REACTIONS OF CYCLAMMONIUM CATIONS

XX.* REACTION OF QUINALDINE AND LEPIDINE WITH ACYLATING AGENTS

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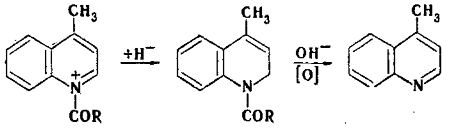
The action of acylating agents on 2-methylquinoline gives extremely unstable N-acyl salts, which, as a result of hydride-ion capture, are converted to 1-acyl-2-methyl-1,2,3,4-tetrahydroquinolines. Under similar conditions, 1-acyllepidinium salts form 1-acyl-4-methyl-1,2-dihydroquinolines or dimerize.

The reaction of quinoline or its benzo-substituted derivatives with acyl halides gives N-acylquinolinium salts, which can be used in situ for the introduction of a quinoline residue into nucleophilic organic compounds [2-4]. These sorts of quinolination reactions, cannot, however, be carried out with lepidine and quinaldine [2,4], although their capacity for the formation of N-acyl salts should be higher than for unsubstituted quinoline. This cannot be explained by the effect of steric factors (in the case of 2-methylquinoline), since high yields of quinolination products are obtained with 8-methylquinoline [4].

We have been able to demonstrate that the reaction of acyl halides with 2- or 4-methylquinoline also forms extremely unstable 1-acyl salts, which, under the quinolination conditions (in the presence of dialkylanilines), do not undergo heteroarylation but are converted (during hydride-ion capture) to N-acyl derivatives of 1,2-dihydroquinolines. We obtained the same compounds by carrying out the reaction of acyl halides with excess quinaldine or lepidine without the addition of dialkylanilines, but in an inert solvent with an equimolecular ratio of reacting components we did not observe the formation of partially hydrogenated methylquinoline derivatives. In this case, 1-acyllepidinium and -quinaldinium salts behave differently. Depending on the conditions used to carry out the reaction, acyllepidinium cations are converted to either 1-acyl-4-methyl-1,2-dihydroquinolines (I) (at 50°C) or to dimers (at 100°). The structure of I was proved by means of the UV, IR, PMR, and mass spectra. The alkaline hydrolysis of I gives lepidine, which also confirms the structure of I:



I

In elucidating the structures of the dimers we proceeded from two possibilities for their formation – as a result of dimerization of I through the double bond, as occurs in the case of 2,2,4-trimethyl-1,2-dihydroquinoline [5, 7];or by dimerization of the 1-acyllepidinium cation through the CH_3 group, similar to the process described for the dimerization of 1-alkyllepidinium salts [8]. An examination of the mass spectrum of dimer V demonstrated that it consists of two dihydroquinoline fragments, which made it possible to immediately reject the first assumption. In our case, anhydro base III, which, like other nucleophilic agents, attacks the cation of I in the α position to form derivative IV, apparently is formed readily

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*See [1] for communication XIX.

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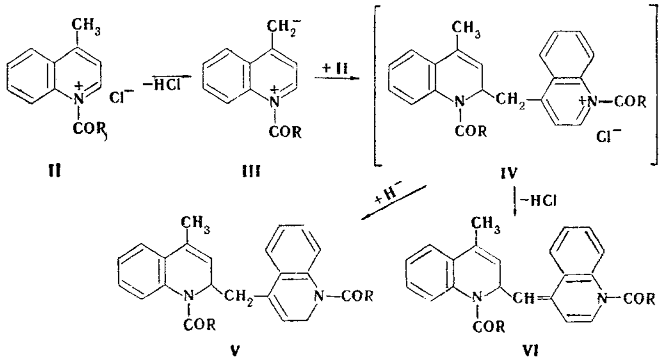
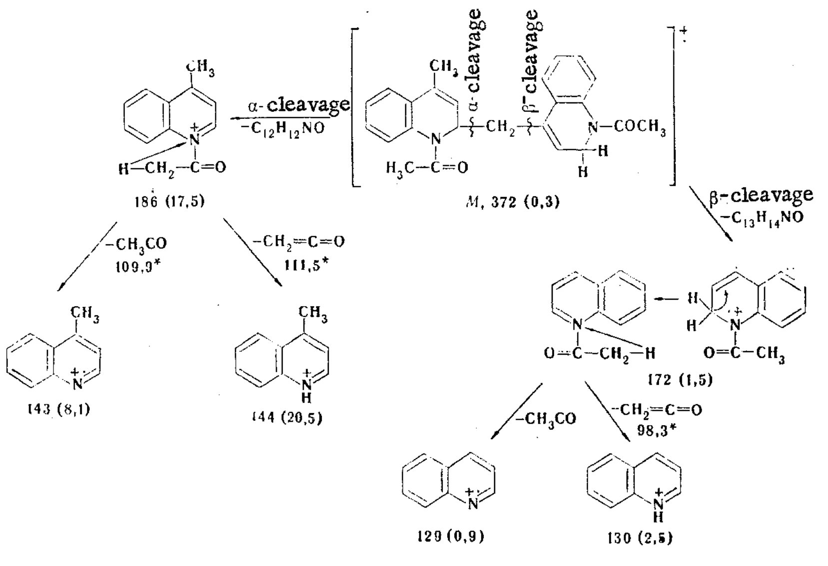
as a result of strong activation of the methyl group in 1-acyllepidinium cation II [9]. Derivative IV, as a result of the addition of a hydride ion, is converted to V or to anhydro base VI, which is similar to that which is formed in the dimerization of anhydro bases of 1-alkyllepidinium salts [8]:



The interpretation of the mass spectrum of the dimer is difficult because of the extremely low resistance of the molecular ion to electron impact (W_M = 0.3% of the total ion current). By analyzing the mass spectrum of one of the dimers (R = CH_3), we arrived at the following conclusions. The charge localization in the molecular ion is equally probable on any of the two nitrogen atoms of both partially hydrogenated quinoline rings. The most intense peaks of the fragment ions in the mass spectrum of the investigated compound are peaks with masses 186, 172, 144, 143, 142, 130, 129, 116, 115, and 89. Fragments with mass 186 can be expected during the disintegration of the molecular ion at the C−C bond connecting the two cyclic fragments, which have any one of the proposed structures V or VI, and the given peak therefore cannot serve for purposes of identification of the structure. The appearance of intense fragment ions with masses 172 and 130 in the mass spectrum is possible only in the case of disintegration of the molecular ion with structure V as a result of cleavage of the chain at the α or β bond (see Scheme 1) with subsequent splitting out of an alkyl radical. These processes lead to the formation of a pseudomolecular ion with the 4-methylquinoline or quinoline structure (m/e 143 and 129, respectively), the disintegration of which has been studied in detail [10] and is illustrated by the presence of fragment ions with masses 142, 128, 115, 101, and 89 in the spectrum of V.

The maximum peak in the mass spectrum of V is the peak of a fragment ion with mass 144, the development of which is due to the possibility of the formation of the energetically advantageous structure of the 4-methylquinolinium cation (see Scheme 1) as a result of a rearrangement process associated with the migration of a labile hydrogen atom of the CH_3 group of the acyl grouping attached to the nitrogen atom with simultaneous splitting out of the resulting $O{=}C{=}CH_2$ group. The stable structure of the quinolinium cation (m/e 130) similarly develops from the fragment ion with mass 172. It should be noted that, from the

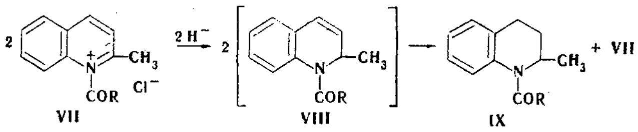
Scheme 1



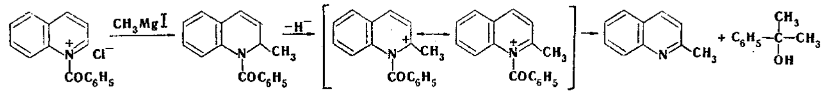
point of view of the disintegration of this molecular ion (structure V), it is difficult to explain the absence of a fragment with mass 200 in the mass spectrum, which may be evidence in favor of structure VI. However, if the molecular ion has the VI structure, the presence of intense peaks of ions with masses 172 and 130 in the mass spectrum cannot be explained.

Thus the molecular ion of the investigated compound most likely has structure V, the disintegration of which under the influence of electron impact proceeds via Scheme 1.

The reaction of acyl halides with quinaldine proved to be more complex. Dimer formation was not observed in this case, apparently because of the lesser activation of the methyl group in the 1-acylquinaldinium ion as compared with the 1-acyllepidinium ion [9]. When we carried out the reaction under different conditions, we always obtained 1-acyl-1,2,3,4-tetrahydroquinaldines (IX), probably as a result of disproportionation (with hydride transfer) of the intermediately formed 1-acyl-2-methyl-1,2-dihydroquinolines:



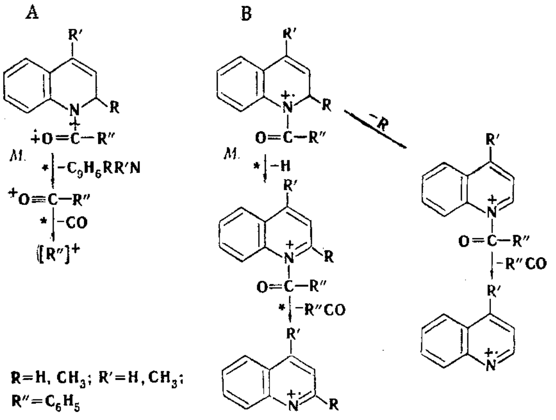
The IX structure was proved by means of the PMR, IR, and mass spectra and was confirmed by alternative synthesis. To elucidate the intermediate formation of 1,2-dihydro derivative VIII, we used an independent route to synthesize an authentic sample of 1-benzoyl-2-methyl-1,2-dihydroquinoline by the reaction of the 1-benzoylquinolinium salt with methylmagnesium iodide:



With respect to its melting point and mobility on aluminum oxide in various solvent systems, the compound was almost identical to IX, but its PMR and mass spectra unambiguously confirmed the structure assigned to it. Thus an intense doublet of the CH_3 group at δ 1.17 ppm (J = 6 Hz) and a quartet of the α proton (J = 6 Hz) at weaker field (δ 5.2 ppm for VIII and 4.72 ppm for IX) are observed in the PMR spectra of VIII and IX. However, the spectrum of VIII does not contain the signal of two CH_2 groups of the tetrahydroquinaldine ring at 2.1-2.8 ppm, and the signals of ethylene protons (3-H and 4-H) appeared at 5.9-6.3 ppm.

Compound VIII undergoes alkaline hydrolysis to give quinaldine, but we always obtained 1,2,3,4-tetrahydroquinaldine from the hydrolysis of IX, which definitely confirms their structure.

Our attempts to detect intermediately formed VIII in the reaction medium by means of paper and thin-layer chromatography were unsuccessful. In this connection and for confirmation of the structures of all of the synthesized compounds, we investigated their mass spectra and attempted to use them for the identification of the intermediate reaction products. The disintegration of the molecular ions of I, VIII, and IX should be characterized by competition between two principal directions of dissociation – disintegra-



tion originating from the molecular ion of structure A with a localized positive charge on the oxygen atom of the acyl group, and disintegration developing during the dissociative ionization of the molecular ion of structure B with charge localized on the nitrogen heteroatom.

In examining the mass spectra of these compounds it is seen that the predominant direction in the disintegration is disintegration of the molecular ion with structure A (the overall contribution of the disintegration processes due to structure A reaches about 65% of the total ion current). This molecular ion, with a localized charge on the oxygen atom of the carbonyl group, can be considered to be a representative of carboxylic acid amides, the character of disintegration of which has been adequately studied [11]. The α cleavage, which is expressed in splitting out of a methyl-substituted tetrahydro- (IX) or dihydroquinoline radical, that is characteristic for the disintegration of such compounds (ketones, acid derivatives, etc.) leads to the appearance of a stable fragment peak of the benzoyl cation ($C_6H_5-C\equiv O^+$) with mass 105, which is the maximum peak in the spectrum. A phenyl cation is formed from this fragment ion by subsequent elimination of carbon monoxide. The existence of this process is distinctly recorded in the spectrum by the corresponding metastable transition and by a number of fragment ions with masses 107, 92, 77, and 51 [9].

When the charge is localized on the nitrogen atom of the quinoline ring (structure B), the initial act of disintegration is detachment of a hydrogen atom or a methyl group from the α position of the quinoline ring, which leads to aromatization and stabilization of the system as a whole [the peaks of the $(M-H)^+$ or $(M-CH_3)^+$ fragments are generally more intense than the molecular ion peaks of all of the compounds, the intensities of which are 0.9-3.5% of the total ion current] with subsequent splitting out of an R"CO radical. The pseudomolecular ions with the methyl-substituted quinoline structure that are formed in this case undergo further disintegration to form a number of fragment ions with masses 142, 129, 128, 115, and 101 [10, 11]. For IX, which contains a tetrahydroquinoline ring, dehydrogenation of the system occurs after the above-described successive processes – M^+ (structure B) $\rightarrow (M-CH_3)^+ \rightarrow [(M-CH_3)-R''CO]^+$ – and the maximum number of eliminated hydrogen atoms is determined by the possibility of retention of the aromatic structure by the ions [13].

Thus the presence of a molecular ion peak (0.9-3.5% of ΣJ) in the mass spectra of the investigated compounds and a number of intense fragment ions – fragments of the molecule with the proposed structure (the peaks of fragment ions with intensities >1% of the total ion current were considered) – in the mass spectra of the investigated compounds completely confirms the structures assigned to them.

EXPERIMENTAL

The PMR spectra of carbon tetrachloride or pyridine solutions of the compounds were obtained with a JNM-C-60 spectrometer with hexamethyldisiloxane as the internal standard. The IR spectra of chloroform solutions were obtained with a UR-20 spectrophotometer. The UV spectra of ethanol solutions were recorded with an SF-4A spectrophotometer. Activity II aluminum oxide and benzene–hexane–chloroform (6 : 1 : 30) were used for the thin-layer chromatography. The gas-liquid chromatography was carried out with a UKh-1 chromatograph. The mass spectra of samples of I, II, IV, and V were recorded with an MKh-1303 spectrometer at an ionizing electron voltage of 50 eV, a cathode emission current of 1.5 mA, and a source and admission system temperature of 250°. The spectrum of III was recorded with an MS-7 spectrometer at an ionizing electron voltage of 70 eV, a cathode emission current of 1.0 mA, and an ionizing chamber temperature of 165°.

1-Benzoyl-2-methylquinolinium Chloride. The addition of a solution of 14.3 g (0.1 mole) of quinaldine in 10 ml of tetrahydrofuran to a cooled (to −60°) solution of 14 g (0.1 mole) of freshly distilled benzoyl chloride in 30 ml of absolute tetrahydrofuran gave 16 g (57%) of a colorless crystalline precipitate, which had mp 207-208° after repated washing with absolute ether. The product decomposed on standing in air. Found: Cl 13.0%. $C_{17}H_{14}ClNO$. Calculated: Cl 12.5%.

1-Benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline (IX). A. A mixture of 14.3 g (0.1 mole) of anhydrous quinaldine and 7 g (0.05 mole) of benzoyl chloride was allowed to stand at 50° for 2 h, after which it was treated with ammonium hydroxide and steam-distilled. The residue in the flask was separated, dried, and recrystallized three times from acetone to give 9 g (72%) of snow-white crystals with mp 117-118° (mp 117.5-118° [12]), R_f 0.51, and λ_{max} 265 nm (log ε 4.62).

B. A 14.1-g (0.1 mole) sample of benzoyl chloride was added dropwise to a cooled (to −5°) solution of 14.7 g (0.1 mole) of 1,2,3,4-tetrahydroquinaldine in 16 ml of anhydrous pyridine, after which the reaction mixture was allowed to stand at 0° for 3 h. The resulting precipitate was removed by filtration, washed with sodium carbonate solution and water, dried, and recrystallized to give 17.7 g (69%) of a product with mp 117-118° (from acetone). The product did not depress the melting point of the compound described in method A, and their IR spectra were identical.

Hydrolysis of the compounds obtained by both methods by refluxing in alcoholic alkali for 5 h gave 1,2,3,4-tetrahydroquinaldine (identified by means of GLC by the addition of an authentic sample of 1,2,3,4-tetrahydroquinaldine to the reaction mixture).

The same substance (mp 117-118°) was isolated in 45% yield from the reaction of quinaldine and benzoyl chloride with dimethylaniline (as previously described in [3]) or with diethylaniline. The formation of I was not observed in the absence of excess quinaldine or the other tertiary amine.

1-Benzoyl-2-methyl-1,2-dihydroquinoline (VIII). A total of 100 ml of a Grignard reagent, prepared from 14.2 g (0.1 mole) of methyl iodide and 2.5 g (0.1 g-atom) of magnesium in absolute ether, was added gradually to a previously heated (at 100° for 1.5 h) and cooled (to 0°) mixture of 12.9 g (0.1 mole) of anhydrous quinoline and 14 g (0.1 mole) of benzoyl chloride. The reaction mixture was heated for another 3 h, after which it was decomposed with 200 ml of saturated ammonium chloride solution. The ether layer was separated, and the aqueous layer was extracted several times with ether. The ether layer and extracts were dried, the ether was evaporated, and the residual material was recrystallized from acetone to give 8.2 g (33%) of a product with mp 119-120° and R_f 0.50; λ_{max}, nm (log ε): 265 (4.45), 320 (shoulder) (3.85). Found: C 81.6; H 6.2; N 5.8%; mol. wt. 249. $C_{17}H_{15}NO$. Calculated: C 81.9; H 6.0; N 5.6%; mol. wt. 249.

Hydrolysis of this compound with alcoholic alkali gave quinaldine, which was identified by means of GLC.

1-Benzoyl-4-methyl-1,2-dihydroquinoline (I). A 7-g (0.05 mole) sample of benzoyl chloride was added dropwise to a solution of 7.2 g (0.05 mole) of lepidine in 30 ml of absolute benzene, after which the mixture was allowed to stand at 50° for 2 h and steam-distilled. The solid residue was separated, dried, and recrystallized from petroleum ether to give 11 g (89%) of colorless crystals with mp 105-106° and R_f 0.45. Found: C 81.2; H 6.2; N 5.8%; mol. wt. 249 (mass spectrum). $C_{17}H_{15}NO$. Calculated: C 81.9; H 6.0; N 5.6%; mol. wt. 249.3.

Under similar conditions, 12.0 g (96%) of colorless crystalline dimer V ($R = C_6H_5$) with mp 188-190° [from dimethylformamide–water (2:1)] and R_f 0.13 was obtained after 6 h at 100°. The IR spectrum contained $\nu_{C=O}$ at 1650 cm^{-1}. Found: C 81.8; H 5.9; N 6.4%; mol. wt. 498. $C_{31}H_{30}N_2O_2$. Calculated: C 81.9; H 6.0; N 5.6%; mol. wt. 499.

The following dimers were similarly obtained: dimer V ($R = CH_3$), mp 151-152° (from butyl alcohol), R_f 0.10, $\nu_{C=O}$ 1650 cm^{-1}. Found: C 77.3; H 6.5; N 7.5%; mol. wt. 372 (mass spectrum). $C_{24}H_{24}N_2O_2$. Calculated: C 77.4; H 6.4; N 7.7%; mol. wt. 372. Dimer V ($R = \alpha$-furyl), mp 201-202° (from ethanol), R_f 0.12. Found: C 75.5; H 5.6; N 6.0%. $C_{30}H_{24}N_2O_4$. Calculated: C 75.3; H 5.0; N 5.9%.

Similar dimers are also formed in the reaction of acyl halides with lepidine in the presence of dialkylanilines or 1-alkyl-1,2,3,4-tetrahydroquinolines. Dimer formation was not observed when the reaction was carried out without excess lepidine or the other nitrogen base.

1-Benzoyl-2,4-dimethyl-1,2-dihydroquinoline. A 7-g (0.05 mole) sample of benzoyl chloride was added to 15.7 g (0.1 mole) of 2,4-dimethylquinoline, and the mixture was held at 100° for 1.5 h and steam-distilled. The solid residue was separated and dried to give 10.1 g (76%) of a lemon-yellow crystalline substance with mp 65-66° (from petroleum ether) and R_f 0.76. Found: C 82.5; H 6.6; N 5.2%. $C_{18}H_{17}NO$. Calculated: C 82.4; H 6.5; N 5.3%.

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