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Condensation of Isophorone and Isophorone Oxime with Amines and Aldehydes

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Abstract—Mannich condensations of isophorone (3,5,5-trimethylcyclohex-2-en-1-one) with paraformaldehyde and dimethylamine, benzylamine, and piperidine hydrochlorides were studied. The reactions were not selective, and they involved both activated methylene group and vinylic carbon atom, as well the exocyclic methyl group at the double bond. The corresponding isomeric amino ketones were formed in comparable amounts (42, 30, and 28%). The *E* and *Z* isomers of isophorone oxime reacted with paraformaldehyde and dimethylamine hydrochlride to give mixtures of analogous Mannich condensation products, but the fraction of the addition product at the carbon atom spatially close to the oxime hydroxy group was larger. Under analogous conditions, the reaction of isophorone with aromatic amines and aromatic aldehydes gave products of two-component condensation of isophorone with aldehydes, and the reactions involved exclusively the activated methylene group in the initial enone with formation of the corresponding *trans*,*trans*-isomeric 7-arylmethylidene derivatives.

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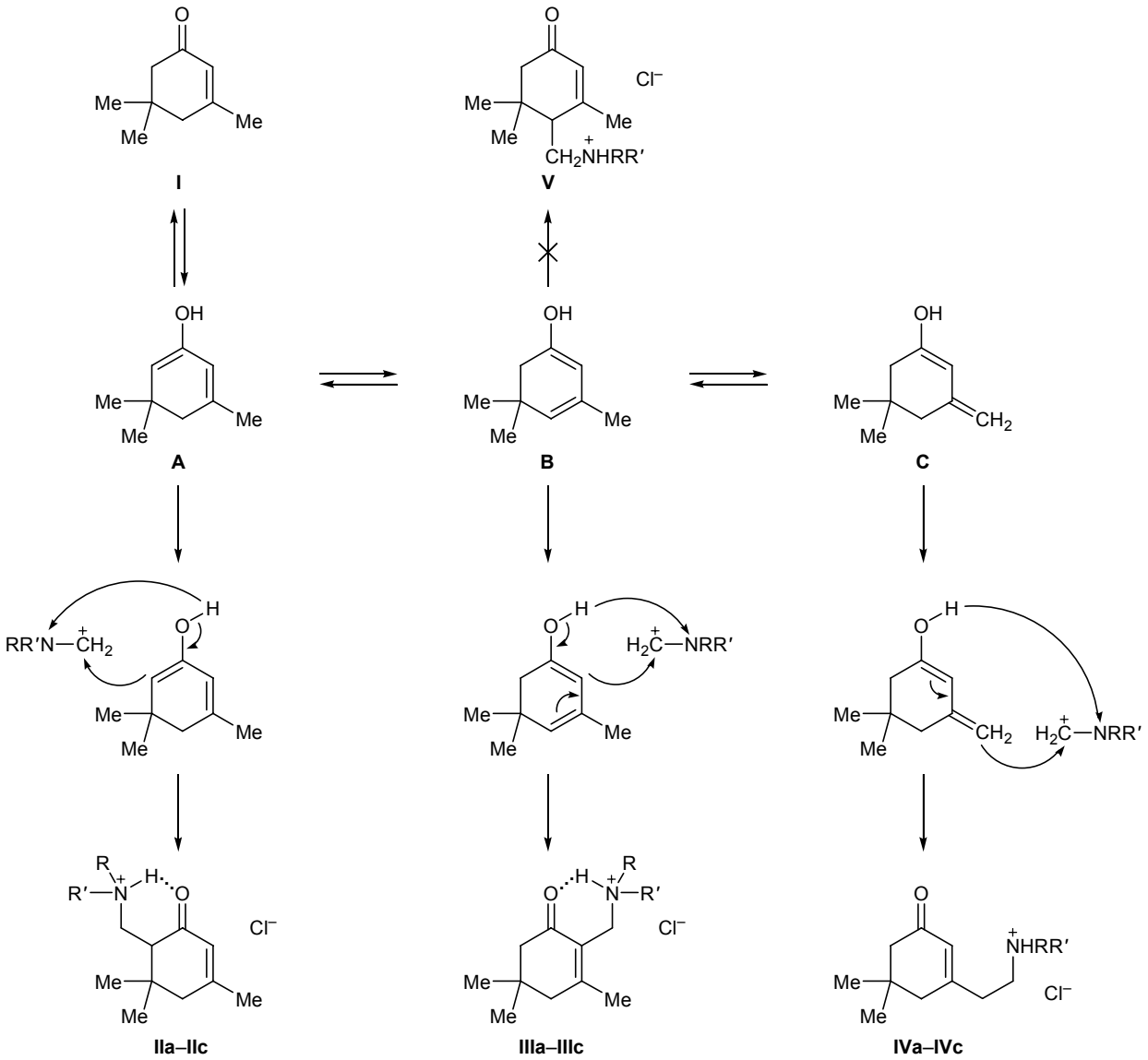
α-Aminomethylation of carbonyl compounds with iminium intermediates generated from amines and aldehydes, which is known as Mannich condensation [1], is widely used in organic synthesis. The significance of this reaction is determined primarily by the fact that the resulting β-amino ketones or their quaternary salts readily undergo deamination with formation of α,β-unsaturated carbonyl compounds; high reactivity of the latter underlies their application in the synthesis of a broad series of derivatives. Using as an example 3-methylideneisocamphanone prepared by deamination of the corresponding Mannich base, we demonstrated the possibility for synthesizing a number of terpene derivatives with various functional groups, heterocyclic compounds, and carbocyclic analogs of prostaglandin endoperoxides [2–4]. The behavior of α,β-unsaturated ketones under the Mannich condensation conditions was studied very poorly. A probable reason is high lability of such compounds, especially under acid catalysis necessary for the Mannich reaction.

We examined transformations of isophorone (**I**, 3,5,5-trimethylcyclohex-2-en-1-one) in the Mannich reaction. This α,β-unsaturated ketone was selected as substrate taking into account primarily its accessibility, as well as cyclic structure and high degree of substitution in the enone fragment, which make it relatively stable and weakly prone to undergo polymerization (tarring). The isophorone molecule possesses an enolizable $CH_2C{=}O$ fragment, which is a classical reaction center for Mannich condensation. Therefore, the formation of 6-aminomethylisophorone derivatives **II** might be expected.

In fact, β-amino ketones like **II** were formed as a result of Mannich condensation of **I** with paraformaldehyde and amines, but they were not the only products (42% in the product mixture). Simultaneously, α-aminomethylation occurred at both C^2 vinylic carbon atom and methyl carbon atom (C^7) at the double bond (γ-aminomethylation). The fractions of 2- and 7-aminomethyl derivatives **III** and **IV** in the product mixtures (30 and 28%, respectively) were slightly smaller than that of the classical condensation product **II**, but the ratio of regioisomers **II**–**IV** was the same in the reactions with dimethylamine, benzylamine, and piperidine hydrochlorides.

Mixtures of regioisomeric amino ketones **II**–**IV** were separated by fractional crystallization. The most difficult was isolation of *N*,*N*-dimethylamino derivatives **IIa**–**IVa**, for these hydrochlorides are relatively

Scheme 1.



R = R′ = Me (**a**); R = H, R′ = $PhCH_2$ (**b**); RR′ = $(CH_2)_5$ (**c**).

low-melting substances and are extremely hygroscopic. Therefore, our attempt to isolate compounds **IIa**–**IVa** according to the procedure reported previously [5] (precipitation with diethyl ether or acetone from a solution in alcohol), instead of separation of the corresponding hydrochloride, resulted in formation of two layers, one of which contained all three components of the reaction mixture, initial solvents, and a small amount of water. Samples enriched in each regioisomer (no less than 80%) were obtained by repeated precipitation with anhydrous tetrahydrofuran from anhydrous acetone. Amino ketone hydrochlorides obtained from benzylamine and piperidine were separated using mixtures of anhydrous diethyl ether, chloroform, and/or acetone.

The stucture of the isolated compounds was determined on the basis of their IR, ^{1}H NMR, and mass spectra. The IR spectrum of 6-(dimethylaminomethyl)-isophorone hydrochloride (**IIa**) contained absorption bands typical of stretching vibrations of conjugated carbonyl group (1665 cm^{-1}) and N–H bond (3400 cm^{-1}) and a series of bands in the region 2400–2700 cm^{-1}, corresponding to vibrations of protonated amines. In the mass spectrum of **IIa** the molecular ion peak had an *m*/*z* value of 196 (protonated form) and a relative intensity of 7%. Reliable proofs for the struc-

ture of **IIa** as 6-aminomethyl derivative were obtained by ^{1}H NMR spectroscopy. Compound **IIa** displayed in the ^{1}H NMR spectrum signals from methyl groups at δ 1.02 (6H, 5-CH_3) and 1.98 ppm (d, 3H, 3-CH_3, ^4J = 1.4 Hz), a quartet from the olefinic proton at δ 5.97 ppm (^4J = 1.4 Hz), and a broadened two-proton singlet at δ 2.26 ppm due to methylene protons on C^4. The 6-H signal was a doublet of doublets at δ 3.32 ppm with vicinal coupling constants of 8 and 6 Hz. Protons on C^{10} resonated at δ 3.64 (d.d, ^2J = 11, ^3J = 6 Hz) and 3.54 ppm (d, ^2J = 11, ^3J = 8 Hz). Nonequivalence of the geminal protons on C^{10} [as in saturated analog, 2-(dimethylaminomethyl)dihydroisophorone] indicates formation of a strong intramolecular hydrogen bond between the amino and carbonyl groups, which restricts rotation of the aminomethyl substituent [5]. The differences in the chemical shifts of protons on C^{10} and in the vicinal coupling constants are smaller than those observed for the saturated analog, which may be due to distortion of bond angles caused by the presence of a planar enone fragment in molecule **IIa**.

The IR and mass spectra of the second product (32%) were analogous to those of compound **IIa**. This product was assigned the structure of 2-(dimethylaminomethyl)isophorone hydrochloride (**IIIa**) on the basis of the ^{1}H NMR data. The ^{1}H NMR spectrum of **IIIa** lacked signal from olefinic proton but contained two broadened two-proton singlets at δ 2.20 and 2.64 ppm, corresponding to the C^4H_2 and C^6H_2 methylene groups, respectively. These findings indicate that the dimethylaminomethyl group is attached to the double-bonded carbon atom (C^2). Signals from protons on C^{10} appear as two doublets at δ 3.08 and 3.12 ppm with a distinct "roof" effect and a geminal coupling constant ^2J of 12 Hz (*AB* system). The multiplicity of these signals indicates the absence of proton in the vicinal position, in keeping with the proposed structure. The same follows from the presence of a singlet at δ 1.99 ppm, which belongs to the methyl group on C^3 (no allylic coupling typical of compound **IIa** was observed).

Aminomethylation at the double-bonded carbon atom in the α-position with respect to the carbonyl group in molecule **I** was unexpected; this reaction path is not consistent with the classical scheme of alkylation of enolates. In keeping with the generally accepted views on the mechanism of Mannich condensation, the reaction center should possess an effective negative charge. Taking into account that the double C=C bond in the enone fragment is polarized due to high electronegativity of the carbonyl oxygen atom, the above interaction becomes possible.

The structure of the minor component of the product mixture (28%) was even more surprising. Its IR spectrum was similar to the spectra of regioisomers **IIa** and **IIIa**. The mass spectrum of this compound also contained the molecular ion peak with *m*/*z* 196, but the fragmentation pattern was essentially different, indicating considerable differences in the structure. Analysis of the ^{1}H NMR data showed that compound **IVa** is the condensation product at the methyl group attached to the double-bonded carbon atom, 3-[2-(dimethylamino)ethyl]-5,5-dimethylcyclohex-2-en-1-one hydrochloride. The ^{1}H NMR spectrum of **IVa** lacked signal typical of 3-methyl group at about δ 2 ppm, whereas a two-proton multiplet appeared as δ 2.36 ppm, and the olefinic 2-H proton resonated as a triplet at δ 5.98 ppm (^4J = 1.4 Hz), indicating the presence of only two protons in the *cis*-allylic position. The $C^{10}H_2$ protons gave a triplet at δ 3.06 ppm (2H) with a coupling constant ^3J of 7 Hz due to vicinal interaction with protons of the neighboring methylene group. The fact that protons on C^{10} are magnetically equivalent suggests conformational mobility of the aminomethyl fragment and its remoteness from the carbonyl group; therefore, intramolecular hydrogen bonding is impossible.

Likewise, the IR, ^{1}H NMR, and mass spectra of benzylaminomethyl and piperidinomethyl derivatives **IIb–IVb** and **IIc–IVc** confirmed the assumed structures (see Experimental).

Thus, the molecule of 3,5,5-trimethylcyclohex-2-en-1-one (**I**) was found to possess three reaction centers capable of being involved in Mannich condensation. Apart from the classical reaction path, i.e., aminomethylation at the activated α-methylene group, the reaction also occurred at the α-olefinic and γ-allylic carbon atoms. Isophorone molecule possesses one more γ-allylic carbon atom (C^4), but no aminomethylation products at C^4 (**V**) were detected in the reaction mixtures. Presumably, the presence of three methyl groups in the α-positions to C^4 hampers reaction at that center for steric reasons.

It is commonly believed that the α-methylene group in ketones is activated during the Mannich condensation as a result of enolization of the carbonyl group [6]. Such enolization of isophorone should give rise to hydroxy diene **A**. It may be presumed that compound **I** may be converted into both normal dienol **A** and analogous intermediates **B** and **C**, in which the activat-

ed atoms are C^2 and C^4 or C^2 and C^7, respectively. The product ratio is determined by the probability for formation of the corresponding dienols and spatial accessibility of the reaction centers therein. Therefore, the reaction of intermediate **B** with methylideneiminium cation should lead to 2-aminomethyl derivative **III**, while intermediate **C** should be converted mainly into compound **IV** (Scheme 1).

The reaction mechanism involving the corresponding enols is not the only possible, for compounds that could not give rise to enols are also capable of reacting with aldehydes and amines according to Mannich; such compounds are, e.g., ketone oximes [5, 7, 8]. We synthesized isophorone oxime as a mixture of *E* and *Z* isomers **VI** and **VII** whose ratio depended on the oximation conditions. The reaction at room temperature gave a mixture of *E* and *Z* isomers at a ratio of 1:3, whereas at elevated temperature the **VI**:**VII** ratio was 8:11 (according to the ^{1}H NMR data; see below). Separation of isomeric oximes is difficult; both isomers are very readily soluble in most organic solvents, and they crystallized jointly from strongly concentrated solutions even in the cold. We succeeded in obtaining a sample slightly enriched in the major *Z* isomer (**VII**) by crystallization from aqueous acetone (acetone–water ratio 6:1). By repeated dissolution–crystallization we isolated a sample containing no less than 92% of isomer **VII**. A sample consisting mainly of the *E* isomer (**VI**) was obtained by repeated crystallization from aqueous methanol of the substance isolated from the mother liquor (see Experimental).

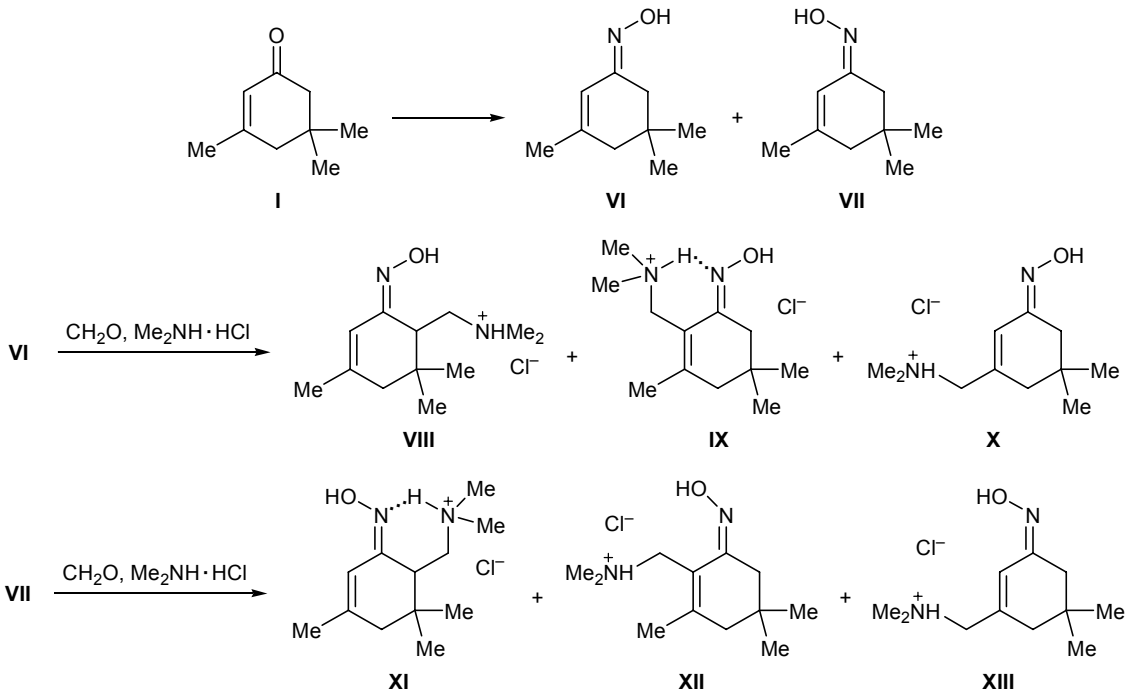
The structure of *E* and *Z* stereoisomers was assigned to compounds **VI** and **VII** on the basis of their ^{1}H NMR spectra. It is known [9] that proton located in the vicinity of the oxime hydroxy group gives a signal in a weaker field due to deshielding effect of the hydroxy group. In our case, the signal from the olefinic proton in the major isomer appears at δ 6.64 ppm, and that from the minor isomer, at δ 5.92 ppm; therefore, the former was assigned *Z* configuration where the hydroxy group on the nitrogen is oriented toward the C^2 atom. By contrast, the signal from methylene protons on C^6 in the *E* isomer is located in a weaker field (δ 2.37 ppm) relative to the corresponding signal of the *Z* isomer (δ 2.08 ppm).

Oximes **VI** and **VII** were used as substrates in the Mannich condensation with paraformaldehyde and dimethylamine hydrochloride. These reactions also afforded mixtures of aminomethylation products at C^2, C^6, and C^7, though in a smaller yield because of considerable tarring. The major product obtained from *E* isomer **VI** was 6-(dimethylaminomethyl)isophorone oxime hydrochloride (**VIII**, 55%), while the fractions of 2- and 7-dimethylaminomethyl derivatives **IX** and **X** were 24 and 21%, respectively. Under similar conditions, *Z*-oxime **VII** gave rise to a mixture of products consisting of 34% of 6-(dimethylaminomethyl) derivative **XI**, 43% of 2-(dimethylaminomethyl) isomer **XII**, and 23% of 7-aminomethyl analog **XIII** (Scheme 2). The products were separated by the same procedure as that described above for the separation of analogous amino ketones.

The structure of amino oximes **VIII**–**XIII** was confirmed by their IR, ^{1}H NMR, and mass spectra. The IR spectra of **VIII**–**XIII** contained an absorption band at 1650 cm^{-1}, corresponding to stretching vibrations of C=N bond in α,β-unsaturated oximes, and a band at 3400 cm^{-1}, which is typical of vibrations of oxime hydroxy group. In the mass spectra of **VIII**–**XIII**, the molecular ion peaks (*m*/*z* 211) had a relative intensity of 5–6%. The products were assigned the structure of particular regioisomers on the basis of the same considerations as in the structure assignment of the amino ketone analogs. Amino oximes **VIII** and **XI** displayed in the ^{1}H NMR spectra signals from both olefinic proton and methyl group at the double bond, as well as a downfield signal from 6-H; therefore, these compounds were assigned the structure of 6-dimethylaminomethyl derivatives. The spectra of **IX** and **XII** lacked olefinic proton signal, which is consistent with the structure of 2-(dimethylaminomethyl)isophorone oxime hydrochlorides, while in the spectra of minor products **X** and **XIII** we observed no signal assignable to methyl group at the double bond (δ 2 ppm), which indicated that aminomethylation occurred at the C^7 atom of the initial oxime.

Unlike amino ketones **II** and **III**, strong intramolecular hydrogen bond is formed only in amino oximes **IX** and **XI** where the hydroxy group on the oxime nitrogen atom is oriented in the opposite direction to the amino group, so that there are no steric hindrances for hydrogen bonding between the NH proton and oxime nitrogen atom. As a result of intramolecular hydrogen bonding, protons in the methylene group neighboring to the amino nitrogen atom become nonequivalent, and they appear in the ^{1}H NMR spectra as two doublets of doublets with the same coupling constants as in the spectra of analogous amino ketones (see Experimental). Signals from the corresponding protons in the spectra of regioisomeric amino oximes **VIII** and **XII** were two-proton doublets with a vicinal

Scheme 2.



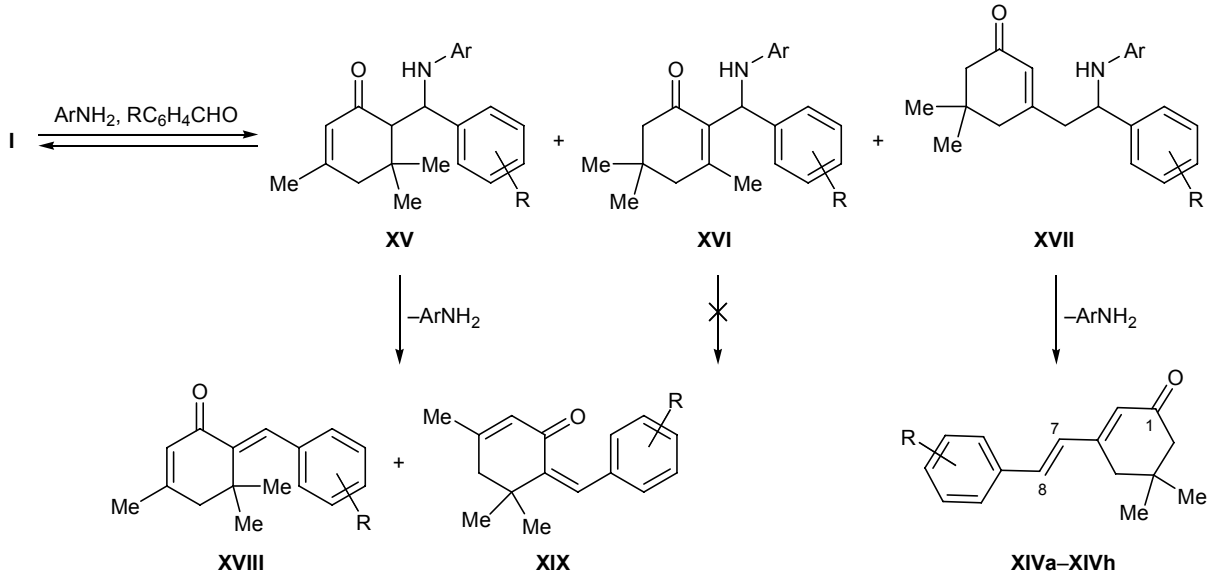
coupling constant ^3J of 7 Hz. These protons in molecules **VIII** and **XII** are magnetically equivalent due to conformational mobility of the aminomethyl fragment.

Thus the transformations of oximes **VI** and **VII** in the Mannich reaction are generally similar to those occurring with isopohorone. The only difference is slightly increased fraction of the aminomethylation product at the carbon atom neighboring to the oxime fragment (compounds **VIII** and **XII** for the *E* and *Z* isomers, respectively). As we noted previously [5], this may be due to association of intermediate iminium carbocation with the hydroxy group at the stage preceding its addition. As concerns other aspects, the mechanism of Mannich condensation of non-enolizable ketone oximes remains unclear.

We also made an attempt to perform Mannich condensation of isophorone (**I**) with paraformaldehyde and aromatic amines. However, the reactions with aromatic amines (*p*-toluidine, *p*-chloroaniline, *p*-methoxyaniline, and methyl *p*-aminobenzoate) as both free bases and hydrochlorides were accompanied by fast tarring, and we failed to isolate appreciable amounts of the target Mannich bases from the reaction mixtures. Tarring also occurred in the reactions of isophorone (**I**) with aromatic aldehydes and aromatic amine hydrochlorides. When aromatic amines were taken as free bases, we isolated products of two-component condensation of isophorone with the corresponding aldehyde. This process was strictly regio- and stereoselective, and the corresponding *trans*,*trans*-7-(arylmethylidene)isophorones **XIV** were isolated in good yields (Scheme 3). Analogous compounds were not obtained in the condensation with salicylaldehyde and *m*- and *p*-nitrobenzaldehydes; in these cases, only the corresponding Schiff bases were isolated from the reaction mixture. Probable reasons are discussed below. The expected Mannich bases were detected but only as minor components (no more than 5%).

The structure of dienones **XIV** was determined by IR and ^{1}H NMR spectroscopy. The IR spectra of these compounds contained an absorption band at 1630–1650 cm^{-1}, which is typical of stretching vibrations of carbonyl group in conjugated systems, and bands belonging to vibrations of conjugated and aromatic C=C bonds. In the ^{1}H NMR spectra we observed signals from protons in the aromatic fragment, a singlet from methyl protons (6H, δ ~1.1 ppm), and broadened singlets due to methylene protons on C^4 and C^6 (2H each, δ ~2.30 and 2.45 ppm). The 2-H olefinic proton resonated as an unresolved multiplet. Its chemical shift (δ ~6 ppm) insignificantly differed from that of initial isophorone, indicating the absence of shielding by the arylvinyl fragment and hence *s-trans* orientation of the latter with respect to the endocyclic C=C bond. Signals from protons at the C^7=C^8 double bond were two doublets with a clearly pronounced "roof" effect (*AB*

Scheme 3.



R = 4-F (**a**), 4-Br (**b**), 4-HO (**c**), 4-MeO (**d**), 4-Me_2N (**e**), 3-EtO-4-HO (**f**), 3-MeO-4-HO (**g**), 3,4-$(MeO)_2$ (**h**);
Ar = 4-MeC_6H_4, 4-$MeOC_6H_4$, 1-naphthyl, 2-naphthyl, etc.

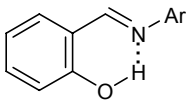
system, δ ~6.8 and ~6.9 ppm). An exception was 7-(*p*-bromobenzylidene) derivative **XIVb**; the 7-H and 8-H protons resonated in the spectrum of **XIVb** as one two-proton singlet (the protons turned out to be accidentally equivalent). The vicinal coupling constant for 7-H and 8-H in all other compounds **XIV** was 16 Hz, which corresponds to *trans* configuration of the double bond and hence *trans* arrangement of the isophorone and aromatic fragments.

A probable mechanism for formation of compounds **XIV** is as follows. It is known that aromatic amines readily react with aldehydes to give the corresponding Schiff bases. Addition of CH acid at the activated C=N bond in Schiff bases could lead to β-arylamino ketones. Insofar as the addition step is reversible, Mannich base always exists in equilibrium with initial isophorone and Schiff base. Another possible decomposition path typical of Mannich bases is their deamination (Hofmann elimination). Compound **XVI** cannot undergo elimination according to Hofmann, for it lacks proton in the β-position with respect to the amino group. Deamination of the addition product at C^6 (**XV**) is possible; however, this process is not favorable for thermodynamic and steric reasons: as a result, compounds **XVIII** and **XIX** would be formed with cross-conjugated system of double bonds, one of which is strained and oriented *cis* with respect to the carbonyl group; moreover, van der Waals repulsion between the aryl substituents and the carbonyl or geminal dimethyl group is possible in both these structures. By contrast, deamination of β-enamino ketone **XVII** seems to be quite advantageous, for it could lead to the formation of linear conjugated double bond system in thermodynamically favorable *trans*,*trans* configuration. As follows from the NMR data, just dienones having structure **XIV** were obtained.

Taking into account that the formation of amino ketones **XV** and **XVI** is reversible and that compound **XIV** is chemically inert (it does not undergo further transformations), just the latter accumulates as product under the given conditions. Furthermore, it is very probable that the formation of Mannich bases **XV**–**XVII** is characterized by different regioselectivity than in the synthesis of analogs **II**–**IV**, for the intermediate Schiff base has a much larger size than iminium intermediate generated from formaldehyde; therefore, the C^7 atom (methyl group) in isophorone is the most accessible for the addition of Schiff base molecule.

The assumed formation of aryldienone **XIV** through intermediate Mannich base **XVII** rather than direct condensation is supported by the following. First of all, the corresponding Schiff bases were isolated as by-products from all reaction mixtures, and in some cases traces of compounds **XV**–**XVII** were detected. Second, we found that isophorone does not react with aromatic aldehydes in the presence of tertiary amines (e.g., *N*,*N*-dimethylaniline) despite their higher acidity, other conditions being equal. Third, as we already

noted, neither salicylaldehyde nor *m*- and *p*-nitrobenzaldehydes reacted with isophorone and aromatic amines, and only the corresponding Schiff bases were isolated from the reaction mixtures. Obviously, compounds **XX** formed from aromatic amines and salicylaldehyde are stabilized by intramolecular hydrogen bond which prevents them from being involved in subsequent Michael addition process.



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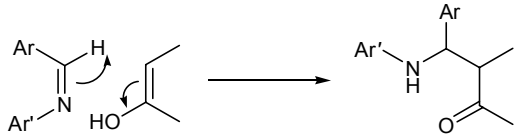
In the case of Schiff bases derived from nitrobenzaldehydes, electronic factors are likely to be crucial. It is generally accepted that the addition involves cyclic transition state **XXI** which is converted into Mannich base **XXII** via bond migration (Scheme 4). The presence of a strong electron-withdrawing substituent (nitro group) in the benzene ring reduces the electron density on the double C=N bond, so that its reactivity weakens. If dienones **XIV** were formed according to a different scheme, i.e., that not involving formation and subsequent addition of Schiff bases, chemical reactivity of the latter would not affect the condensation of isophorone with aldehydes.

Scheme 4.



XXI **XXII**

Our attempts to obtain compounds analogous to dienones **XIV** from *E*- and *Z*-isomeric isophorone oximes **VI** and **VII** were unsuccessful: in all cases, complete tarring occurred.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Protégé-460 spectrometer with Fourier transform. The ^{1}H NMR spectra were measured on a Bruker Avance instrument (500 MHz) from solutions in $CDCl_3$ using tetramethylsilane as internal reference. The mass spectra were obtained on a Hewlett–Packard 5890/5972 GC–MS system (HP-5MS column; electron impact, 70 eV). The progress of reactions was monitored, and the reaction mixtures were analyzed, by GLC on a Chrom-5 chromatograph (glass column, 2000×2 mm, stationary phase Apiezon L on Chromaton N-AW-DMCS, 0.16–0.20 mm).

Isophorone oximes were synthesized according to the procedure described in [10]. Prolonged stirring of the reaction mixture at room temperature resulted in the formation of a mixture of *E* and *Z* isomers **VI** and **VII** at a ratio of 1:3. Crystallization of the isomer mixture from acetone–water (6:1) increased the fraction of the major isomer, (*Z*)-**VII**. After five crystallizations, the product contained no less than 92% of *Z* isomer **VII**. When the reaction was carried out at elevated temperature (under reflux), the ratio of *E*- and *Z*-isomeric isophorone oximes **VI** and **VII** was 8:11. The product was recrystallized from acetone–water (6:1), and the mother liquor enriched in minor component **VI** was evaporated. The residue was a semicrystalline material which was dissolved in methanol, water was added to the solution until it turned turbid, the mixture was evaporated, and the precipitate enriched in *E* isomer **VI** was filtered off. After six recrystallizations we obtained a sample containing ~93% of *E* isomer **VI**.

(*E*)-3,5,5-Trimethylcyclohex-2-en-1-one oxime (VI). mp 90–92°C. IR spectrum, ν, cm^{-1}: 3400 br, v.s (OH), 3050 v.w (=C–H), 2965 s, 2930 m (C–H$_{aliph}$), 1650 s (C=N), 960 m (N–O). ^{1}H NMR spectrum, δ, ppm: 0.96 s (6H, 5-CH$_3$), 1.83 d (3H, 3-CH$_3$, ^4J = 1.4 Hz), 1.98 br.s (2H, 4-H), 2.08 br.s (2H, 6-H), 6.64 q (1H, 2-H, ^4J = 1.4 Hz), 9.60 br.s (1H, OH).

(*Z*)-3,5,5-Trimethylcyclohex-2-en-1-one oxime (VII). mp 99–101°C. IR spectrum, ν, cm^{-1}: 3420 br, v.s (OH), 3050 v.w (=C–H), 2960 s, 2930 m (C–H$_{aliph}$), 1650 s (C=N), 950 m (N–O). ^{1}H NMR spectrum, δ, ppm: 1.00 s (6H, 5-CH$_3$), 1.80 d (3H, 3-CH$_3$, ^4J = 1.4 Hz), 1.94 br.s (2H, 4-H), 2.37 br.s (2H, 6-H), 5.92 q (1H, 2-H, ^4J = 1.4 Hz), 9.80 br.s (1H, OH).

Mannich condensations of isophorone (I) and its oximes VI and VII were carried out according to the procedure described in [5]. After addition of diethyl ether to the solution in ethanol obtained by reaction with dimethylamine hydrochloride, the mixture divided into layers. The bottom layer containing the target products was separated and evaporated on a rotary evaporator. Compounds obtained in the reactions with benzylamine and piperidine hydrochlorides were isolated by evaporation of the reaction mixture to 1/5 of the initial volume and subsequent precipitation with excess anhydrous acetone.

Dimethylaminomethyl ketone hydrochlorides IIa–IVa were isolated as a dark thick oily substance (overall yield 60%). The isomers were separated as

follows. The product mixture was dissolved in anhydrous acetone, anhydrous tetrahydrofuran was added until the solution turned turbid, and the mixture was placed in a refrigerator with protection from atmospheric moisture (the obtained hydrochlorides are very hygroscopic). The precipitate was filtered off, THF was added to the filtrate until it turned turbid and so on. Following this procedure, first crystallization fractions were enriched in compound **IIa**, last crystallization fractions were enriched in **IIIa**, and the mother liquor was enriched in isomer **IVa**.

6-(Dimethylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one hydrochloride (IIa) was isolated after four dissolution–precipitation cycles, purity ≥87%. IR spectrum, ν, cm^{-1}: 3400 br.s (NH), 3050 v.w (=C–H), 2960 s, 2930 m (C–H_{aliph}), 2730–2350 (several bands, NH^+), 1665 s (C=O), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.03 s (6H, 5-CH_3), 1.98 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.30 br.s (2H, 4-H), 2.95 s (6H, NCH_3), 3.32 d.d (1H, 6-H, ^3J = 6, 8 Hz), 3.54 d.d (1H, 10-H, ^2J = 11, ^3J = 8 Hz), 3.64 d.d (1H, 10-H, ^2J = 11, ^3J = 6 Hz), 5.97 q (1H, 2-H, ^4J = 1.4 Hz), 9.80 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 196 (7) $[M]^+$, 150 $[M - Me_2NH_2]^+$, 135, 121, 118, 108, 96, 93, 67 (100), 52, 41.

2-(Dimethylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one hydrochloride (IIIa) was isolated after five recrystallization from dioxane of a fraction enriched in this isomer, purity ≥83%. IR spectrum, ν, cm^{-1}: 3410 br.s (NH), 2960 s, 2930 m (C–H_{aliph}), 2730–2350 (several bands, NH^+), 1665 s (C=O), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.82 s (6H, 5-CH_3), 1.99 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.20 br.s (2H, 4-H), 2.64 br.s (2H, 6-H), 2.88 s (6H, NCH_3), 3.08 d (1H, 10-H, ^2J = 12 Hz), 3.16 d (1H, 10-H, ^2J = 12 Hz), 9.60 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 196 (9) $[M]^+$, 150 $[M - Me_2NH_2]^+$, 135, 121, 118, 108, 96, 93, 67 (100), 52, 41.

3-[2-(Dimethylamino)ethyl]-5,5-dimethylcyclohex-2-en-1-one hydrochloride (IVa) with a purity of ≥80% was isolated after four recrystallizations from anhydrous acetone of the product isolated from the mother liquor. IR spectrum, ν, cm^{-1}: 3350 br.s (NH), 3050 v.w (=C–H), 2960 s, 2930 m (C–H_{aliph}), 2730–2350 (several bands, NH^+), 1670 s (C=O), 1620 (C=C). ^{1} NMR spectrum, δ, ppm: 1.34 s (6H, 5-CH_3), 2.24 br.s (2H, 4-H), 2.36 m (2H, 7-H), 2.58 br.s (2H, 6-H), 2.90 s (6H, NCH_3), 3.06 t (2H, 10-H, ^3J = 7 Hz), 5.98 t (1H, 2-H, ^4J 1.4 Hz), 8.40 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 196 (5) $[M]^+$, 150 $[M - Me_2NH_2]^+$, 136, 123, 108, 92, 83, 67 (100), 55, 41.

Benzylaminomethyl ketone hydrochlorides IIb–IVb were isolated as a light yellow semicrystalline material with an overall yield of 64%. To isolate particular regioisomers, the mixture was dissolved in chloroform, and the products were fractionally precipitated with diethyl ether. The first fractions were enriched in compound **IVb**, the last fractions were enriched in **IIIb**, and the mother liquor was enriched in isomer **IIb**.

6-(Benzylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one hydrochloride (IIb) was isolated by fourfold dissolution in acetone and precipitation with diethyl ether of the product isolated from the mother liquor, purity ≥90%. IR spectrum, ν, cm^{-1}: 3400 br.s (NH), 3060 m (C–H_{arom}), 2960 s, 2930 m (C–H_{aliph}), 2730–2400 (several bands, NH^+), 1665 s (C=O), 1620 (C=C), 1590 s (C=C_{arom}), 745 s, 695 m (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.05 s (6H, 5-CH_3), 1.97 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.27 br.s (2H, 4-H), 3.28 d.d (1H, 6-H, ^3J = 6, 8 Hz), 3.57 d.d (1H, 10-H, ^2J = 10, ^3J = 8 Hz), 3.62 d.d (1H, 10-H, ^2J = 10, ^3J = 6 Hz), 4.08 d and 4.16 d (1H each, PhC**H**$_2$, ^2J = 13.2 Hz), 5.93 q (1H, 2-H, ^4J = 1.4 Hz), 7.38 m (3H) and 7.66 m (2H) (Ph), 8.60 br.s (1H, NH, free), 10.2 br.s (1H, NH, chelated). Mass spectrum, *m*/*z* (I_{rel}, %): 258 (5) $[M]^+$, 150 $[M - PhCH_2NH_2]^+$, 135, 121, 118, 108, 107 (100), 96, 93, 67, 52, 41.

2-(Benzylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one hydrochloride (IIIb) was isolated by fivefold recrystallization from acetone of a fraction enriched in this isomer, purity ≥88%. IR spectrum, ν, cm^{-1}: 3410 br.s (NH), 3060 m (C–H_{arom}), 2960 s, 2930 m (C–H_{aliph}), 2730–2400 (several bands, NH^+), 1665 s (C=O), 1620 (C=C), 1590 s (C=C_{arom}), 750 s, 700 m (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 0.84 s (6H, 5-CH_3), 1.96 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.18 br.s (2H, 4-H), 2.58 br.s (2H, 6-H), 3.12 d (1H, 10-H, ^2J = 12 Hz), 3.18 d (1H, 10-H, ^2J = 12 Hz), 4.12 d and 4.18 d (1H each, PhC**H**$_2$, ^2J = 13.2 Hz), 7.32 m (3H) and 7.60 m (2H, Ph), 8.80 br.s (1H, NH, free), 10.4 br.s (1H, NH, chelated). Mass spectrum, *m*/*z* (I_{rel}, %): 258 (6) $[M]^+$, 150 $[M - PhCH_2NH_2]^+$, 135, 121, 118, 108, 107 (100), 96, 93, 67, 52, 41.

3-[2-(Benzylamino)ethyl]-5,5-dimethylcyclohex-2-en-1-one hydrochloride (IVb) was isolated by fourfold precipitation with diethyl ether from chloroform, purity ≥85%. IR spectrum, ν, cm^{-1}: 3350 br.s (NH), 3060 m (C–H_{arom}), 2960 s, 2930 m (C–H_{aliph}), 2730–2380 (several bands, NH^+), 1670 s (C=O), 1620 (C=C), 1580 s (C=C_{arom}), 760 s, 690 m (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.37 s (6H, 5-CH_3),

2.27 br.s (2H, 4-H), 2.34 m (2H, 7-H), 2.56 br.s (2H, 6-H), 3.05 t (2H, 10-H, ^3J = 7 Hz), 4.09 d and 4.17 d (1H each, PhC**H**$_2$, ^2J = 13.2 Hz), 5.96 t (1H, 2-H, ^4J = 1.4 Hz), 7.37 m (3H) and 7.64 m (2H) (Ph), 8.70 br.s (2H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 258 (3) $[M]^+$, 150 $[M - PhCH_2NH_2]^+$, 136, 123, 108, 107 (100), 92, 83, 67, 55, 41.

Piperidinomethyl ketone hydrochlorides IIc–IVc were isolated as a light brown semicrystalline material in an overall yield of 55%. Particular regioisomers were isolated by dissolution of their mixture in anhydrous acetone and fractional precipitation with diethyl ether. The first fractions were enriched in compound **IVc**, the subsequent fractions were enriched in compound **IIIc**, and the mother liquor was enriched in isomer **IIc**.

3,5,5-Trimethyl-6-(piperidinomethyl)cyclohex-2-en-1-one hydrochloride (IIc) was isolated by fourfold dissolution in chloroform and precipitation with diethyl ether of the product isolated from the mother liquor, purity ≥90%. IR spectrum, ν, cm^{-1}: 3420 br.s (NH), 3050 v.w (=C–H), 2960 s, 2930 m (C–H_{aliph}), 2750–2380 (several bands, NH^+), 1665 s (C=O), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.98 s (6H, 5-CH_3), 1.90 m (6H, 3′-H, 4′-H, 5′-H), 2.08 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.23 br.s (2H, 4-H), 2.90 m (4H, 2′-H, 6′-H), 3.20 d.d (1H, 10-H, ^2J = 11, ^3J = 8 Hz), 3.49 d.d (1H, 10-H, ^2J = 11, ^3J = 6 Hz), 3.54 d.d (1H, 6-H, ^3J = 6, 8 Hz), 5.84 q (1H, 2-H, ^4J = 1.4 Hz), 10.00 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 236 (4) $[M]^+$, 150 $[M - (CH_2)_5NH]^+$, 135, 121, 118, 108, 96, 93, 85 (100), 67, 52, 41.

3,5,5-Trimethyl-2-(piperidinomethyl)cyclohex-2-en-1-one hydrochloride (IIIc) was isolated by fivefold recrystallization from butanol of a fraction enriched in this isomer, purity ≥82%. IR spectrum, ν, cm^{-1}: 3430 br.s (NH), 2960 s, 2930 m (C–H_{aliph}), 2750–2390 (several bands, NH^+), 1665 s (C=O), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.78 s (6H, 5-CH_3), 1.90 m (6H, 3′-H, 4′-H, 5′-H), 2.06 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.21 br.s (2H, 4-H), 2.56 br.s (2H, 6-H), 2.90 m (4H, 2′-H, 6′-H), 2.99 d (1H, 10-H, ^2J = 12 Hz), 3.07 d (1H, 10-H, ^2J = 12 Hz), 10.20 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 236 (5) $[M]^+$, 150 $[M - (CH_2)_5NH]^+$, 135, 121, 118, 108, 96, 93, 85 (100), 67, 52, 41.

5,5-Dimethyl-3-(2-piperidinoethyl)cyclohex-2-en-1-one hydrochloride (IVc) was isolated by fourfold crystallization from anhydrous acetone of the product isolated from the first fractions (see above), purity ≥84%. IR spectrum, ν, cm^{-1}: 3340 br.s (NH), 3050 v.w (=C–H), 2960 s, 2930 m (C–H_{aliph}), 2760–2390 (several bands, NH^+), 1670 s (C=O), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.32 s (6H, 5-CH_3), 1.87 m (6H, 3′-H, 4′-H, 5′-H), 2.22 br.s (2H, 4-H), 2.37 m (2H, 7-H), 2.61 br.s (2H, 6-H), 2.88 m (6H, 2′-H, 6′-H, 10-H), 5.87 t (1H, 2-H, ^4J = 1.4 Hz), 8.50 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 236 (3) $[M]^+$, 150 $[M - (CH_2)_5NH]^+$, 136, 123, 108, 92, 85 (100), 83, 67, 55, 41.

Mannich base hydrochlorides VIII–XIII were synthesized from the *E* and *Z* isomers of isophorone oxime according to the standard procedure (see above). Insofar as the reaction mixtures underwent considerable tarring, excess diethyl ether was added to the resulting alcoholic solution, and the upper (diethyl ether) layer was separated. The remaining ethanol solution contained mush less polymeric products. If necessary, a fresh portion of ethanol was added to the solution, and treatment with diethyl ether was repeated.

Compounds **VIII–X** (overall yield 49%) were obtained from *E* isomer **VI** by removal of the solvent by distillation. Particular isomers were isolated according to the same procedure as in the isolation of analogous amino ketone hydrochlorides.

(*E*)-6-(Dimethylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one oxime hydrochloride (VIII) was isolated by fivefold recrystallization from acetonitrile of a fraction enriched in this isomer, purity ≥81%. IR spectrum, ν, cm^{-1}: 3400 br.s (NOH), 3260 (NH), 3060 w (=C–H), 2960 s, 2900 m, 2870 m (C–H_{aliph}), 2690–2440 (several bands, NH^+), 1650 s (C=N), 1620 m (C=C), 950 (NOH). ^{1}H NMR spectrum, δ, ppm: 1.02 s (6H, 5-CH_3), 1.87 d (3H, 3-CH_3, ^4J = 1.4 Hz), 1.97 br.s (2H, 4-H, 2.98 s (6H, NCH_3), 3.28 t (2H, 10-H, ^3J = 7 Hz), 3.65 t (1H, 6-H, ^3J = 7 Hz), 5.98 q (1H, 2-H, ^4J = 1.4 Hz), 8.40 br.s (1H, NH), 9.60 br.s (1H, NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 211 (3) $[M]^+$, 195 $[M - OH]^+$, 165 $[M - Me_2NH_2]^+$, 148 $[M - Me_2NH_2 - OH]^+$, 133, 120, 117, 107, 96, 93, 67 (100), 52, 41.

(*E*)-2-(Dimethylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one oxime hydrochloride (IX) was isolated by triple reprecipitation with anhydrous acetone from a chloroform solution, purity ≥80%. IR spectrum, ν, cm^{-1}: 3390 br.s (NOH), 3280 (NH), 2960 s, 2910 m, 2880 m (C–H_{aliph}), 2670–2440 (several bands, NH^+), 1650 s (C=N), 1620 m (C=C), 950 (NOH). ^{1}H NMR spectrum, δ, ppm: 0.88 s (6H, 5-CH_3), 1.89 d (3H, 3-CH_3, ^4J = 1.4 Hz), 2.00 br.s (2H, 4-H), 2.77 s

(6H, NCH_3), 2.87 d (1H, 10-H, ^2J = 12 Hz), 2.91 br.s (2H, 6-H), 3.02 d (1H, 10-H, ^2J = 12 Hz), 9.6 br.s (2H, NH, NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 211 (3) $[M]^+$, 195 $[M - OH]^+$, 165 $[M - Me_2NH_2]^+$, 148 $[M - Me_2NH_2 - OH]^+$, 133, 121, 117, 108, 96, 93, 67 (100), 52, 41.

3-[2-(Dimethylamino)ethyl]-5,5-dimethylcyclohex-2-en-1-one hydrochloride (X) was isolated by fourfold crystallization from anhydrous acetone of the product isolated from fractions enriched with this isomer, purity ≥80%. IR spectrum, ν, cm^{-1}: 3350 br.s (NOH, NH), 3050 v.w (=C–H), 2960 s, 2920 m, 2850 w (C–H_{aliph}), 2680–2420 (several bands, NH^+), 1650 s (C=N), 1620 (C=C), 960 (NOH). ^{1}H NMR spectrum, δ, ppm: 1.13 s (6H, 5-CH_3), 2.10 br.s (2H, 4-H), 2.22 m (2H, 7-H), 2.82 br.s (2H, 6-H), 2.81 s (6H, NCH_3), 2.92 t (2H, 10-H, ^3J = 7 Hz), 5.97 t (1H, 2-H, ^4J = 1.4 Hz), 8.40 br.s (1H, NH), 9.60 br.s (1H, NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 211 (2) $[M]^+$, 195 $[M - OH]^+$, 165 $[M - Me_2NH_2]^+$, 148 $[M - Me_2NH_2 - OH]^+$, 135, 122, 108, 92, 83, 67 (100), 55, 41.

Compounds **XI**–**XIII** were obtained in an overall yield of 47% from *Z* isomer **VII** by washing with diethyl ether (see above) and removal of the solvent by distillation. Particular regioisomers were isolated according to the same procedure as in the isolation of analogous amino ketone hydrochlorides.

(*Z*)-6-(Dimethylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one oxime hydrochloride (XI) was isolated by fivefold crystallization from acetonitrile of a fraction enriched in this isomer, purity ≥83%. IR spectrum, ν, cm^{-1}: 3400 br.s (NOH), 3280 (NH), 3060 w (=C–H), 2960 s, 2900 m, 2870 m (C–H_{aliph}), 2660–2440 (several bands, NH^+), 1650 s (C=N), 1620 m (C=C), 950 (NOH). ^{1}H NMR spectrum, δ, ppm: 1.01 s (6H, 5-CH_3), 1.88 d (3H, 3-CH_3, ^4J = 1.4 Hz), 1.98 br.s (2H, 4-H), 3.00 s (6H, NCH_3), 3.20 d.d (1H, 10-H, ^2J = 11, ^3J = 8 Hz), 3.29 d.d (1H, 6-H, ^3J = 6, 8 Hz), 3.37 d.d (1H, 10-H, ^2J = 11, ^3J = 6 Hz), 6.62 q (1H, 2-H, ^4J = 1.4 Hz), 9.50 br.s (1H, NH), 9.80 br.s (1H, NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 211 (3) $[M]^+$, 195 $[M - OH]^+$, 165 $[M - Me_2NH_2]^+$, 148 $[M - Me_2NH_2 - OH]^+$, 133, 120, 117, 107, 96, 93, 67 (100), 52, 41.

(*Z*)-2-(Dimethylaminomethyl)-3,5,5-trimethylcyclohex-2-en-1-one oxime hydrochloride (XII) was isolated by fourfold precipitation with anhydrous acetone from chloroform of fractions enriched in this isomer, purity ≥81%. IR spectrum, ν, cm^{-1}: 3380 br.s (NOH), 3300 (NH), 2960 s, 2910 m, 2880 m (C–H_{aliph}), 2680–2440 (several bands, NH^+), 1650 s (C=N), 1620 m (C=C), 950 (NOH). ^{1}H NMR spectrum, δ, ppm: 0.90 s (6H, 5-CH_3), 1.87 d (3H, 3-CH_3, ^4J = 1.4 Hz), 1.98 br.s (2H, 4-H), 2.40 br.s (2H, 6-H), 2.72 s (6H, NCH_3), 3.05 br.s (2H, 10-H), 8.40 br.s (1H, NH), 9.60 br.s (1H, NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 211 (3) $[M]^+$, 195 $[M - OH]^+$, 165 $[M - Me_2NH_2]^+$, 148 $[M - Me_2NH_2 - OH]^+$, 133, 121, 117, 108, 96, 93, 67 (100), 52, 41.

(*Z*)-3-[2-(Dimethylamino)ethyl]-5,5-dimethylcyclohex-2-en-1-one oxime hydrochloride (XIII) was isolated by fourfold crystallization from anhydrous acetone of the product isolated from the mother liquor, purity ≥80%. IR spectrum, ν, cm^{-1}: 3370 br.s (NOH + NH), 3050 v.w (=C–H), 2960 s, 2920 m, 2850 m (C–H_{aliph}), 2680–2420 (several bands, NH^+), 1650 s (C=N), 1620 (C=C), 960 (NOH). ^{1}H NMR spectrum, δ, ppm: 1.12 s (6H, 5-CH_3), 2.11 br.s (2H, 4-H), 2.19 m (2H, 7-H), 2.36 br.s (2H, 6-H), 2.73 s (6H, NCH_3), 2.96 t (2H, 10-H, ^3J = 7 Hz), 6.64 t (1H, 2-H, ^4J = 1.4 Hz), 8.50 br.s (1H, NH), 9.50 br.s (1H, NOH). Mass spectrum, *m*/*z* (I_{rel}, %): 211 (2) $[M]^+$, 195 $[M - OH]^+$, 165 $[M - Me_2NH_2]^+$, 148 $[M - Me_2NH_2 - OH]^+$, 135, 122, 108, 92, 83, 81, 67 (100), 55, 41.

3-[(*Z*)-2-Arylethenyl]-5,5-dimethylcyclohex-2-en-1-ones XIVa–XIVh (*general procedure*). As noted above, compounds **XIV** were obtained in most cases instead of expected Mannich bases by heating a solution of equimolar amounts of isophorone, aromatic amine, and aromatic aldehyde in ethanol under reflux. The best yields of **XIVa–XIVh** were obtained in the reactions with *p*-toluidine as amine component; reduction of the amount of the latter to 0.3 equiv decreased tarring and impurity of the corresponding Schiff base.

3-[(*Z*)-2-(4-Fluorophenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVa). Yield 64%, mp 116–117°C. IR spectrum, ν, cm^{-1}: 3070, 3050, 3030 (=C–H, C–H_{arom}), 2950, 2920, 2865 (C–H_{aliph}), 1655 (C=O), 1615 (C=C), 1590, 1580, 1505 (C=C_{arom}), 1155 (C–F), 840 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.09 s (6H, 5-CH_3), 2.29 br.s (2H, 6-H), 2.43 d (2H, 4-H, ^4J = 1.2 Hz), 6.05 t (1H, 2-H, ^4J = 1.2 Hz), 6.84 d (1H, 7-H, ^3J = 16.0 Hz), 6.89 d (1H, 8-H, ^3J = 16.0 Hz), 7.04 t (2H, 3′-H, 5′-H, $^3J_{HH}$ = $^3J_{HF}$ = 8.6 Hz), 7.46 d.d (2H, 2′-H, 6′-H, $^3J_{HH}$ = 8.6, $^4J_{HF}$ = 5.5 Hz).

3-[(*Z*)-2-(4-Bromophenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVb). Yield 67%, mp 121–122°C. IR spectrum, ν, cm^{-1}: 3060, 3040, 3030 (=C–H, C–H_{arom}), 2950, 2920, 2865 (C–H_{aliph}), 1655 (C=O), 1615 (C=C), 1575, 1485 (C=C_{arom}), 835 (δC–H_{arom}),

540 (C–Br). ^{1}H NMR spectrum, δ, ppm: 1.13 s (6H, 5-CH_3), 2.32 br.s (2H, 6-H), 2.46 d (2H, 4-H, ^4J = 1.2 Hz), 6.08 t (1H, 2-H, ^4J = 1.2 Hz), 6.91 s (2H, 7-H, 8-H), 7.37 d (2H, 3′-H, 5′-H, ^3J = 8.5 Hz), 7.47 d (2H, 2′-H, 6′-H, ^3J = 8.5 Hz).

3-[(*Z*)-2-(4-Hydroxyphenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVc). Yield 72%, mp 192–194°C. IR spectrum, ν, cm^{-1}: 3200 br.s (OH), 3060, 3045 (=C–H, C–H_{arom}), 2950, 2920, 2865 (C–H_{aliph}), 1645 (C=O), 1615 (C=C), 1600, 1515 (C=C_{arom}), 1285 (C–O), 835 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.11 s (6H, 5-CH_3), 2.32 br.s (2H, 6-H), 2.48 d (2H, 4-H, ^4J = 1.2 Hz), 6.07 t (1H, 2-H, ^4J = 1.2 Hz), 6.84 d (1H, 7-H, ^3J = 16.0 Hz), 6.90 d (1H, 8-H, ^3J = 16.0 Hz), 6.96 d (2H, 3′-H, 5′-H, ^3J = 8.5 Hz), 7.80 d (2H, 2′-H, 6′-H, ^3J = 8.5 Hz), 9.87 (1H, OH).

3-[(*Z*)-2-(4-Methoxyphenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVd). Yield 75%, mp 135–136°C. IR spectrum, ν, cm^{-1}: 3080, 3050, 3020 (=C–H, C–H_{arom}), 2970, 2935, 2870 (C–H_{aliph}), 1635 (C=O), 1610 (C=C), 1600, 1510 (C=C_{arom}), 1250 (C–O–C), 840 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.11 s (6H, 5-CH_3), 2.31 br.s (2H, 6-H), 2.47 d (2H, 4-H, ^4J = 1.2 Hz), 3.88 s (3H, OCH_3), 6.07 t (1H, 2-H, ^4J = 1.2 Hz), 6.84 d (1H, 7-H, ^3J = 16.0 Hz), 6.90 d (1H, 8-H, ^3J = 16.0 Hz), 6.98 d (2H, 3′-H, 5′-H, ^3J = 8.5 Hz), 7.85 d (2H, 2′-H, 6′-H, ^3J = 8.5 Hz).

3-[(*Z*)-2-(4-Dimethylaminophenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVe). Yield 55%, mp 138–140°C. IR spectrum, ν, cm^{-1}: 3080, 3050, 3020 (=C–H, C–H_{arom}), 2970, 2935, 2870 (C–H_{aliph}), 1645 (C=O), 1615 (C=C), 1590, 1505 (C=C_{arom}), 1175 (C–N), 830 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.10 s (6H, 5-CH_3), 2.31 br.s (2H, 6-H), 2.46 d (2H, 4-H, ^4J = 1.2 Hz), 3.03 s (6H, NCH_3), 6.07 t (1H, 2-H, ^4J = 1.2 Hz), 6.78 d (2H, 3′-H, 5′-H, ^3J = 8.5 Hz), 6.84 d (1H, 7-H, ^3J = 16.0 Hz), 6.89 d (1H, 8-H, ^3J = 16.0 Hz), 7.74 d (2H, 2′-H, 6′-H, ^3J = 8.5 Hz).

3-[(*Z*)-2-(3-Ethoxy-4-hydroxyphenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVf). Yield 88%, mp 146–148°C. IR spectrum, ν, cm^{-1}: 3135 (OH), 3060, 3040 (=C–H, C–H_{arom}), 2960, 2930, 2870 (C–H_{aliph}), 1635 (C=O), 1610 (C=C), 1590, 1570, 1520 (C=C_{arom}), 1280 (C–O), 1260 and 1240 (C–O–C), 840 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.12 s (6H, 5-CH_3), 1.50 t (3H, $CH_2C\mathbf{H}_3$, ^3J = 7 Hz), 2.32 br.s (2H, 6-H), 2.47 d (2H, 4-H, ^4J = 1.2 Hz), 4.19 q (2H, OCH_2, ^3J = 7 Hz), 6.07 t (1H, 2-H, ^4J = 1.2 Hz), 6.79 d (1H, 7-H, ^3J = 16.0 Hz), 6.86 d (1H, 5′-H, ^3J = 8.5 Hz), 6.90 d (1H, 8-H, ^3J = 16.0 Hz), 6.96 s (1H, 2′-H), 7.05 d (1H, 6′-H, ^3J = 8.5 Hz), 10.0 (1H, OH).

3-[(*Z*)-2-(4-Hydroxy-3-methoxyphenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVg). Yield 81%, mp 158–159°C. IR spectrum, ν, cm^{-1}: 3135 (OH), 3070, 3050 (=C–H, C–H_{arom}), 2950, 2935, 2925 (C–H_{aliph}), 1630 (C=O), 1610 (C=C), 1585, 1570, 1525 (C=C_{arom}), 1285 (C–O), 1260, 1235 (C–O–C), 850 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.11 s (6H, 5-CH_3), 2.31 br.s (2H, 6-H), 2.47 d (2H, 4-H, ^4J = 1.2 Hz), 3.95 s (3H, OCH_3), 6.06 t (1H, 2-H, ^4J = 1.2 Hz), 6.80 d (1H, 7-H, ^3J = 16.0 Hz), 6.86 d (1H, 5-H, ^3J = 8.5 Hz), 6.90 d (1H, 8-H, ^3J = 16.0 Hz), 6.96 s (1H, 2′-H), 7.05 d (1H, 6′-H, ^3J = 8.5 Hz), 10.0 (1H, OH).

3-[(*Z*)-2-(3,4-Dimethoxyphenyl)ethenyl]-5,5-dimethylcyclohex-2-en-1-one (XIVh). Yield 76%, mp 139–141°C. IR spectrum, ν, cm^{-1}: 3060, 3035 (=C–H, C–H_{arom}), 2960, 2930, 2855 (C–H_{aliph}), 1630 (C=O), 1610 (C=C), 1595, 1575, 1515 (C=C_{arom}), 1275, 1240 (C–O–C), 860 (δC–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.12 s (6H, 5-CH_3), 2.31 br.s (2H, 6-H), 2.47 d (2H, 4-H, ^4J = 1.2 Hz), 3.94 s and 3.97 s (3H each, OCH_3), 6.07 t (1H, 2-H, ^4J = 1.2 Hz), 6.79 d (1H, 7-H, ^3J = 16.0 Hz), 6.88 d (1H, 5′-H, ^3J = 8.5 Hz), 6.90 d (1H, 8-H, ^3J = 16.0 Hz), 6.96 s (1H, 2′-H), 7.08 d (1H, 6′-H, ^3J = 8.5 Hz).

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