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It is shown that the rearrangement of phenylacetic acid hydrazides obtained from 8-substituted N-amino-1,2,3,4-tetrahydroquinolines under the influence of PCl₅ proceeds through a step involving the formation of a cyclohexadienoneimine derivative (which was isolated and characterized), which is formed by attack on the 10 position of the tetrahydroquinoline ring. A subsequent 1,3-sigmatropic shift of the cyanobenzyl group leads to nitriles of [6-(8-R-1,2,3,4-tetrahydroquinoly1)]phenylacetic acids. The possibility of their formation through another cyclohexadienoneimine intermediate (formed as a result of attack at the 8 position) is assumed. The nature and pathways for the formation of the side products in the rearrangement were ascertained.

In our preceding paper [1] we examined various rearrangements of 2,6-disubstituted phenylhydrazones that take place in the Fischer indole synthesis.

It is known from recent studies by Kost and co-workers that N_2 -acylarylhydrazines undergo an interesting rearrangement under the influence of phosphorus oxychloride to give 2aminoindoles [2-5]. This reaction may find wide application for the synthesis of indole derivatives that are difficult to obtain by other methods.

Since the Kost synthesis is based on a mechanism similar to the mechanism of the Fischer indole synthesis, we decided to carry out this reaction in the case of 2,6-disubstituted arylhydrazides in order to establish whether similar rearrangements occur in this case.

It was found that hydrazide I, obtained from phenylacetyl chloride and N-amino-1,2,3,4tetrahydroquinoline after refluxing for 2 h with phosphorus pentachloride (1 mole) in benzene, formed II, III, and IV, which were isolated by chromatography [6].



Hydrolysis of III in 20% HCl solution gave acid V, from which 6-benzyl-8-methylquinoline (VI) was formed by refluxing in xylene in the presence of Pd/C and decarboxylation and aromatization.



In order to prove the position of the benzyl group we synthesized 8-methylquinolines with a benzyl group in the 5, 6, and 7 positions and then established that VI is the 6-substituted derivative.

The structure of cyclohexadienoneimine intermediate II was proved by analytical and spectral methods and by the results of its reaction with 20% HCl, in which the same acid

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(V) as that obtained from III was formed due to a 1,3-sigmatropic shift of the cyanobenzyl group and subsequent hydrolysis [7].

The mechanism of the formation of II and III recalls, at least in the first steps, the formation of aminoindoles in the Kost synthesis, but it differs in the last steps, since the formation of an indole ring is impossible in this case. It is extremely likely that III is formed from II, although the possibility that the reaction proceeds through a step involving a different cyclohexadienoneimine intermediate (VIII) cannot be excluded.



Similarly, diphenylacetic acid hydrazide IX immediately gives tetrahydroquinoline derivative X, the structure of which was ascertained by means of spectral and analytical data and in analogy with the preceding rearrangement.



Hydrazide XI reacted similarly to give XII.



We observed that XIII, which has a methyl group in the 6 position, gives cyclohexadienoneimine XIV in 40% yield and a number of side products.



All of the side products are evidently obtained from cyclohexadienoneimine XIV. For example, α -chlorophenylacetonitrile and tetrahydroquinoline XV can be formed by the action of HCl on this imine.



If phenylacetonitrile is split out, the initially formed dihydroquinoline should undergo disproportionation to give a mixture of tetrahydroquinoline XV and quinoline XVI. The formation of diphenylsuccinonitrile (IV) is possibly related to the homolytic cleavage of imine XIV. This hypothesis is confirmed by the results of acid treatment (by refluxing with 20% HCl) of dienoneimine XIV, which leads to the same substances, i.e., to quinolines XV and XVI and dinitrile IV. In addition, phenylacetic acid and benzaldehyde, which are evidently formed as a result of conversion of the primary reaction products, were identified.

EXPERIMENTAL

<u>N-(6,8-Dimethyl-1,2,3,4-tetrahydro-1-quinolyl)phenylacetamide</u> (XIII). An 8.8-g (0.06 mole) sample of phenylacetyl chloride was added slowly to a solution of 10 g (~0.06 mole) of N-amino-6,8-dimethyl-1,2,3,4-tetrahydroquinoline and 8.5 ml of triethylamine in 100 ml of dry chloroform while maintaining the temperature of the reaction mixture below 20°C. The solvent was then removed by evaporation, and the residue was treated with a 5% solution of HCl and ether. Insoluble hydrazide XIII was removed by filtration and crystallized from ethanol to give 12 g (70%) of hydrazide XIII with mp 177-179°C. IR spectrum: 3333 (NH) and 1667 cm⁻¹ (CO). PMR spectrum (CDCl₃): 7.25 (5H, s, C₆H₅), 6.92 (1H, s, NH), 6.70 (2H, d, aromatic protons), 3.47 (2H, s, COCH₂), 3.28 (2H, m, NCH₂), 2.70 (2H, t, benzyl group of the hydrogenated ring), 2.20 (3H, d, 6-CH₃), 2.09 (3H, s, 8-CH₃), and 1.75 ppm (2H, m, CH₂ attached to a saturated carbon atom).

Reaction of Hydrazide XIII with PCl₅. A mixture of 11.5 g (0.04 mole) of hydrazide XIII and 8.5 g of PCl₅ in dry benzene was refluxed for 2 h, and the resulting solution was treated with water. The aqueous layer was made alkaline with 5% NaOH solution and extracted with ether to give 4 g of the dienoneimine derivative with mp 75°C (from diisopropyl ether). PMR spectrum (CDCl₃): 7.40 (5H, m, C₆H₅), 6.78 (2H, d, aromatic protons), 5.40 (1H, s, CH₂), 3.00 (2H, m, NCH₂), 2.70 (2H, m, benzyl group of the hydrogenated ring), 2.31 (3H, s, 6-CH₃), 2.22 (3H, s, 8-CH₃), and 1.60 (2H, m, CH₂ attached to a saturated carbon atom).

The precipitate (3.3 g) that formed from the mother liquor was chromatographed with a column filled with silica gel (elution with benzene) to give, successively, 6,8-dimethyl-1,2,3,4-tetrahydroquinoline (XV) and 6,8-dimethylquinoline (XVI).

The precipitate from the benzene layer was treated with alcohol to give 0.5 g of 2,3diphenylsuccinonitrile [8] (IV) with mp 228°C. Fractional distillation of the mother liquor also gave unchanged hydrazide XIII, phenylacetonitrile, and α -chlorophenylacetonitrile.

Reaction of Cyclohexadienoneimine XIV with 20% HCl Solution. This reaction was carried out at the boiling point for 1 h, as a result of which basic, acidic, and neutral compounds were formed. The principal fraction consisted of 6,8-dimethylquinoline (XVI) and its tetrahydro derivative (XV), which was isolated in pure form by chromatography. The acidic fraction was treated with diazomethane, and the resulting compound was identified by comparison with an authentic sample as methyl phenylacetate. The neutral fraction was vacuum evaporated, and the residue was worked up to give benzaldehyde in the form of the 2,4-dinitrophenylhydrazone and 2,4-diphenylsuccinonitrile (IV).

<u>N-(8-Methyl-1,2,3,4-tetrahydro-1-quinolyl)diphenylacetamide (IX)</u>. This compound, with mp 207°C (from diisopropyl ether), was obtained as white crystals by the method described for hydrazides I [6] and XIII. IR spectrum (Nujol): 3333 (NH) and 1667 cm⁻¹ (CO). PMR spectrum (CDCl₃): 7.19 (10H, s, 2C₆H₅), 6.88 (3H, s, aromatic protons), 4.70 (1H, s, COCH), 3.29 (2H, m, NCH₂), 2.71 (2H, t, benzyl protons), 2.02 (3H, s, CH₃), and 1.70 ppm (2H, m, CH₂ attached to a saturated carbon atom).

Reaction of Hydrazide IX with PCl₅. The reaction was carried out under the conditions described for I and XIII. Workup of the basic fraction gave only nitrile X with mp 126°C (from methanol). IR spectrum (Nujol): 3430 (MH) and 2247 cm⁻¹ (CN). PMR spectrum (CDCl₃): 7.27 (10H, m, 2C₆H₅), 6.65 (2H, s, aromatic), 3.35 (3H, m, NHCH₂), 2.70 (2H, t, benzyl protons), and 1.90 ppm (5H, m, CH₃ and CH₂ attached to a saturated carbon atom).

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STERIC EFFECT OF SUBSTITUENTS ON THE NATURE OF THE CHROMOPHORE IN $\Delta^{9,10}$ -OCTAHYDRO-4-QUINOLONES*

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The study of the behavior of cisoid two-ring ketones from substituted cyclohexanones and (-)-menthone was continued. The steric effect of a bulky substituent attached to the 8-C atom of the quinolone system on the conformation of the molecule was established; this effect leads to disruption of the conjugation of the p-electron pair of the nitrogen atom in the enamino ketone portion of the chromophore.

During a comparison of the spectral characteristics of 1-butyl-5-methyl-8-isopropyl- $\Delta^{9,10}$ -octahydro-4-quinolone (Ia) [2] and the previously investigated two-ring enamino ketones IV [3, 4] we observed a shift of 70 nm to the short-wave region of the band of the $\pi \rightarrow \pi^*$ transition in the UV spectrum of Ia. This change in the spectral behavior evidently may be associated with the steric effect of the substituent in the carbocyclic ring on the conformation of the molecule. In this connection we investigated a number of enamino ketones (I-III) containing various substituents in the 1, 5, and 8 positions of the octa-hydroquinoline system.



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I a $R = C_4H_5$, $R^1 = CH_3$, $R^2 = CH(CH_3)_2$; b $R = CH_3C_6H_5$, $R^1 = CH_3$, $R^2 = CH(CH_3)_2$; II $R = CH_2C_6H_5$, $R^1 = H$, $R^2 = CH_2CH(CH_3)_2$, III a $R = CH_2C_6H_5$, $R^1 = CH_3$, $R^2 = H$; b $R = CH_2C_6H_5$, $R^1 = H$, $R^2 = CH_3$; IV $R^1 \approx R^2 = H$; a $R \approx CH(C_6H_5)CH_3$; b $R = CH(C_2H_5)CH_3$

Two-ring cisoid enamino ketones I-III were obtained by the methods described in [3, 4]. Their compositions and structures were confirmed by the results of elementary analysis and PMR spectroscopic data (Table 1). The mass spectral fragmentation of the enamino ketones confirms their structures and is characteristic for compounds of this series [2].

It should be noted that the UV spectra of enamino ketones IV in heptane are characterized by the band of a $\pi \rightarrow \pi^*$ transition of the enamino ketone chromophore at 305-315 nm. In contrast to this, the band of the $\pi \rightarrow \pi^*$ transition in the UV spectra of enamino ketones I obtained from (-)-menthone appears at 240 nm, and an inflection is also observed at 280-310 nm (Fig. 1).

In the IR spectra of compounds I, II and III, IV we also observed these differences; in enamino ketones III and IV bands appeared at 1540-1560 and 1620-1630 cm^{-1} , characteristic of the stretching vibrations of the conjugated C=C bond and the carbonyl group. In the spectra of compounds I and II these bands converge strongly at 1638 and 1670 cm^{-1} .

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