5-CH$_3$-*eq*), 29.4 d (C^5), 38.3 s (C^3), 41.9 t (C^{10}), 48.9 t (C^4), 49.0 t (C^6), 51.6 t (C^{11}), 55.6 d (C^2), 129.0 d (2C), 129.3 d (1C, C^p), 130.0 d (2C), 130.5 s (1C, C$_{arom}$), 211.9 s (C^1). Mass spectrum, *m*/*z*, (I_{rel}, %): 198 $[M]^+$ (1), 152 $[M - PhCH_2NH_2]^+$, 137, 119, 109, 91, 83, 69 (100), 53, 44.

Dimethylamino oxime hydrochlorides VIIIa and IXa (a mixture of isomers) were isolated from the reaction mixture by partial removal of the solvent under reduced pressure, followed by precipitation with anhydrous acetone (yield 36%). A dark yellow thick oily material thus obtained was dissolved in anhydrous chloroform, and anhydrous diethyl ether was carefully added. The precipitate was enriched in major isomer **VIII**, and the mother liquor, with minor isomer **IX**. The procedure was repeated three times to isolate samples containing no less than 90% of the corresponding regioisomer.

(*Z*)-2-Dimethylaminomethyl-3,5,5-trimethylcyclohexanone oxime hydrochloride (VIIIa). A sample isolated as described above was recrystallized from anhydrous *tert*-butyl alcohol. mp 85–87°C. IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2955, 2910, 2870, 2840 (C–H); 2700, 2655, 2430, 2330 (NH$^+$); 1670 (C=N); 960 (NOH). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 0.92 s (3H, 5-CH$_3$-*ax*), 1.02 s (3H, 5-CH$_3$-*eq*), 1.10 d (3H, 3-CH$_3$, ^3J = 6.8 Hz), 1.58 t (4-H$_{ax}$, ^2J = 10.0, $^3J_{ax,ax}$ = 10.0 Hz), 1.65 d.d.d (4-H$_{eq}$, ^2J = 10.0, $^3J_{eq,ax}$ = 3.6, ^WJ = 1.6 Hz), 1.81 m (3-H$_{ax}$), 2.02 d (6-H$_{ax}$, ^2J = 13.6 Hz), 2.30 d.d (6-H$_{eq}$, ^2J = 13.6, ^WJ = 1.6 Hz), 2.83 s [6H, N(CH$_3$)$_2$], 3.06 m (2H, 10-H), 3.50 d.t (2-H$_{ax}$, $^3J_{ax,ax}$ = 10.0, $^3J_{2,10}$ = 7.2 Hz), 8.20 br.s (NH), 9.51 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 213 $[M]^+$ (1), 167 $[M - Me_2NH_2]^+$, 150 $[M - Me_2NH_2 - OH]^+$, 135, 118, 109, 97, 96, 83, 68 (100), 53, 43.

(*E*)-2-Dimethylaminomethyl-3,3,5-trimethylcyclohexanone oxime hydrochloride (IXa). A sample isolated as described above was recrystallized twice

from anhydrous *tert*-butyl alcohol. mp 93–95°C. IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2950, 2910, 2870, 2840 (CH); 2700, 2655, 2435, 2330 (NH^+); 1655 (C=N); 930 (NOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.99 d (3H, 5-CH_3, ^3J = 7.0 Hz), 1.03 s (3H, 3-CH_3-*ax*), 1.10 s (3H, 3-CH_3-*eq*), 1.61 m (2H, 4-H_{ax}, 4-H_{eq}), 1.89 m (5-H_{ax}), 2.21 d.d (6-H_{ax}, ^2J = 13.8, $^3J_{ax,ax}$ = 10.0 Hz), 2.72 d.d (2-H_{ax}, $^3J_{2,10\text{-}trans}$ = 9.8, $^3J_{2,10\text{-}gauche}$ = 4.5 Hz), 2.86 s [6H, $N(CH_3)_2$], 2.90 d.d.d (6-H_{eq}, ^2J = 13.8, $^3J_{eq,ax}$ = 3.6, ^WJ = 1.6 Hz), 2.96 d.d (*gauche*-10-H, ^2J = 10.0, $^3J_{10\text{-}gauche,2}$ = 4.5 Hz), 3.02 t (*trans*-10-H, ^2J = 10.0, $^3J_{10\text{-}trans,2}$ = 9.8 Hz), 10.21 br.s (NH), 10.68 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 213 $[M]^+$ (1), 167 $[M - Me_2NH_2]^+$, 150 $[M - Me_2NH_2 - OH]^+$, 135, 118, 109, 91, 83, 69 (100), 53, 44.

Benzylamino oxime hydrochlorides VIIIb and IXb (a mixture of isomers) were isolated from the reaction mixture by evaporation under reduced pressure, followed by reprecipitation from anhydrous acetone with excess anhydrous diethyl ether (yield 42%). To separate the isomers, the semicrystalline material was again dissolved in acetone, and crystals enriched in the major isomer (**VIIIb**) were precipitated by carefully adding anhydrous diethyl ether. The procedure was repeated to isolate amino oxime **VIIIb** containing ~92% of the main substance. The subsequent recrystallization from acetonitrile gave pure isomer **VIIIb**. An additional small amount of diethyl ether was added to the first mother liquor in order to separate isomer **VIIIb** more completely, the mother liquor was evaporated, and the residue was recrystallized thrice from 2-propanol to isolate pure (*E*)-oxime **IXb**.

(*Z*)-2-Benzylaminomethyl-3,5,5-trimethylcyclohexanone oxime hydrochloride (VIIIb). mp 175–177°C. IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2960, 2910, 2870, 2840 (CH); 2700, 2650, 2430, 2330 (NH^+); 1670 (C=N); 1570 (C–C_{arom}); 960 (NOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.93 s (3H, 5-CH_3-*ax*), 1.02 s (3H, 5-CH_3-*eq*), 1.11 d (3H, 3-CH_3, ^3J = 6.8 Hz), 1.52 t (4-H_{ax}, ^2J = 10.0, $^3J_{ax,ax}$ = 10.0 Hz), 1.57 d.d.d (4-H_{eq}, ^2J = 10.0, $^3J_{eq,ax}$ = 3.5, ^WJ = 1.6 Hz), 1.69 m (3-H_{ax}), 1.99 d (6-H_{ax}, ^2J = 13.6 Hz), 2.27 d.d (6-H_{eq}, ^2J = 13.6, ^WJ = 1.6 Hz), 3.08 m (2H, 10-H), 3.45 d.t (2-H_{ax}, $^3J_{ax,ax}$ = 10.0, $^3J_{2,10}$ = 7.0 Hz), 4.12 d and 4.20 d (PhC**H**$_2$, ^2J = 13.0 Hz), 7.38 m (3H) and 7.63 d (2H (H_{arom}); 7.64 br.s (NH), 10.50 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 275 $[M]^+$ (1), 167 $[M - PhCH_2NH_2]^+$, 150 $[M - PhCH_2NH_2 - OH]^+$, 135, 118, 109, 97, 96, 83, 68 (100), 53, 43.

(*E*)-2-Benzylaminomethyl-3,3,5-trimethylcyclohexanone oxime hydrochloride (IXb). mp 186–187°C. IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2960, 2910, 2870, 2840 (CH); 2700, 2650, 2430, 2330 (NH^+); 1650 (C=N); 1570 (C–C_{arom}); 930 (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 275 $[M]^+$ (1), 167 $[M - PhCH_2NH_2]^+$, 150 $[M - PhCH_2NH_2 - OH]^+$, 135, 118, 109, 91, 83, 69 (100), 53, 43. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.64 s (3H, 3-CH_3-*ax*), 1.02 s (3H, 3-CH_3-*eq*), 1.04 d (3H, 5-CH_3, ^3J = 7.0 Hz), 1.56 m (2H, 4-H_{ax}, 4-H_{eq}), 1.89 m (5-H_{ax}), 2.19 d.d (6-H_{ax}, ^2J = 13.6, $^3J_{ax,ax}$ = 10.0 Hz), 2.74 d.d (2-H_{ax}, $^3J_{2,10\text{-}trans}$ = 9.8, $^3J_{2,10\text{-}gauche}$ = 4.5 Hz), 2.92 d.d.d (6-H_{eq}, ^2J = 13.6, $^3J_{eq,ax}$ = 3.6, ^WJ = 1.6 Hz), 3.03 d.d (*gauche*-10-H, ^2J = 10.0, $^3J_{10\text{-}gauche,2}$ = 4.0 Hz), 3.08 t (*trans*-10-H, ^2J = 10.0, $^3J_{10\text{-}trans,2}$ = 9.8 Hz), 4.08 d and 4.21 d (PhC**H**$_2$, ^2J = 13.2), 7.36 m (3H) and 7.60 d (2H (H_{arom}), 8.35 br.s (NH, free), 10.20 br.s (NH, chelated), 10.80 br.s (NOH).

Regioisomeric amino oxime hydrochlorides Xa and XIa (a mixture of isomers) were isolated from the reaction mixture as an oily material (yield 40%). The isomers were separated by the procedure described above for compounds **VIIIa** and **IXa**.

(*Z*)-2-Dimethylaminomethyl-3,3,5-trimethylcyclohexanone oxime hydrochloride (Xa). mp 76–77°C (from anhydrous *tert*-butyl alcohol). IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2960, 2910, 2870, 2840 (CH); 2700, 2655, 2430, 2330 (NH^+); 1665 (C=N); 960 (NOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.94 d (3H, 5-CH_3, ^3J = 7.0 Hz), 1.02 s (3H, 3-CH_3-*ax*), 1.11 s (3H, 3-CH_3-*eq*), 1.59 m (2H, 4-H_{ax}, 4-H_{eq}), 1.87 m (5-H_{ax}), 2.05 d.d (6-H_{ax}, ^2J = 13.6, $^3J_{ax,ax}$ = 10.0 Hz), 2.28 d.d.d (6-H_{eq}, ^2J = 13.6, $^3J_{eq,ax}$ = 3.6, ^WJ = 1.6 Hz), 2.82 s [6H, $N(CH_3)_2$], 3.12 m (2H, 10-H), 3.45 t (2-H_{ax}, $^3J_{2,10}$ = 7.2 Hz), 8.12 br.s (NH), 9.60 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 213 $[M]^+$ (1), 167 $[M - Me_2NH_2]^+$, 150 $[M - Me_2NH_2 - OH]^+$, 135, 118, 109, 91, 89, 83, 69 (100), 53, 44.

(*E*)-2-Dimethylaminomethyl-3,5,5-trimethylcyclohexanone oxime hydrochloride (XIa). mp 89–91°C (from anhydrous *tert*-butyl alcohol). IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2960, 2910, 2870, 2840 (CH); 2700, 2655, 2430, 2330 (NH^+); 1650 (C=N), 930 (NOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 s (3H, 5-CH_3-*ax*), 1.03 d (3H, 3-CH_3, ^3J = 7.0 Hz), 1.12 s (3H, 5-CH_3-*eq*), 1.64 m (2H, 4-H_{ax}, 4-H_{eq}), 1.77 m (3-H_{ax}), 2.15 d (6-H_{ax}, ^2J = 13.6 Hz), 2.58 d.t (2-H_{ax}, $^3J_{ax,ax}$ = 10.0, $^3J_{2,10\text{-}trans}$ = 10.0, $^3J_{2,10\text{-}gauche}$ = 4.0 Hz), 2.78 d.d (6-H_{eq}, ^2J = 13.6, ^WJ = 1.6 Hz), 2.87 s [6H, $N(CH_3)_2$], 2.95 d.d (*gauche*-10-H, ^2J = 10.0, $^3J_{10\text{-}gauche,2}$ = 4.0 Hz), 3.01 t (*trans*-10-H, ^2J = 10.0, $^3J_{10\text{-}trans,2}$ = 10.0 Hz), 10.25 br.s (NH), 10.64 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 213 $[M]^+$ (1), 167

$[M - Me_2NH_2]^+$, 150 $[M - Me_2NH_2 - OH]^+$, 135, 118, 109, 97, 96, 83, 68 (100), 53, 43.

Benzylamino oxime hydrochlorides Xb and XIb (a mixture of isomers) were obtained in 44% yield. The isomers were separated as described above for compounds **VIIIb** and **IXb**.

(*Z*)-2-Benzylaminomethyl-3,3,5-trimethylcyclohexanone oxime hydrochloride (Xb). mp 168–169°C (from acetonitrile). IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2960, 2910, 2870, 2840 (CH); 2700, 2650, 2430, 2330 (NH^+); 1670 (C=N); 1570 (C–C_{arom}); 960 (NOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.78 s (3H, 3-CH_3-*ax*), 0.90 d (3H, 5-CH_3, ^3J = 7.0 Hz), 0.94 s (3H, 3-CH_3-*eq*), 1.51 m (2H, 4-H_{ax}, 4-H_{eq}), 1.86 m (5-H_{ax}), 2.09 d.d (6-H_{ax}, ^2J = 13.6, $^3J_{ax,ax}$ = 10.0 Hz), 2.24 d.d.d (6-H_{eq}, ^2J = 13.6, $^3J_{eq,ax}$ = 3.6, ^WJ = 1.6 Hz), 3.15 m (2H, 10-H), 3.49 t (2-H_{ax}, $^3J_{2,10}$ = 7.0 Hz), 4.12 d and 4.21 d (PhC**H**$_2$, ^2J = 13.0 Hz), 7.36 m (3H) and 7.64 d (2H) (H_{arom}), 7.88 br.s (NH), 10.60 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 275 $[M]^+$ (1), 167 $[M - PhCH_2NH_2]^+$, 150 $[M - PhCH_2NH_2 - OH]^+$, 135, 118, 109, 91, 83, 69 (100), 53, 43.

(*E*)-2-Benzylaminomethyl-3,5,5-trimethylcyclohexanone oxime hydrochloride (XIb). mp 180–182°C (from acetonitrile). IR spectrum, ν, cm^{-1}: 3450 (NOH, NH); 2960, 2910, 2870, 2840 (CH); 2700, 2650, 2430, 2330 (NH^+); 1650 (C=N); 1570 (C–C_{arom}); 930 (NOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.70 s (3H, 5-CH_3-*ax*), 1.02 d (3H, 3-CH_3, ^3J = 7.0 Hz), 1.04 s (3H, 5-CH_3-*eq*), 1.49 m (2H, 4-H_{ax}, 4-H_{eq}), 1.66 m (3-H_{ax}), 2.08 d (6-H_{ax}, ^2J = 13.6 Hz), 2.64 d.t (2-H_{ax}, $^3J_{ax,ax}$ = 10.0, $^3J_{2,10\text{-}trans}$ = 10.0, $^3J_{2,10\text{-}gauche}$ = 4.0 Hz), 2.72 d.d (6-H_{eq}, ^2J = 13.6, ^WJ = 1.6 Hz), 2.98 d.d (*gauche*-10-H, ^2J = 10.0, $^3J_{10\text{-}gauche,2}$ = 4.0 Hz), 3.03 t (*trans*-10-H, ^2J = 10.0, $^3J_{10\text{-}trans,2}$ = 10.0 Hz), 4.09 d and 4.22 d (PhC**H**$_2$, ^2J = 13.2 Hz), 7.38 m (3H) and 7.60 d (2H) (H_{arom}), 7.85 br.s (NH, free), 10.21 br.s (NH, chelated), 10.64 br.s (NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 275 $[M]^+$ (1), 167 $[M - PhCH_2NH_2]^+$, 150 $[M - PhCH_2NH_2 - OH]^+$, 135, 118, 109, 97, 96, 83, 68 (100), 53, 43.

Trimethyl(trimethyl-2-oxocyclohexylmethyl)-ammonium iodides and (2-hydroxyiminotrimethylcyclohexylmethyl)trimethylammonium iodides (*general procedure*). Sodium hydroxide, 400 mg (10 mmol), was added to a solution of 10 mmol of hydrochloride **IVa**, **Va**, **VIIIa**, **IXa**, **Xa**, or **XIa** in 10 ml of ethanol. The precipitate of sodium chloride was filtered off, 1 ml (~16 mmol) of methyl iodide was added to the resulting solution of the corresponding free Mannich base, and the mixture was left to stand at 12–14°C. From the solutions containing amino oximes **VIIIa** and **Xa**, trimethylamine hydroiodide separated in 30 min. Deamination of oximes **IXa** and **XIa** occurred at a lower rate and required several hours. No deamination of amino ketones **IVa** and **Va** was observed under these conditions, but it occurred during evaporation of alcoholic solutions of the quaternary salts on a rotary evaporator. By crystallization from ethanol (evaporation of an ethanolic solution on exposure to air in the cold) we succeeded in isolating only a small amount (~300 mg) of pure trimethyl-(4,4,6-trimethyl-2-oxocyclohexylmethyl)ammonium iodide (**XII**). mp 88°C (decomp.). IR spectrum, ν, cm^{-1}: 2960, 2910, 2870, 2840 (CH); 1720 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.79 s (3H, 5-CH_3-*ax*), 1.06 s (3H, 5-CH_3-*eq*), 1.32 d (3H, 3-CH_3, ^3J = 7.0 Hz), 1.70 m (2H, 4-H_{ax}, 4-H_{eq}), 1.88 m (3-H_{ax}), 2.06 d (6-H_{ax}, ^2J = 14.0 Hz), 2.35 d.d (6-H_{eq}, ^2J = 14.0, ^WJ = 1.6 Hz), 2.98 d.t (2-H_{ax}, $^3J_{ax,ax}$ = 10.0, $^3J_{2,10}$ = 6.9 Hz), 3.42 s [9H, $N(CH_3)_3$], 3.52 m (2H, 10-H). Mass spectrum, *m*/*z* (I_{rel}, %): 212 $[M]^+$ (<1), 152 $[M - Me_3NH]^+$, 137, 119, 109, 97, 96, 83, 68 (100), 53, 43.

We failed to isolate α,β-unsaturated compounds formed as a result of deamination, for they underwent fast polymerization during the reaction.

REFERENCES

1. Voitkevich, S.A., *865 Dushistykh veshchestv dlya parfyumerii i bytovoi khimii* (865 Fragrant Substances for Perfumes and Household Chemicals), Moscow: Pishchevaya Promyshlennost', 1994, p. 225.
2. *Osnovy biokhimii* (Principles of Biochemistry), Moscow: Mir, 1981, vol. 3, p. 1759.
3. *Comprehensive Organic Chemistry*, Barton, D. and Ollis, W.D., Eds., Oxford: Pergamon, 1979, vol. 1. Translated under the title *Obshchaya organicheskaya khimiya*, Moscow: Khimiya, 1982, vol. 2, pp. 585, 643.
4. Pashkovskii, V.S., Lakhvich, F.A., Koval'skaya, S.S., and Kozlov, N.G., *Russ. J. Org. Chem.*, 2001, vol. 37, p. 375.
5. Koval'skaya, S.S. and Kozlov, N.G., *Russ. J. Org. Chem.*, 1997, vol. 33, p. 177.
6. Koval'skaya, S.S. and Kozlov, N.G., *Russ. J. Org. Chem.*, 2000, vol. 36, p. 785.
7. Dailing, D.K. and Grant, D.M., *J. Am. Chem. Soc.*, 1972, vol. 94, p. 5318.
8. Daniel, A. and Pavia, A.A., *Tetrahedron Lett.*, 1967, p. 1145.
9. Vatsuro, K.V. and Mishchenko, G.L., *Imennye reaktsii v organicheskoi khimii* (Name Reactions in Organic Chemistry), Moscow: Khimiya, 1976, p. 268.
10. Soloducho, J. and Zabza, A., *Pol. J. Chem.*, 1979, vol. 53, p. 1497.