Pyrrolanthrone-1-carboxylic Acid Azides (XIII, XIV). A solution of 0.028 mole of sodium nitrite in 6 ml of water was added gradually at 0-5°C to a suspension of 0.028 mole of hydrazide XI or XII in 80 ml of acetic acid and 20 ml of water, after which the mixture was stirred for 1 h. It was then diluted with 370 ml of cold water, and the resulting precipitate was removed by filtration to give 7.3 g (90%) of azide XIII [IR spectrum (KBr): 2165 cm^{-1} (N$_3$)] or 8 g (96%) of azide XIV [IR spectrum (KBr): 2140 cm^{-1} (N$_3$)].

1-Aminopyrrolanthrones (IV, V). An 8-g sample of azide XIII or XIV in 40 ml of acetic acid and 40 ml of water was heated at 80-85°C for 1-2.5 h, after which the mixture was cooled, and the resulting precipitate was removed by filtration and dried to give amine IV or V. Amine V was chromatographed on SiO$_2$ (40-100 mμ) (elution with chloroform and alcohol) to obtain a sample for analysis.

Pyrrolanthrone (II). A 0.5-g sample of acid I was heated in 25 ml of 85-88% phosphoric acid at 160-175°C for 2 h, after which the mixture was cooled and diluted with 125 ml of water. The aqueous mixture was neutralized with ammonium hydroxide, and the precipitate was removed by filtration, washed, dried, and chromatographed on Al$_2$O$_3$ (elution with chloroform) to give 0.29 g (70%) of pyrrolanthrone (II) with mp 258-260°C (from benzene). Compound II was identical to the substance obtained by the method in [1] with respect to its melting point and IR spectrum.

N-Methylpyrrolanthrone (III). A) 0.5-g sample of acid VIII was heated in 25 ml of 85-88% phosphoric acid at 120-130°C for 1 h. The product was isolated and purified by the methods used in the preparation of II.

B) A 0.5-g (1.65 mmole) sample of azide XIV was added to a solution of 1 g (14.5 mmole) of sodium nitrite in 25 ml of acetic acid and 25 ml of water, and the mixture was stirred at room temperature for 6 h. It was then diluted with 100 ml of water, and the resulting precipitate was removed by filtration, dried, and chromatographed on SiO$_2$ (100-250 mμ) (elution with benzene) to give 0.13 g (32%) of III.

LITERATURE CITED

1. M. V. Kazankov, N. P. Makshankova, and E. G. Kuznetsova, Khim. Geterotsikl. Soedin., No. 8, 1103 (1977).
2. A. Gossauer, Die Chemie der Pyrrole, Ber., **37**, 259 (1974).
3. H. Fischer, O. Süs, and F. G. Weilgung, Ann., **481**, 159 (1930).

AUTOXIDATIVE TRANSFORMATIONS OF 2-SUBSTITUTED 3-ALKYL-4-HYDROXY-1-OXO-1,2-DIHYDROISOQUINOLINES

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A method for the preparation of 2-substituted 3-alkyl-4-hydroxy-1-oxo-1,2-dihydro-isoquinolines is described. It is shown that 2,3-dialkyl-substituted derivatives readily undergo autoxidation and dealkylation to give N-methylphthalonimide and 3-hydroperoxy- and 3-hydroxy-2,3-dialkyl-1,4-dioxo-1,2,3,4-tetrahydroisoquino-lines.

2,3-Dialkyl-5-1-oxo-hydroxy-1,2-dihydroisoquinolines are capable of facile oxidative transformations, whereas their 3-aryl analogs are resistant to autoxidation by air oxygen [1].

It is known [2, 3] that compounds with a double bond in the β position relative to the nitrogen atom in many cases are capable of oxidation. 3-Hydroperoxypyrrolenines and other

oxygen-containing substances are formed from C-substituted pyrroles by oxidation with air oxygen with migration of the double bond. Similarly, the oxidation of imidazoles gives hydroperoxides and their decomposition products. It has been established that the oxidation of 3-substituted indoles to 3-hydroperoxides is realized only when there is an alkyl substituent in the 3 position. If there is an electron-withdrawing phenyl group in this position, oxidation does not take place. N-substituted 1,2,3,4-tetrahydroisoquinolines are also easily oxidized in benzene with the formation of a peroxide bridge in the 1,1' position [4]. Compounds that contain the same system of bonds also include 1-phenylamino-2-arylphenylimino-2-indenes, which give 2,3-diaryl-3-hydroxy-3-aryl-4-phenyliminodehydroisoquinolines when they are refluxed in chloroform [5]. The formation of intermediate cyclic peroxides is postulated in this reaction.

The aim of the present research was to synthesize and study the properties (primarily the zutoxidative transformations with air oxygen) of 2-substituted 3-alkyl-4-hydroyl-1-oxo-1,2-dihydroisoquinolines (IIa-c), which were obtained by reaction of the previously described [6, 7] 2-alkylamino- and 2-anilino-2-alkylindanediones (Ia-c) with nucleophilic agents.

I, II, IV, V a Alk=C$_2$H$_5$, R=C$_6$H$_5$;
b Alk=C$_2$H$_5$, R=CH$_3$; c Alk=n-C$_3$H$_7$,
R=CH$_3$;
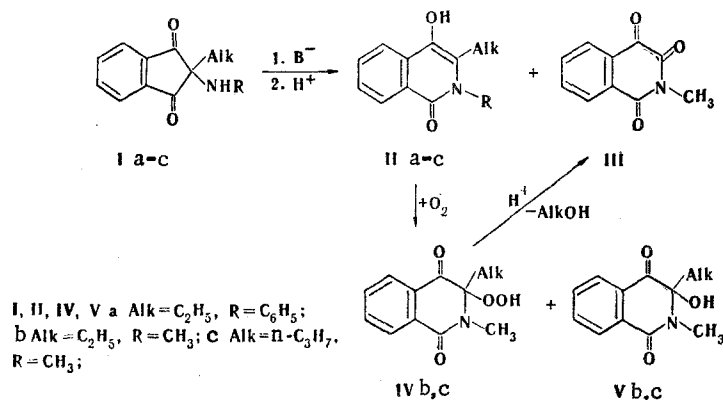
Compound IIa was obtained by isomerization of 2-anilino-2-ethylindane-1,3-dione (Ia) in the presence of sodium methoxide. The IR spectrum of IIa contains absorption maxima at 1599, 1613, 1643, and 3200 cm^{-1}; this is characteristic for a structure of the II type [1]. A triplet of the protons of the methyl group at δ 0.9 ppm, a quartet of methylene protons at 2.2-2.6 ppm, and the signal of an enol hydroxy group at 8.12 ppm (confirmed by deuteration with D$_2$O) are observed in the PMR spectrum of IIa in dimethyl sulfoxide (DMSO). Enol IIa was characterized by its O-acetyl derivative, in the IR spectrum of which the absorption of an acetyl carbonyl is observed at 1740 cm^{-1}.

The known N-methylphthalonimide (III) [8-10] was isolated as a result of the reaction of aminoindanediones Ib and Ic with nucleophilic agents. Its formation may be the result of acid decomposition of hydroperoxides IV; this was confirmed in the case of IVb. The decomposition of hydroperoxides IV evidently is realized via a mechanism similar to the mechanism of acid decomposition of cumene hydroperoxide and other peroxides [11, 12]. It was established that imide III is also formed from amino ketone Ib when the reaction with nucleophiles is carried out in a nitrogen or argon atomosphere; however, since the reaction products are isolated in air, this confirms the decisive role of the rapid oxidative transformations of the the intermediates.

In addition to imide III, the corresponding 3-hydroperoxy- and 3-hydroxy-1,2,3,4-tetrahydroisoquinolines (IV and V) are found among the products of the reaction of amino ketones Ib, c with nucleophiles; IV and V are formed as a result of autoxidation of the intermediate 1-oxo-4-hydroxy-1,2-dihydroisoquinolines IIb, c.

The structure of 2-methyl-3-ethyl-3-hydroperoxy-1,4-dioxo-1,2,3,4-tetrahydroisoquinoline (IVb) was proved unambiguously by iodometric determination of the peroxide oxygen and by spectral methods. Absorption of an amide carbonyl group at 1655 cm^{-1} and of a keto group at 1710 cm^{-1} is observed in the IR spectrum. A broad absorption band of a hydroxyl group is found at 3270 cm^{-1}. The addition of triethylamine to a solution of the hydroperoxide in chloroform does not give rise to any changes in the absorption in the region of the stretching vibrations of the double bonds; this confirms the absence of a carboxyl group in the compound. The ν_{OH} absorption vanishes because of the formation of a triethylammonium grouping.

The protons of the ethyl group resonate at strongest field in the PMR spectrum of IVb in deuterochloroform: a triplet (^3J = 7.0 Hz) of a methyl fragment at δ 0.70 ppm and a multiplet of a methylene fragment at ~2.0 ppm are observed. Analysis of the latter shows that both protons are anisochronic and form an AB system (^2J = 13 Hz), each line of which is split into a quartet because of spin—spin coupling with the methyl group. Nonequivalence of both protons can develop only if the ethyl group is attached to a chiral carbon atom [13, 14]. A singlet of N—CH$_3$ protons appears at 3.13 ppm. A multiplet of aromatic protons of the ABCD type is found in the weak-field portion of the spectrum (7.6–8.3 ppm). Consequently, the carbonyl groups adjacent to the phenylene ring were retained but have a different environment. The O—H proton resonates at weak field (12.3 ppm) in the form of a broad singlet.

A molecular ion does not appear in the mass spectrum of IVb; however, the peak with m/e 201 and the elementary composition $C_{12}H_{11}NO_2$ corresponds to the fragment peroxide. This sort of elimination of H_2O_2 from hydroperoxides upon electron impact is characteristic for this series of compounds [15]. A peak with m/e 219 also appears in the mass spectrum, and this constitutes evidence for the presence of hydroxy derivative Vb. A third reaction product (ethanol) is detected by gas—liquid chromatography (GLC).

A distinctive sign of the reaction of 2-methylamino-2-propylindane-1,3-dione (Ic) with nucleophiles is the fact that in this case unstable 1-oxo-4-hydroxy-1,2-dihydroisoquinoline IIc, the IR spectrum of which is characterized by maxima at 1582, 1614, and 1643 cm^{-1} and a broad maximum of an enol hydroxyl group at 3400 cm^{-1}, was also isolated along with imide III. The O-acetyl derivative has intense C=O absorption at 1762 cm^{-1} and is resistant to autoxidation. After IIc is stored in air or crystallized from ethanol, its IR spectrum changes, and maxima of amide and ketone carbonyl groups at, respectively, 1645 and 1709 cm^{-1} and absorption of a hydroxyl group at 3270 cm^{-1} appear; this is in agreement with the structure of hydroxy derivative Vc or hydroperoxide IVc. Since the mass spectrum contains a molecular ion peak (M$^+$) with m/e 233 and elementary composition $C_{13}H_{15}NO_3$, it may be strictly asserted that enol IIc gives intermediate hydroxy derivative Vc when it undergoes autoxidation. The presence of small amounts of hydroperoxide IVc was also proved by iodometry.

If one studies the PMR spectrum of the product of the reaction of amino diketone Ic with nucleophiles in deuterochloroform immediately after its isolation from the reaction medium, one finds confirmation for the structure of enol IIc: a multiplet of aromatic protons (6.7–8.15 ppm), a singlet of N—CH$_3$ protons (3.54 ppm), and three signals of protons of a propyl group [the triplet of an α—CH$_2$ group (2.83 ppm, ^3J = 6.5 Hz), the multiplet of a β—CH$_2$ group (1.3–1.9 ppm), and the triplet of a methyl group (1.00 ppm, ^3J = 6.1 Hz)] are observed. Treatment with D_2O revealed that the signal of the hydrogen atom of the enol hydroxyl group is hidden under the multiplet at 7.5 ppm. If the PMR spectrum of the same substance is recorded after prolonged storage in air or crystallization from ethanol, one notes appreciable changes: the multiplet of aromatic protons (δ 7.6–8.3 ppm) is shifted significantly to weak field, and the resonance of the N—CH$_3$ protons (3.16 ppm) and the propyl group (multiplets at 1.7–2.3 and 1.0–1.3 and triplet at 0.84 ppm) is shifted to stronger field. The hydrogen atom of the hydroxyl group gives a broad singlet at 10.3 ppm. The spectrum thus confirms the structure of tetrahydroisoquinoline Vc.

Thus in contrast to the corresponding 3-aryl derivatives, facile autoxidation and dealkylation is characteristic for 2,3-dialkyl-4-hydroxy-1-oxo-1,2-dihydroisoquinolines.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in Nujol or hexachlorobutadiene were recorded with a UR-20 spectrometer. The mass spectra were recorded with an AEI MS-905 spectrometer at an ionizing voltage of 70 eV with introduction of the samples through a glass inlet system at a cylinder temperature of 150°C. The PMR spectra of ~10% solutions of the compounds were recorded with a Perkin—Elmer R12A spectrometer with tetramethylsilane as the internal standard. Gas—liquid chromatography (GLC) was carried out with a Tsvet 1-64A chromatograph with a flame-ionization detector and helium as the carrier gas under isothermal conditions.

3-Ethyl-2-phenyl-4-hydroxy-1-oxo-1,2-dihydroisoquinoline (IIa). A 2.65-g (0.01 mole) sample of 2-anilinoindanedione Ia was reflexed for 3 h in a solution of sodium methoxide prepared from 50 ml of methanol and 0.9 g of sodium, and the resulting yellow solution was poured into 200 ml of water. The aqueous mixture was acidified with hydrochloric acid, and

the precipitate was removed by filtration to give 1.8 g (68%) of a colorless substance with mp 158°C (from ethanol). Found: C 77.2; H 5.8; N 5.1%; M 265 (by mass spectrometry). $C_{17}H_{15}NO_2$. Calculated: C 77.0; H 5.7; N 5.3%; M 265. The O-acetyl derivative was prepared as follows. A sample of IIa was refluxed in a mixture of acetyl chloride and acetic anhydride (1:1) for ~15 min, after which the mixture was poured into water. Workup gave a colorless substance with mp 203°C (from ethanol). Found: C 73.8; H 5.3; N 4.2%. $C_{19}H_{17}NO_3$. Calculated: C 74.2; H 5.6; N 4.6%.

Reaction of 2-Methylamino-2-ethylindane-1,3-dione (Ib) with Aqueous Alkali. A solution of 3.4 g (0.06 mole) of potassium hydroxide in 20 ml of water was added to a solution of 7.2 g (0.03 mole) of the hydrochloride of Ib in 80 ml of water, and the mixture was heated on a water bath for 3 h. The resulting solution was diluted with 200 ml of water, and the aqueous mixture was acidified with hydrochloric acid and allowed to stand overnight at 0°C. The resulting precipitate was removed by filtration* and crystallized from ethanol to give 1 g (18%) of N-methylphthalonimide (III) with mp 186°C. The properties of the product were in agreement with the properties described in [8-10, 16]. Careful addition of water to the filtrate after crystallization of imide III precipitated 1.8 g (26%) of hydroperoxide IVb with mp 138°C (from ethanol). Found: C 61.0; H 5.8; N 5.9%. $C_{12}H_{13}NO_4$. Calculated: C 61.3; H 5.6; N 5.9%. Determination of the peroxide oxygen by iodometry [17] established that the product contained ~98% hydroperoxide IVb.

Acid Decomposition of Hydroperoxide IVb. A solution of hydroperoxide IVb in ether was saturated with dry hydrogen chloride. N-Methylphthalonimide (III) was isolated after the solvent was removed.

Reaction of Aminoindanedione Ib with Sodium Methoxide. A 4.06-g (0.02 mole) sample of Ib was refluxed for 3 h in a solution of sodium methoxide, prepared from 1.8 g of sodium and 100 ml of methanol, after which the mixture was poured into 300 ml of water, and the aqueous mixture was acidified with hydrochloric acid and worked up to give III and IVb, as in the preceding experiment.

The same substances (III and IVb) were obtained when the reaction of Ib with nucleophilic agents was carried out in a nitrogen or argon atmosphere and the products were isolated under the usual conditions.

Reaction of 2-Methylamino-2-propylindane-1,3-dione (Ic) with Sodium Methoxide. A 2.17-g (0.01 mole) sample of Ic was refluxed in a solution of sodium methoxide, prepared from 50 ml of methanol and 0.9 g of sodium, after which the yellowish solution was poured into 200 ml of water. Acidification of the aqueous mixture with hydrochloric acid precipitated 1.8 g of a colorless mixture consisting of enol IIc and imide III [confirmed by TLC on Silufol UV-254 plates, elution with chloroform—ethanol—hexane (5:4:5)]. The product had mp 98-102°C and dissolved in aqueous alkali to give a yellow solution. Crystallization from ethanol gave 0.2 g of imide III with mp 186°C. Dilution of the filtrate with water after separation of imide III precipitated 2-methyl-3-propyl-4-hydroxy-1-oxo-1,2-dihydroisoquinoline (IIc) with mp 129-131°C. Found: C 70.9; H 6.6; N 7.2%. $C_{13}H_{15}NO_2$. Calculated: C 71.9; H 7.0; N 6.5%.

Crystallization from ethanol gave 2-methyl-3-propyl-3-hydroxy-1,4-dioxo-1,2,3,4-tetrahydroisoquinoline (Vc), which contained hydroperoxide IVc (proved by iodometry). Found: C 67.7; H 6.3; N 6.1%; M 233 (by mass spectrometry). $C_{13}H_{15}NO_3$. Calculated: C 66.9; H 6.5; N 6.0%; M 233. The O-acetyl derivative was a colorless substance with mp 86°C (from ethanol). Found: C 68.5; H 6.5; N 5.0%; M 259 (by mass spectrometry). $C_{15}H_{17}NO_3$. Calculated: C 69.5; H 6.6; N 5.4%; M 259.

LITERATURE CITED

1. I. P. Lentsberg, Author's Abstract of His Master's Dissertation, Riga (1972).
2. V. Karnozhitskii, Usp. Khim., 46, 263 (1977).
3. W. Bartok, D. D. Rosenfeld, and A. Schriesheim, J. Org. Chem., 28, 410 (1963).
4. A. Rieche, E. Höft, and H. Schultze, Chem. Ber., 97, 195 (1964).
5. V. A. Usov and Ya. F. Freimanis, Khim. Geterotsikl. Soedin., No. 4, 640 (1969).
6. Ya. Ya. Ozol, S. K. Germane, A. K. Aren, and G. Ya. Vanag, Izv. Akad. Nauk Latv. SSR, Ser. Khim., No. 5, 583 (1969).

*Ethanol was detected in the filtrate by GLC.

7. Ya. Ya. Ozol, G. Ya. Vanag, and S. K. Germane, Zh. Org. Khim., 2, 1691 (1966).
8. N. J. Mruk and H. Tieckelmann, Tetrahedron Lett., No. 14, 1209 (1970).
9. I. G. Hinton and F. G. Mann, J. Chem. Soc., No. 2, 599 (1959).
10. R. A. Henry, C. A. Heller, and D. W. Moore, J. Org. Chem., 40, 1760 (1975).
11. W. Pritzkow, Chem. Ber., 88, 572 (1955).
12. M. S. Kharasch, A. Fono, W. Nudenberg, and B. Bischof, J. Org. Chem., 17, 207 (1952).
13. K. Mislow and M. Raban, in: Selected Problems in Stereochemistry [Russian translation], Mir, Moscow (1970), p. 32.
14. R. H. Bible, Jr., Interpretation of NMR Spectra: An Empirical Approach, Plenum Publ. (1965).
15. A. R. Burgess, R. D. G. Lane, and D. K. Sharma, J. Chem. Soc., B, No. 4, 341 (1969).
16. C. Fournier and J. Decombe, Bull. Soc. Chim. France, No. 9, 3367 (1967).
17. V. Karnozhitskii, Organic Peroxides [Russian translation], Inostr. Lit., Moscow (1961), p. 116.

ACETALS OF LACTAMS AND ACID AMIDES.

XXV.* LACTIM—LACTAM TAUTOMERISM OF 6-DIALKYLAMINO-3-CYANO-2-

PYRIDONE DERIVATIVES

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It is shown that the alkylation of 1-methyl-6-cyano-1,2,3,4-tetrahydro-1,8-naphthyrid-7-one under various conditions takes place at the oxygen atom of the oxo group in the 7 position. It was established by UV, IR, and mass spectroscopy that lactim—lactam tautomerism is observed in 6-dimethylamino-2-pyridone, pyrrolo[2,3-b]pyrid-6-one, 1,8-naphthyrid-7-one, and 8-oxopyrido[2,3-b]azepine derivatives. The tautomeric equilibrium constants (K_T) in various solvents were calculated. It is shown that the position of the equilibrium is shifted from the lactam to the lactim form when the polarity of the solvent decreases, when an electron-acceptor CN group is introduced, and when a 6-NR_2 group is included in the ring condensed with the pyridone ring.

Unsubstituted 2- and 4-pyridones undergo both N- and O-alkylation under various conditions. Since it has been recently established that the alkylation of dialkylamino-4-pyridones proceeds selectively at the oxygen atom [2], in the present research we investigated the problem of the direction of alkylation of similar 2-pyridone derivatives.

Alkylation of 1-methyl-6-cyano-1,2,3,4-tetrahydro-1,8-naphthyrid-7-one (I) with triethyloxonium tetrafluoroborate and methyl iodide [with dimethylformamide (DMF) (in the presence of NaH) or alcohol containing KOH as the solvent] gave II and III, the UV spectra of which in polar solvents are similar to one another but differ from the spectrum of starting I. When III is heated with hydrobromic acid, it undergoes processes involving demethylation, saponification of the cyano group, and decarboxylation, as a result of which 1-methyl-1,2,3,4-tetrahydro-1,8-naphthyrid-7-one (IV), which was also synthesized from naphthyridone I by refluxing with HBr, is formed.

It follows from these data that II and III are O-alkylation products. Ethoxy derivatives VI and VII, respectively, were synthesized from naphthyridone IV and pyridoazepine V by the method used to prepare II. Since 2-pyridone derivatives that contain (in the 6 position) a substituent with a heteroatom display lactim—lactam tautomerism [3, 4], in the

*See [1] for communication XXIV.