REACTIONS OF 1,2-DIHYDROQUINOLINES

IV.* REACTION OF 2,2,4-TRIMETHYL-1,2-DIHYDROQUINOLINES WITH CYCLOHEXANE

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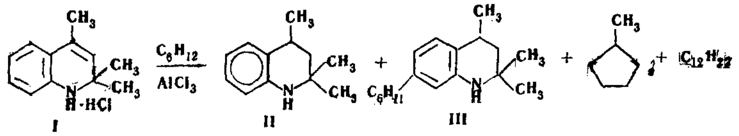
Under the influence of anhydrous aluminum chloride, cyclohexane converts 2,2,4-trimethyl-1,2-dihydroquinoline to the tetrahydro derivative and alkylates it at the 7-position with simultaneous reduction of the Δ^3-bond.

In [2,3] it was shown that 2,2,4-trimethyl-1,2-dihydroquinolines readily add aromatic hydrocarbons under the conditions of the Friedel-Crafts reaction to form 2,2,4-trimethyl-4-aryl-1,2,3,4-tetrahydroquinolines.

We were able to establish that cyclohexane also reacts with 2,2,4-trimethyl-1,2-dihydroquinoline hydrochloride (I) under the influence of aluminum chloride, but, in contrast to the reaction with aromatic hydrocarbons, instead of addition at the Δ^3-bond, dihydroquinoline I is reduced to give primarily 2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline (II), whose yield reaches 60%. In addition, 2,2,4-trimethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline (III), methylcyclopentane, and a small amount of a $C_{12}H_{22}$ hydrocarbon are obtained.



Compound III has a UV spectrum [λ_{max} 247 and 300 nm (log ε 3.86 and 3.40)] similar to the UV spectrum of 2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline [λ_{max} 250 and 305 nm (log ε 4.00 and 3.40)]. The PMR spectrum of III (Fig. 1) contains the signals of the two interacting $H_{(6)}$ and $H_{(5)}$ protons (doublets at 6.29

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*See [1] for communication III.

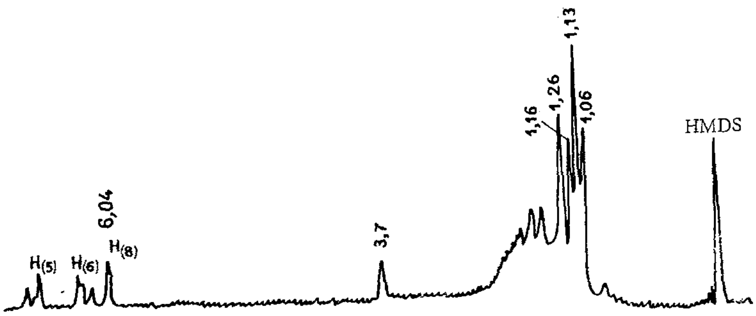

Fig. 1. PMR spectrum of 2,2,4-trimethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline (III) in CCl_4.

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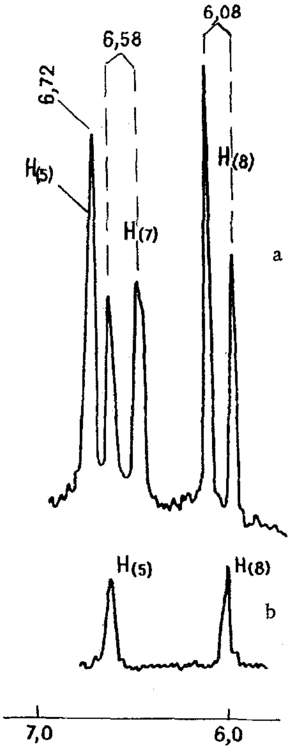

Fig. 2. PMR spectra (in CCl_4) of: a) 2,2,4,6-tetramethyl-1,2,3,4-tetrahydroquinoline (VI); b) 2,2,4,6-tetramethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline (VII).

and 6.83 ppm with J 8 Hz) and a one-proton, slightly split (as a result of meta interaction) singlet at 6.04 ppm. This indicates the presence of a substituent in the 7-position of the aromatic ring, since the singlet should be related to $H_{(8)}$, which has the greatest diamagnetic shift under the influence of the amino group. This conclusion is confirmed by a comparison of its PMR spectrum with the PMR spectra of 2,2,4,7-tetramethyl-1,2-dihydroquinoline (IV) [4], 2,2,4,6-tetramethyl-1,2-dihydroquinoline (V) [4], and 2,2,4,6-tetramethyl-1,2,3,4-tetrahydroquinoline (IV). The chemical nonequivalence of the $H_{(8)}$ (IV) and $H_{(5)}$ (V) protons results in a sharp difference in their chemical shifts (singlets at 6.17 and 6.90 ppm, respectively), and the $H_{(8)}$ signal experiences a diamagnetic shift as compared with the $H_{(5)}$ signal under the influence of the nitrogen atom.

The spectral data for the aromatic part of VI (Fig. 2a) are in complete agreement with the data for IV and V. The singlet at 6.72 ppm, which belongs to $H_{(5)}$, has a paramagnetic shift relative to the quartet of the signals of the interacting $H_{(7)}$ and $H_{(8)}$ protons (the corresponding doublets centered at 6.58 and 6.08 ppm with J 8 Hz).

The possibility of the migration of one of the methyl groups to the ring is excluded, since there is no signal for a methyl group bonded to the aromatic ring in the spectrum (Fig. 1).

The signals of the gem-methyl groups (1.13 and 1.26 ppm) and the signal of the methyl group in the 4-position (1.06 and 1.16 ppm), which is split into a doublet (J 6 Hz) under the influence of the $H_{(4)}$ proton, are situated in the strong-field region. The absorption band of the protons of the cyclohexyl group is superimposed on these signals and also on the signals of the methylene group of the nitrogen ring.

The addition of cyclohexane to 2,2,4,6-tetramethyl-1,2-dihydroquinoline, in which the 6-position is occupied by a CH_3 group, proceeds similarly. The PMR spectrum of the 2,2,4,6-tetramethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline (VII) (Fig. 2b) formed in the process has signals at 6.05 and 6.66 ppm, which pertain to $H_{(8)}$ and $H_{(5)}$, respectively. This first of all confirms the position of the cyclohexyl group, and, secondly, the correctness of the assignment of the signal at 6.04 ppm of III to the $H_{(8)}$ proton.

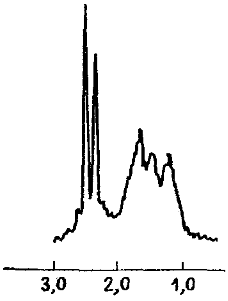

Fig. 3. PMR spectrum of 2,4-dimethyl-7-cyclohexylquinoline (VIII) in CCl_4.

Dehydrogenation of III on a palladium catalyst gave, as the primary products, two compounds with different percentages of hydrogen than in the starting compound, which did not have primary or secondary amino groups. On the basis of elementary analysis and PMR spectra they were assigned the 2,4-dimethyl-7-cylohexylquinoline (VIII) and 2,4-dimethyl-7-phenylquinoline (IX) structures. The absence of a signal of a methyl group bonded to the aliphatic carbon atom in the PMR spectrum of VIII (Fig. 3) excludes alternative structures, in which there is a methylcyclopentyl radical in place of a cyclohexyl group. The presence of a cyclopentyl ring is consequently unlikely in the starting III, since methylcyclopentane is not isomerized under similar conditions [5].

As noted above, 2,2,4-trimethyl-1,2-dihydroquinoline hydrochloride reacts readily with aromatic hydrocarbons to form 4-aryltetrahydroquinolines. The first act of this reaction is probably protonation of the double bond with induction of a considerable positive charge on $C_{(4)}$. The ion formed electrophilically attacks the aromatic ring via the well-known mechanism and gives a substituted aryltetrahydroquinoline. However, if a saturated hydrocarbon, cyclohexane, for example, is present in the reaction mixture, there is a possibility for the removal of a hydride ion by the dihydroquinoline cation and for its reduction to a tetrahydroquinoline derivative. The cyclohexyl cation generated as a result of removal of a hydride ion from cyclohexane can electrophilically attack the aromatic ring or give the transformation products that are common for such carbonium ions (the formation of methylcyclopentane, etc.). The protonation of the NH group orients entry of the substituent at the 7-position.

The chemical properties of III are similar to the properties of 2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline. It is not reduced by sodium in alcohol, is not aromatized with the cleavage of methane on heating with potassium amide, and is readily acylated by acetic anhydride; in addition, the acetyl derivative is just as readily hydrolyzed by refluxing with hydrochloric acid.

A $C_{12}H_{22}$ hydrocarbon with mp 46.5°, to which the 2,2'-dimethyldicyclopentyl structure was assigned, was described by Nenitzescu and co-workers in [6-8]. We isolated it from the hydrocarbon fraction that has the same quantitative composition and is probably a mixture of isomeric hydrocarbons.

EXPERIMENTAL

Reaction of 2,2,4-Trimethyl-1,2-dihydroquinoline (I) with Cyclohexane. Anhydrous aluminum chloride [119.7 g (0.9 mole)] was added to a suspension of 94.5 g (0.45 mole) of hydrochloride I in 162 ml of anhydrous cyclohexane, and the mixture was shaken for 1 h while maintaining the temperature at 25-30°. The upper layer was decanted, and the lower layer was poured into 500 ml of ice water. Sodium hydroxide (80 g) was added gradually to the latter, and the freed base was extracted with 200 ml of ether. The extract was dried with potassium hydroxide and vacuum distilled with collection of two fractions, one (52 g) with bp 82-85° (2 mm), and the other (21 g) with bp 140-145° (2 mm). Recrystallization of the first fraction from n-heptane gave 50 g (60%) of 2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline (II) with mp 41° (from n-heptane) and λ_{max} 250 and 305 nm (log ε 4.0 and 3.4) (in methanol). The hydrochloride of II had mp 212-213°. The acetyl derivative had mp 86° [9, 10].

The second fraction was dissolved in a triple volume of n-heptane and treated with 120 ml of 10% HCl. The precipitated crystals were filtered by suction and washed with n-heptane. Hot water (100 ml) was added, followed by 25 ml of 20% sodium hydroxide. The mixture was cooled and extracted with ether. The ether extract was dried with KOH, the ether was removed by distillation, and the residue was refluxed for 1 h with a small excess of acetic anhydride. The mixture was made alkaline and extracted with ether. The ether extract was dried with KOH, the ether was removed, and the residue was crystallized, initially from n-heptane and then from acetone, to give 15 g of 1-acetyl-2,2,4-trimethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline with mp 126-127° and λ_{max} 255 nm (log ε 4.17). Found %: C 80.0; H 9.7. $C_{20}H_{29}NO$. Calculated %: C 80.2; H 9.8.

The substance obtained was hydrolyzed by refluxing with concentrated HCl for 1 h. Potassium hydroxide solution was added, and the mixture was extracted with ether. The extract was dried, the solvent was removed by distillation, and the residue was vacuum distilled to give 10 g (9%) of 2,2,4-trimethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline (III) as a colorless oil with bp 148-150° (2 mm) and λ_{max} 247 and 300 nm (log ε 3.86 and 3.40). Found %: C 83.8; H 10.5. $C_{18}H_{27}N$. Calculated %: C 84.0; H 10.6.

The decanted upper hydrocarbon layer was washed with weak KOH solution and water, dried with calcium chloride, and fractionated with a column with selection of a fraction (5 g) with bp 70-72° (757 mm), a fraction (cyclohexane) with bp 78-80° (757 mm), a fraction (10 g) with bp 38-40° (2 mm), and a fraction (4 g) with bp 123-126° (2 mm). Methylcyclopentane with bp 71-72°, n_D^{20} 1.4090, and d_4^{20} 0.7485 [11] was isolated from the first fraction.

The second fraction was dissolved in a triple volume of n-hexane, and the solution was washed three times with 10-ml portions of 15% HCl, 3% KOH solution, and water, and dried with calcium chloride. The n-hexane was removed by distillation, and the residue was fractionated with a column to give 6 g of a $C_{12}H_{22}$ hydrocarbon with bp 211-212° (757 mm), n_D^{20} 1.4655, and d_4^{20} 0.8540. Freezing of the alcohol solution with dry ice precipitated crystals with mp 46°. IR spectrum: 885, 985, 1369, 1450, 2850, and 2951 cm^{-1}. Found %: C 86.4; H 13.4; mol. wt. 166 (mass spectrum). $C_{12}H_{22}$. Calculated %: C 86.7; H 13.3; mol. wt. 166.3. The literature data for 2,2'-dimethyldicyclopentyl are as follows: bp 212° (757 mm), mp 46.5° (from methanol), n_D^{20} 1.4655, and d_4^{20} 0.8544 [6].

2,2,4,6-Tetramethyl-7-cyclohexyl-1,2,3,4-tetrahydroquinoline (VII). Aluminum chloride [47 g (0.352 mole)] was added to a suspension of 39 g (0.176 mole) of 2,2,4,6-tetramethyl-1,2-dihydroquinoline hydrochloride in 90 ml of anhydrous cyclohexane, and the mixture was shaken for 1 h and then heated briefly to 50° on a water bath. The upper layer was decanted, and the lower layer was poured into 200 ml of ice water. Sodium hydroxide (32 g) was added to the latter mixture. The bases were extracted with 100 ml of ether, and the extract was washed and dried with KOH. The ether was removed by distillation, and the residue was vacuum distilled. The fraction with bp 90-160° (2 mm) (9.7 g) was dissolved in 30 ml of n-heptane, and the solution was treated with 100 ml of 20% HCl. The salt was filtered and decomposed with hot sodium hydroxide solution. The mixture was extracted with benzene, and the extract was dried. The benzene was removed, and the base was vacuum distilled to give 6 g (12.5%) of VII with bp 145-147° (2 mm). Found %: C 84.1; H 10.7. $C_{19}H_{29}N$. Calculated %: C 84.1; H 10.8. The acetyl derivative of VII had mp 140-141° (from alcohol). Found %: C 80.4; H 9.9. $C_2H_{31}NO$. Calculated %: C 80.5; H 10.0.

2,4-Dimethyl-7-cyclohexylquinoline (VIII) and 2,4-Dimethyl-7-phenylquinoline (IX). A catalyzate was obtained by passing III through a Pyrex tube filled with catalyst (0.8% Pd/C) at 300-310° in vacuo (10 mm) in a stream of nitrogen. Compounds VIII and IX were isolated from the catalyzate by means of thin-layer chromatography (on Brockmann activity II Al_2O_3 with isooctane–ether (3 : 1) as the liquid phase at a layer thickness of 2 mm). Product VIII had mp 77-78° (n-hexane) and λ_{max} 278 nm (log ε 3.65). Found %: C 85.3; H 8.9. $C_{17}H_{21}N$. Calculated %: C 85.3; H 8.8. Product IX had mp 85-86° (from n-hexane). Found %: C 88.7; H 6.7. $C_{17}H_{15}N$. Calculated %: C 88.2; H 7.1.

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