REACTIONS OF 1,2-DIHYDROQUINOLINES

II.* REACTION OF 1,2-DIHYDROQUINOLINES WITH ALKYLBENZENES

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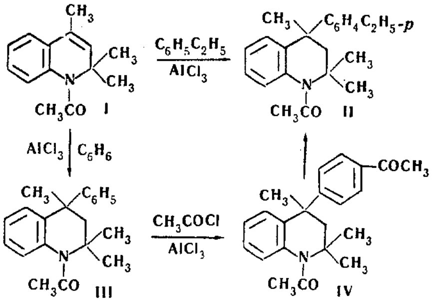
2,2,4-Trimethyl-1,2-dihydroquinolines readily add alkylbenzenes under the influence of aluminum chloride to form 2,2,4-trimethyl-4-(p-alkylphenyl)-1,2,3,4-tetrahydroquinolines.

In [1] it was shown that 2,2,4-trimethyl-1,2-dihydroquinolines in the form of hydrochlorides or 1-acyl derivatives add benzene at the double bond under the influence of aluminum chloride. It turned out that, as with benzene, the reaction proceeds with benzene homologs in rather high yields at room temperature in the presence of a 2-mole excess of aluminum chloride. In fact, 2,2,4-trimethyl-1,2-dihydroquinoline and its 1-acetyl derivative smoothly add toluene, ethylbenzene, isopropylbenzene, and cyclohexylbenzene under these conditions. The yields of addition products decrease with increasing size of the radical in the alkylbenzene, and side products are formed. Thus hydrocarbon $C_{24}H_{30}$, which is apparently the product of condensation of two cyclohexylbenzene molecules, is isolated from the reaction with cyclohexylbenzene. Increasing the reaction time also promotes the formation of side products.

Because of the possibility of isomerization of both the starting alkylbenzenes [2] as well as the final products under the influence of aluminum chloride, we considered it necessary to establish the structures of the compounds obtained.

Destructive oxidation of the aryltetrahydroquinolines, synthesized under various conditions, led to complex mixtures of compounds. In the case of 1-acetyl-2,2,4-trimethyl-4-(p-ethylphenyl)-1,2,3,4-tetrahydroquinoline (II) we carried out an alternative synthesis by acetylation of 4-phenyltetrahydroquinoline (III) in the nucleus with subsequent reduction of the keto group of compound IV and acetylation of the NH group.



Similarly, 2,2,4,6,8-pentamethyl-4-(p-acetylphenyl)-1,2,3,4-tetrahydroquinoline (V) and ketone VI were obtained from 2,2,4,6,8-pentamethyl-1,2-dihydroquinoline. (See scheme on page 1411.)

A singlet at 6.70 ppm (with an intensity of two protons), which belongs to the magnetically equivalent H_5 and H_7 protons, and a quartet (7.14, 7.25, 7.60, 7.80 ppm, J = 8 Hz) from the four protons of the p-phenylene group are observed in the aromatic portion of the PMR spectrum of VI (Fig. 1); this indicates

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*See [1] for Communication I.

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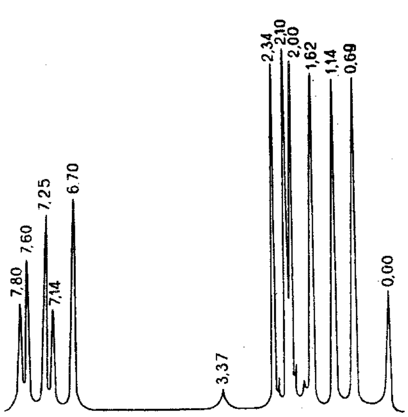


Fig. 1. PMR spectrum of 2,2,4,6,8-pentamethyl-4-(p-acetylphenyl)-1,2,3,4-tetrahydroquinoline (VI).

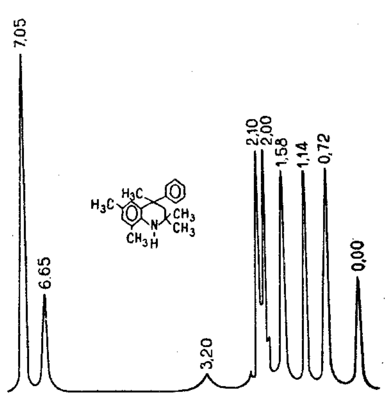
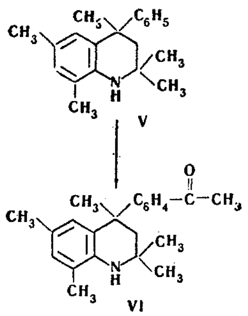


Fig. 2. PMR spectrum of 2,2,4,6,8-pentamethyl-4-phenyl-1,2,3,4-tetrahydroquinoline (V).



that the acetyl group is in the para position. Six singlets from the methyl groups are visible in the right-hand portion of the spectrum; of these, peaks with chemical shifts of 0.69 and 1.14 ppm belong to the gem methyl groups, those at 1.62 ppm relate to the 4-methyl group, those at 2.00 and 2.10 ppm relate to the CH_3 groups in the 6 and 8 positions, while that at 2.34 ppm corresponds to the methyl group of the acetyl group. A quartet from the CH_2 group (the protons are nonequivalent because of the noncoplanarity of the system) is superimposed on the methyl-group region (three signals at 1.69, 1.93, and 2.27 ppm with J = 14 Hz are scanned). The nitrogen proton gives a singlet at 3.37 ppm.

The equivalence of the protons in the 5 and 7 positions of VI is confirmed by the PMR spectrum of V (Fig. 2) for which the aromatic protons give two signals: a phenyl singlet at 7.05 ppm and a singlet from the 5 and 7 protons of the heterocycle at 6.65 ppm (the signal intensity ratio is 5 : 2). The chemical shifts of the protons from the CH_3 groups are almost the same as for VI. The signals of the CH_2 group also are superimposed on the absorption of the CH_3 groups in the 6 and 8 positions.

All of these results and a comparison of the UV and PMR spectra of II-VI (the structure of III was previously determined in [1]) make it possible to consider it to be established that compounds of the II type have the 2,2,4-trimethyl-4-(p-alkylphenyl)-1,2,3,4-tetrahydroquinoline structure. We were unable to detect isomeric compounds in any of these cases. The UV absorption spectra of all of these compounds are identical. The establishment of the structure of II simultaneously demonstrates that Friedel–Crafts acetylation of III proceeds at the phenyl group rather than in the tetrahydroquinoline ring.

EXPERIMENTAL

The purity of the compounds obtained was evaluated by thin-layer chromatography on aluminum oxide [benzene–acetone (19 : 1)]. The PMR spectra were obtained by V. A. Budylin with an RS-60 (60 MHz) spectrometer with carbon tetrachloride as the solvent and hexamethyldisiloxane as the internal standard.

1-Acetyl-2,2,4-trimethyl-4-(p-ethylphenyl)-1,2,3,4-tetrahydroquinoline (II). A. A mixture of 3 g (0.011 mole) of 1-acetyl-2,2,4-trimethyl-1,2-dihydroquinoline, 40 ml of ethylbenzene, and 3.6 g (0.028 mole) of anhydrous aluminum chloride was agitated for 15 min at room temperature. It was then decomposed with ice, the organic layer was separated, and the aqueous layer was extracted with ether. The ether extracts and the organic layer were combined, washed with an alkali solution and water, dried, and the solvent was removed. The solid residue was crystallized from alcohol to give 2.8 g (76%) of a compound with mp 136°. Found %: C 82.3, 82.2; H 8.5, 8.4. $C_{22}H_{27}NO$. Calculated %: C 82.2; H 8.5.

B. A mixture of 3.4 g (0.01 mole) of 1-acetyl-2,2,4-trimethyl-4-(p-acetylphenyl)-1,2,3,4-tetrahydroquinoline (IV) (see below), 20 ml of 85% hydrazine hydrate, 5 g of potassium hydroxide, and 50 ml of diethylene glycol was refluxed until nitrogen evolution ceased. The reaction mass was then cooled, diluted with water, and extracted with petroleum ether. The extract was dried, the solvent was removed, and the residue was crystallized from alcohol to give 3 g (81%) of a compound with mp 136° which was identical to the compound described above. Found %: C 82.3, 82.3; H 8.7, 8.8. $C_{22}H_{27}NO$. Calculated %: C 82.2; H 8.5.

1-Acetyl-2,2,4-trimethyl-4-(p-acetylphenyl)-1,2,3,4-tetrahydroquinoline (IV). A mixture of 4 g (0.014 mole) of 1-acetyl-2,2,4-trimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline and 3.62 g (0.027 mole) of anhydrous aluminum chloride was placed in a flask with a reflux condenser and a calcium chloride drying tube, and 50 ml of dry cyclohexane followed by 2 ml of acetyl chloride were added. The mixture was heated on a water bath until hydrogen chloride evolution ceased. It was then cooled, the cyclohexane was decanted, and the residual complex was decomposed with a small amount of glacial acetic acid. The mixture was then diluted with water (1 : 20), and ketone IV was extracted with benzene. After drying, the solvent was removed and the residue was triturated in boiling n-heptane and crystallized from alcohol to give 2.5 g (55%) of a compound with mp 156-157°. Found %: C 78.6, 78.3; H 7.5, 7.4. $C_{22}H_{25}NO_2$. Calculated %: C 78.8; H 7.4.

1-Acetyl-2,2,4,6,8-pentamethyl-4-(p-acetylphenyl)-1,2,3,4-tetrahydroquinoline. This was obtained, like IV, from 2,2,4,6,8-pentamethyl-4-phenyl-1,2,3,4-tetrahydroquinoline (V) in 51% yield and had mp 150-151° (from ethanol). Found %: C 79.4, 79.2; H 8.2, 8.1. $C_{24}O_{29}NO_2$. Calculated %: C 79.3; H 8.0.

2,2,4,6,8-Pentamethyl-4-(p-acetylphenyl)-1,2,3,4-tetrahydroquinoline (VI). This was obtained in quantitative yield by acid hydrolysis of the 1-acetyl derivative (preceding compound) and had mp 73-74° (from n-hexane). Found %: C 82.2, 82.1; H 8.5, 8.4. $C_{24}H_{29}NO_2$. Calculated %: C 79.3; H 8.0.

1-Acetyl-2,2,4-trimethyl-4-(p-tolyl)-1,2,3,4-tetrahydroquinoline. A mixture of 3 g (0.011 mole) of 1-acetyl-2,2,4-trimethyl-1,2-dihydroquinoline, 50 ml of toluene, and 3.6 g of aluminum chloride was agitated for 15 min. After the usual workup, 3.5 g (83%) of a compound with mp 154° (from n-heptane) and λ_{max} 255 nm, log ε 4.02 (in methanol) was isolated. Found %: C 82.3, 82.2; H 8.2, 8.2. $C_{21}H_{25}NO$. Calculated %: C 82.0; H 8.2.

1-Acetyl-2,2,4-trimethyl-4-(p-isopropylphenyl)-1,2,3,4-tetrahydroquinoline. This was obtained in 55% yield by 10-min agitation of a solution of 1-acetyl-2,2,4-trimethyl-1,2-dihydroquinoline in isopropylbenzene with a 2-mole excess of aluminum chloride and had mp 102-103° (from alcohol). Found %: C 82.2, 82.3; H 8.8, 8.7. $C_{23}H_{29}NO$. Calculated %: C 82.3; H 8.7.

2,2,4-Trimethyl-4-(p-cyclohexylphenyl)-1,2,3,4-tetrahydroquinoline. A suspension of 10.5 g (0.05 mole) of 2,2,4-trimethyl-1,2-dihydroquinoline hydrochloride and 13.3 g (0.1 mole) of aluminum chloride in cyclohexylbenzene (100 ml) was agitated at room temperature for 1 h. After the usual workup, the high-boiling residue was distilled in vacuo, and the base was extracted with dilute (1 : 3) hydrochloric acid. After alkalization and distillation, 13 g (78%) of 2,2,4-trimethyl-4-(p-cyclohexylphenyl)-1,2,3,4-tetrahydroquinoline with bp 190-193° (4 mm) was obtained. Found %: C 86.3, 86.5; H 9.5, 9.3. $C_{24}H_{31}N$. Calculated %: C 86.4; H 9.4. The hydrochloride had mp 209-210°. The benzoyl derivative had mp 141-142° (from alcohol).

A small amount of a hydrocarbon with bp 160-163° (4 mm) and mp 95° could be isolated from the neutral layer by distillation. Found %: C 90.6, 90.6; H 9.5, 9.4. $C_{24}H_{30}$. Calculated %: C 90.5; H 9.5.

LITERATURE CITED

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