microammeter; photoluminescence was excited with an SVDSh-500 lamp, from the spectrum of which light with a wavelength of 365 nm was isolated by means of a DMR-4 quartz monochromator. The IR spectra were obtained with a UR-20 spectrometer.

The hetarylethylene derivatives of 2,5-diphenyloxazole and 2,5-diphenyl-1,3,4-oxadiazole were obtained by the method in [7] and were purified by chromatography on aluminum oxide in benzene with subsequent recrystallization from a suitable solvent.

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POLYNUCLEAR HETEROCYCLIC COMPOUNDS BASED ON THE ADDUCT OF o-CINNAMOYLBENZOIC ACID AND CYCLOHEXANONE

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UDC 547.759.4'751'781: 542.953:543.422

The product of addition of cyclohexanone to o-cinnamoylbenzoic acid, which has the 4-phenyl-8a-hydroxyperhydrochroman-2-spiro-3'-phthalide structure, reacts with nitrogen-containing nucleophiles to give hydrogenated derivatives of oxa-(aza, thia)indolizinespirophthalide and pyrido[1',2':1,2]imidazo[2,3-a]-isoindole, as well as 4-R-1-phthalazones. An isoindolo[1,2-a]quinoline derivative and a compound with a 7,8-diaza-D-homosteroid skeleton were obtained from the latter.

Semicyclic 1,5-diketones that contain reactive substituents in the ortho position relative to the aroyl carbonyl group are convenient starting compounds for the synthesis of polynuclear (including new) heterocyclic systems; in particular, the synthesis of compounds with a heterosteroid skeleton is possible. We have previously described the synthesis and properties of o-hydroxy- and o-amino-substituted semicyclic 1,5-diketones [1, 2]. In order to synthesize an o-carboxy-substituted diketone we realized the addition of cyclohexanone to o-cinnamoylbenzoic acid; we have previously briefly reported the synthesis and some properties of adduct I [3] (see scheme on following page).

The addition proceeds readily in the presence of KOH; adduct I has the 4-phenyl-8a-hydroxyperhydrochroman-2-spiro-3'-phthalide (IA) structure [3]. In the reaction of I with nitrogen nucleophiles we isolated products, the formation of which can be explained by prior opening of the hydropyran and phthalide fragments and conversion of I to the o-carboxy-sub-

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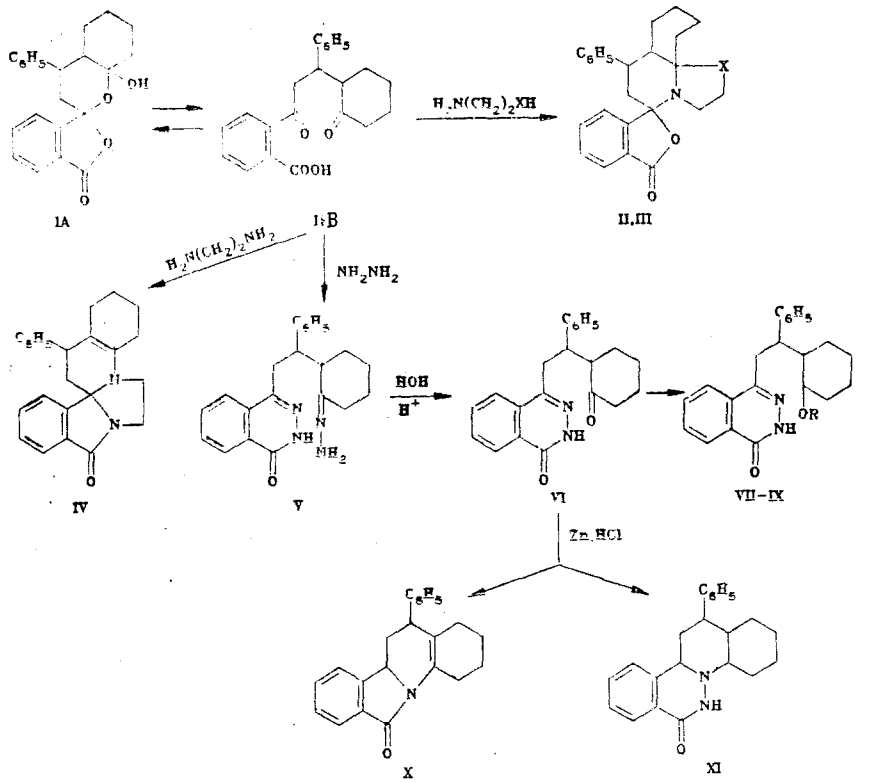
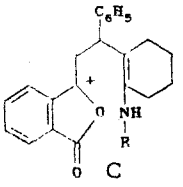


II X = O; III X = S; VII R = H; VIII R = CHO; IX R = $COCH_3$

stituted semicyclic 1,5-diketone form (IB); however, one cannot exclude the possibility that the reactions proceed without opening of the phthalide ring, for example, through intermediate cation C:



Whereas the reaction of I with nucleophiles that contain an aromatic amino group [3] requries heating and acidic catalysis, the reaction with nucleophiles that contain an aliphatic amino group, as well as with hydrazine, proceeds at room temperature in the absence of acidic agents. The products of the reaction of I with ethanolamine and with β-mercaptoethylamine (which has not been previously subjected to reaction with 1,5-diketones) are to a certain extent similar to the products of the reaction of the previously investigated 1,5-diketones with bifunctional nucleophiles [4]; the difference is the presence of the phthalide structure. However, in the case of the reaction with ethylenediamine the reaction proceeds via a different scheme: in addition to the formation of a hydropyridine ring, the second amino group of the nucleophile reacts with the phthalide fragment to give a phthalimidine structure (IV).

The IR spectra of II and III (Table 1) do not contain absorption bands of C=C bonds or OH (II) and SH (III) groups; the carbonyl group of the phthalide fragment gives an intense band at 1745 cm^{-1}. On the other hand, absorption of a C=C bond at 1655 cm^{-1} appears in the spectrum of IV, and, instead of absorption of a phthalide carbonyl group, an intense band at 1700 cm^{-1} (phthalimidine C=O) is observed; absorption of N–H bonds is absent.

In the PMR spectrum of II the protons of the oxazolidine fragment give two multiplets (each 2H) at 4.0 ppm (CH_2–O) and 2.8 ppm (CH_2–N); in the spectrum of III the protons of the thiazolidine fragment give an overall multiplet (4H) centered at 2.9 ppm. Signals of aromatic protons of the phthalide fragment are observed in the spectra at 7.5-7.9 ppm. The signal of a benzyl proton in the 4 position of the piperidine ring shows up in the form of a triplet of doublets with a width of ~30 Hz; this indicates an axial orientation of the 3-H, 4-H, and

TABLE 1. Data from the IR, PMR, and Mass Spectra of II-XI

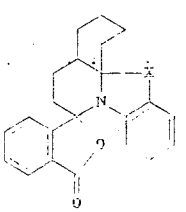
Compound	IR spectum, cm^{-1}	PMR spectrum, ppm (SSCC, Hz)	Mass spectrum,* m/z (relative intensity, %)
II	1495, 1600, 1612, 1744	2,32 t (12), 1H; 2,76 m, 2H; 2,90 q (12; 4), 1H; 3,58 td (12; 4,5), 1H; 4,00 m, 2H; 7,55 t (7), 2H; 7,69 t (7), 1H; 7,89 d (7), 1H	375 (28), 333 (26), 332 (100), 318 (20), 298 (10), 186 (25), 172 (19), 130 (11), 115 (13)
III	1500, 1603, 1614, 1746	2,08 q (12; 4), 1H; 2,35 t (12), 1H; 2,80—3.05 m, 4H; 3,57 td (12; 4.5); 1H; 7,55 t (7), 2H; 7,70 t (7), 1H; 7,88 d (7), 1H	391 (92), 348 (100), 314 (15) 235 (30), 202 (11), 130 (13), 129 (10), 104 (20)
IV	1494, 1600, 1614, 1654, 1700		356 (100), 355 (10), 328 (10), 269 (10), 256 (13), 255 (62), 243 (23), 200 (13), 188 (16), 174 (13), 163 (10)
V	1500, 1600, 1670, 3200, 3320, 3400		360 (8), 344 (24), 248 (34), 160 (100)
VI	1505, 1600, 1665, 1706, 3195†, 3405		346 (3), 249 (21), 248 (100), 247 (28), 160 (53), 149 (14), 91 (39)
VII	1500, 1605, 1660, 3410, 3620		348 (7), 330 (25), 248 (100), 160 (74)
VIII	1500, 1600, 1660, 1720, 3400		376 (15), 348 (11), 330 (19), 248 (80), 160 (100)
IX	1500, 1600, 1660, 1710, 3400		390 (20), 346 (13), 330 (18), 248 (100), 160 (68)
X	1490, 1602, 1685	3,50 d (5)‡, 1H; 4,55 q (12; 3,5), 1H; 7,80 d (6), 1H	315 (100), 300 (10), 287 (15), 286 (25), 238 (20), 211 (30), 141 (9), 114 (8)
XI	1500, 1580, 1602, 1665, 3190, 3400	4,82 br.s 1H; 8,14 d (7), 1H; 8,54 s, 1H	332 (45), 289 (12), 246 (20), 201 (12), 160 (10), 149 (30), 148 (36), 147 (45), 146 (36), 132 (42), 120 (100)

*The M^+ peaks and ion peaks with intensities ≥5% are presented.

†Broad band.

‡The lines of the doublet are broadened.

5-H protons. The PMR spectral data do not make it possible to draw a conclusion regarding the way in which the rings are fused in the perhydroquinoline fragment of II and III; however, an examination of the PMR spectra of previously obtained [3] products (XII, XIII) of the reaction of I with o-aminophenol and o-phenylenediamine makes it possible to assume cis fusion of the perhydroquinoline fragment. It has been previously noted that a significant shift of the signal of one aromatic proton to strong field — to 5.3 ppm [2, 4] — as a consequence of its shielding by the other aromatic ring is observed in the PMR spectra of the products of the reaction of semicyclic 1,5-diketones with o-aminophenol and o-phenylenediamine. This effect is manifested to an even greater degree in the spectra of XII and XIII: their spectra contain doublets (1H, J = 7 Hz) at 4.75 ppm, whereas signals of aromatic protons below 7.0 ppm are absent in the spectra of II and III. An examination of models of XII and XIII shows that such a significant strong-field shift of the signal of an aromatic proton should be observed in the case of an axial orientation of the aromatic substitutent attached to the nitrogen atom of the perhydroquinoline system (and, consequently, in the case of cis fusion of the system); in this case aromatic proton H_A is shielded markedly by the "phthalide" benzene ring. The presence of an acceptor group in the shielding ring intensifies this effect [2].



XII X=O; XIII X=NH

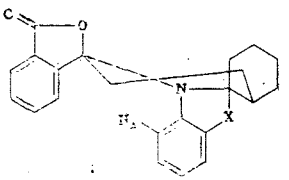


TABLE 2. Characteristics of the Synthesized Compounds

Compound	mp, °C (from ethanol)	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
II	148—149	76,3	6,5	3,7	$C_{24}H_{25}NO_3$	76,8	6,7	3,7	64
III	169—170	73,6	6,4	3,3	$C_{24}H_{25}NO_2$	73,7	6,4	3,6	59
IV	153—155	80,6	7,0	7,8	$C_{24}H_{24}N_2O$	80,9	6,7	7,9	45
V	193—194	73,2	6,7	15,5	$C_{22}H_{24}N_4O$	73,3	6,7	15,6	89
VI	172—173	76,7	6,3	8,0	$C_{22}H_{22}N_2O_2$	76,3	6,4	8,1	98
VII	207—208	75,4	7,1	7,9	$C_{22}H_{24}N_2O_2$	75,8	7,0	8,0	93
VIII	203—204	73,7	6,5	7,1	$C_{23}H_{24}N_2O_3$	73,4	6,4	7,4	71
IX	208—209	74,0	6,9	7,1	$C_{24}H_{26}N_2O_3$	73,9	6,7	7,2	75
X	177—178	83,3	7,1	4,1	$C_{22}H_{21}NO$	83,8	6,7	4,1	35
XI	265—267	79,5	7,5	8,3	$C_{22}H_{24}N_2O$	79,5	7,2	8,4	20

According to the mass-spectral data, the measured molecular masses of II-IV correspond to the calculated values. The mass spectrum of IV contains an $[M - 28]^+$ ion peak; this probably corresponds to detachment of ethylene from the molecular ion as a result of retrodiene decomposition of the cyclohexene fragment. Peaks of $[M - 28]^+$ ions are absent in the spectra of II and III, as well as in the spectra of XII and XIII, but peaks of rearranged $[M - C_3H_7]^+$ ions, which are characteristic for decomposition of the perhydroquinoline structure [5], are observed; this peak is absent in the spectrum of IV. High intensity of the $[M - C_3H_7]^+$ ion peaks is characteristic for cis-decahydroquinoline structures [5]; this also confirms the assumption of cis fusion in XII and XIII and to a certain extent serves as an indication of the same fusion in II and III.

Regardless of the reagent ratio and the reaction conditions, the reaction of I with hydrazine leads to the formation of hydrazonophthalazone V. Absorption bands at 1670 cm^{-1} (phthalazone C=O) and at 3200-3400 cm^{-1} (NH, NH_2) are observed in its IR spectrum; the absorption of the phthalazone C=N bond is overlapped by vibrations of the benzene ring [6], and the band of the hydrazone C=N bond is evidently overlapped by the band of the C=O bond. Compound V is readily converted by acidic hydrolysis to ketophthalazone VI, in the IR spectrum of which an intense band at 1706 cm^{-1} (ketone C=O) additionally appears.

We studied the reduction of ketophthalazone VI to obtain, in particular, a compound with a 7,8-diaza-D-homosteroid skeleton. Reduction with potassium borohydride leads to hydroxyphthalazone VII (the band at 1706 cm^{-1} in the IR spectrum vanishes, and an absorption band of an OH group appears at 3620 cm^{-1}); we also obtained its O-formyl and O-acetyl derivatives (VIII, IX). The presence of intense ion peaks with m/z 248 and 160, which correspond to rearranged ions with 4-styryl- and 4-methyl-1-phthalazone structures, respectively, is characteristic for the mass spectra of V-IX.

We were able to obtain XI, which has a 7,8-diaza-D-homosteroid skeleton, by reduction of ketophthalazone VI with zinc dust and HCl at room temperature. The reaction proceeds very slowly, and XI is formed in low yield. When the reaction temperature is raised, the yield of XI does not increase, and hydrogenated isoindoloquinoline derivative X is formed along with it; this is the result of ring contraction, which occurs rather frequently when phthalazones are heated [7].

Absorption bands at 1685 cm^{-1} (phthalimidine C=O) and at 1656 cm^{-1} (C=C) are observed in the IR spectrum of X; absorption of N—H bonds is absent. The spectrum of XI contains bands at 1665 (phthalazone C=O) and 3200-3400 cm^{-1} (N—H); a band of a C=C bond is not observed According to the mass-spectral data, the measured molecular masses of X and XI correspond to the calculated values. The spectrum of X contains a peak of an $[M - C_2H_4]^+$ fragment ion, which confirms the presence of a cyclohexene fragment, whereas this peak is absent in the spectrum of XI. A weak-field signal (1H) of a proton adjacent to a nitrogen atom and a benzene ring appears in the PMR spectra of X and XI. In the spectrum of X it is observed in the form of a quartet at 4.55 ppm, whereas it is observed in the form of a broad singlet at 4.82 ppm in the spectrum of XI. The singlet form of the signal may serve as an indication of cis-B/C fusion in the heterosteroid system of XI.

EXPERIMENTAL

The IR spectra of the synthesized compounds in mineral oil and chloroform were recorded with a Specord IR-75 spectrometer. The PMR spectra of solutions in deuterochloroform were

obtained with a Bruker HX-90E spectrometer with tetramethylsilane (TMS) as the internal standard. The mass spectra were obtained with an LKB-9000 spectrometer at an ionizing voltage of 70 V. The course of the reactions and the purity of the compounds obtained were monitored by thin-layer chromatography (TLC) on Silufol plates in hexane—ether systems (2:1 and 3:1). The characteristics of the synthesized compounds are presented in Table 2.

Reaction of 4-Phenyl-8a-hydroxyperhydrochroman-2-spiro-3'-phthalide with Aliphatic Amines. A solution of 3.5 g (0.01 mole) of I and 0.012 moles of the amine (ethanolamine, β-mercaptoethylamine, ethylenediamine) in 30 ml of ethanol was maintained at room temperature for 18-30 h, after which it was diluted with water, and the aqueous mixture was extracted with ether. After removal of the ether from the extract, the residue crystallized (II-IV).

1-(2'-Oxocyclohexyl)-1-phenyl-2-(4"-phthalazonyl)ethane Hydrazone (V). A solution of 17.5 g (0.05 mole) of I and 10 g (0.2 mole) of hydrazine hydrate in 150 ml of ethanol was maintained at room temperature for 18 h, after which it was worked up as in the preceding case.

1-(2'-Oxocyclohexyl)-1-phenyl-2-(4"-phthalazonyl)ethane (VI). A mixture of 4 g of V and 40 ml of concentrated HCl was heated on a water bath for 4 h, after which the product was removed by filtration and washed successively with water, sodium carbonate solution, and water.

1-(2'-Hydroxycyclohexyl)-1-phenyl-2-(4"-phthalazonyl)ethane (VII). A 3.5-g (0.01 mole) sample of ketophthalazone VI was added to a solution of 3 g (0.055 mole) of KBH_4 in a mixture of 50 ml of dimethylformamide (DMFA) and 10 ml of water, and the mixture was refluxed for 5 h. It was then cooled and diluted with water, and VII was removed by filtration and washed with water. Compounds VIII and IX, respectively, were obtained by refluxing VII with 85% HCOOH or glacial CH_3COOH for 6 h with subsequent dilution with water.

Reduction of Ketophthalazone VI with Zinc and HCl. A mixture of 3.5 g of VI, 1 g of ainc dust, and 5 ml of concentrated HCl in 30 ml of tetrahydrofuran (THF) was stirred at room temperature for 50 h or refluxed for 5 h; more zinc dust and HCl were added as they were consumed. The mixture was then filtered and diluted with water, and the aqueous mixture was made alkaline with 25% ammonium hydroxide and extracted with ether. After removal of the ether by distillation, the crystalline residue was chromatographed with a column packed with silica gel; products X and XI, as well as the unchanged ketophthalazone VI, were eluted with petroleum ether—diethyl ether.

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