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TRANSFORMATIONS OF MONO- AND BISPHENYLHYDRAZONES OF ALIPHATIC-AROMATIC 1,5-DIKETONES UNDER THE CONDITIONS OF THE FISCHER REACTION

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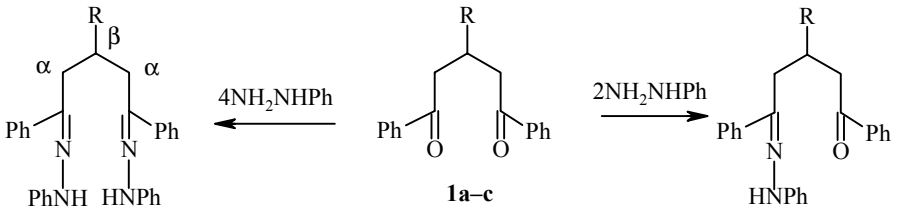
The mono- and bisphenylhydrazones of 3-R-1,5-diphenylpentane-1,5-diones were obtained, and their transformations in the Fischer indole synthesis under various conditions were studied. It was shown that 4-R-2,6-diphenylpyridines, 2-phenylindole, and 5-R-1,3-diphenyl-Δ^2-pyrazolines are formed as the main products in addition to the 3-R-1-phenyl-3-(2-phenyl-3-indolyl)propan-1-ones or their phenylhydrazones produced as a result of indolization. The ways of formation of these compounds are discussed. Some transformations of the obtained ketones were studied.

Keywords: bisphenylhydrazones, 1,5-diketones, 5-R-1,3-diphenyl-Δ^2-pyrazolines, 4-R-2,6-diphenylpyridines, phenylhydrazones, 3-R-1-phenyl-3-(2-phenyl-3-indolyl)propan-1-ones, Fischer reaction.

Earlier we showed that substituted indoloacridines are obtained from alicyclic 1,5-diketones [di(2-oxocyclohexyl)-R-methanes] in reaction with an equimolar amount of phenylhydrazine in an acidic medium [1]. Under analogous conditions substituted pyridocarbazoles are obtained from the semicyclic 1,5-diketones [phenacyl(2-oxocyclohexyl)-R-methanes] [2]. The products result from transformations of the initially formed monophenylhydrazones, i.e., Fischer indolization followed by cyclodehydration.

In a continuation of a study of the reactions of 1,5-dicarbonyl compounds with hydrazines [1,2] and diamines [3] we investigated the reaction of the familiar 3-R-1,5-diphenyl-1,5-pentanediones **1a-c** [4, 5] with phenylhydrazine (Scheme 1) and the subsequent transformations of the obtained mono- and bisphenylhydrazones (Scheme 2).

Scheme 1



3a,**c** **1a–c** **2a–c**

a R = H, **b** R = Me, **c** R = Ph

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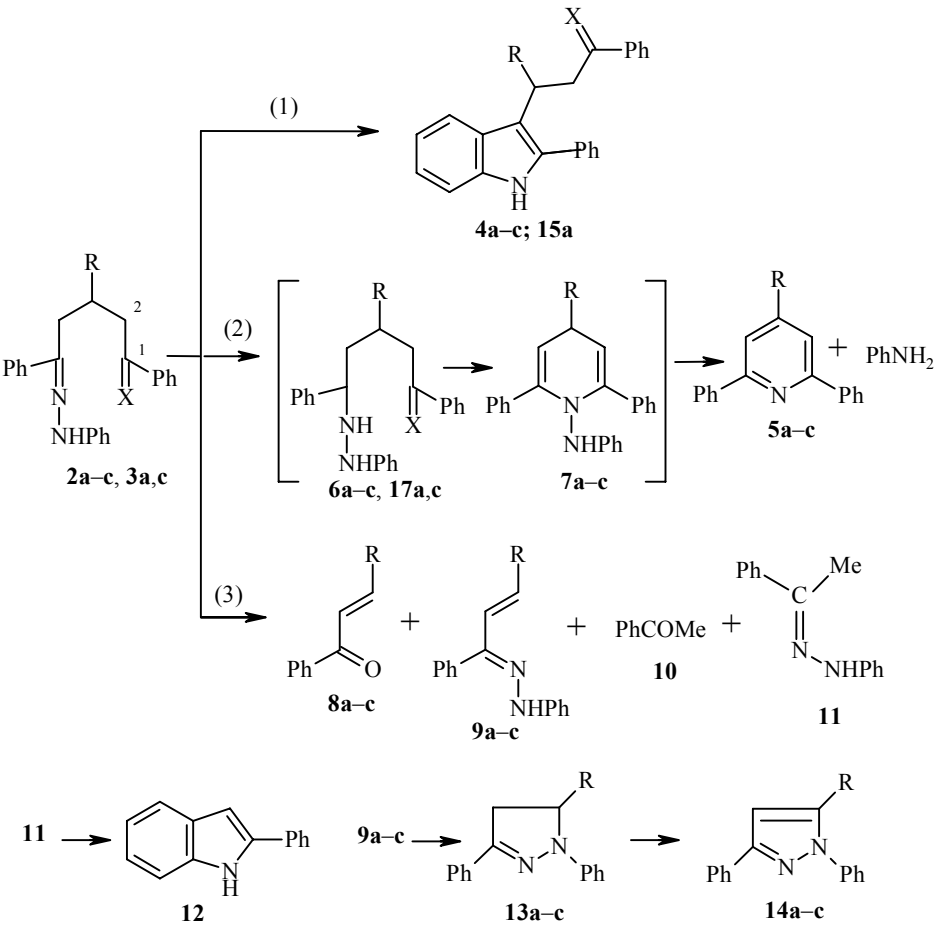
It was possible to obtain the monophenylhydrazones **2a-c** with good yields in the reaction of the diketones **1a-c** with twice the amount of phenylhydrazine in a mixture of acetic acid and ethanol (5:2) at room temperature. Their composition and structure were confirmed by the results of elemental analysis, by data from the IR spectra and mass spectra, and also by the ^{1}H NMR spectra. Thus, in the IR spectra of compounds **2a-c** there are absorption bands at 1680 ($\nu_{C=O}$) and 3300 cm^{-1} (ν_{N-H}), while in the mass spectra there are peaks for the molecular ions with *m/z* 342, 356, and 418 respectively. The strongest peaks in the mass spectra correspond to ions formed during the McLafferty rearrangement (*m/z* 222, 336, and 298 respectively) and to the $C_6H_5CO^+$ ions (*m/z* 105).

Scheme 2



2–**8**, **9**, **13**–**15**, **17** **a** R = H, **b** R = Me, **c** R = Ph; **2**, **6**, **4** X = O; **3**, **15**, **17** X = NNHPh

The reaction of the diketones **1a**,**c** with a fourfold excess of phenylhydrazine under conditions similar to those used for the synthesis of the monohydrazones gave the bisphenylhydrazones **3a**,**c**, which are labile compounds that are soon oxidized in air, particularly in chloroform solutions. Their IR spectra do not contain the absorption of carbonyl groups, while the bands of the stretching vibrations of the N–H groups are observed at 3360 cm^{-1}. In the mass spectra there are peaks for the molecular ions with *m/z* 432 (for **3a**) and *m/z* 508 (for **3c**). The characteristics of the synthesized compounds are presented in greater detail in Table 1.

The transformations of the monohydrazones **2a-c** under various conditions of Fischer indolization (see the Experimental, methods A-D) took place ambiguously. The formation of 4-R-substituted 2,6-diphenylpyridines **5a-c** through the intermediate compounds **6a-c** and **7a-c** (path 2), retro-Michael cleavage

leading to 3-R-1-phenyl-2-propen-1-ones **8a-c**, their phenylhydrazones **9a-c**, acetophenone **10**, and its phenylhydrazone **11** (path 3), and also the associated formation of 2-phenylindole **12** and 5-R-1,3-diphenyl-Δ^2-pyrazolines **13a-c** were probably observed in addition to the desired transformation to 3-R-1-phenyl-3-(2-phenyl-3-indolyl)propan-1-ones (β-indolylpropiophenones) **4a-c** (path 1). The indole **12** (the product from Fischer cyclization of the phenylhydrazone **11**) and the pyrazolines **13a-c** are formed as a result of intramolecular addition of the NH group of the hydrazones **9a-c** at the double bond.

The above-mentioned transformation products **4b**, **c**, **5a-c**, **12**, **13a-c** were isolated, and this included isolation by column chromatography on silica gel. Their structures were confirmed by the spectra and, for the previously known substances, by comparison of their physical constants with published data (Tables 2 and 3).

In addition, the unsaturated ketones **8a-c**, acetophenone **10**, and the products from aromatization of the pyrazolines **13a-c** (the 5-R-1,3-diphenylpyrazoles **14a-c**), identified by comparison of their mass spectra with the mass spectra of the authentic compounds, were detected in the reaction mixtures by chromato-massspectrometric analysis. The mass spectra of compounds **8a-c** contain peaks of molecular ions with *m/z* 132, 146, and 208, and the mass spectra of compounds **14a-c** contain peaks with *m/z* 220, 234, and 296 respectively.

The desired transformation (1) and the side transformations (2, 3) took place to different degrees, depending on the employed conditions and on the structure of the initial hydrazone. The highest yields of the required β-indolylpropiophenones **4b**,**c** (30-36%) were obtained when the reaction was carried out in absolute methanol saturated with hydrogen chloride (method A). The ketone **4a** could not be isolated in the individual state, but chromato-mass-spectrometric analysis demonstrated its presence in the respective reaction mixtures at the rate of 15-20%. The retro-Michael dissociation of the hydrazone **2c** was more intense than for the hydrazones **2a**,**b**. The yield from conversion to pyridines was greatest for the hydrazone **2a** (Table 3).

The obtained ketones **4b**,**c** were previously unknown, and the method proposed here for their synthesis from aliphatic-aromatic 1,5-diketones is new. At the same time other methods for the production of analogous substances, e.g., by the addition of indole derivatives to α,β-unsaturated carbonyl compounds [6, 7] and by the reaction of compounds of the gramine type with derivatives of acetoacetic ester followed by decarboxylation [8, 9], have been described in the literature.

Some derivatives of the products **4b**,**c** were obtained in order to confirm their structure: The phenylhydrazones **15b**,**c** by reaction with phenylhydrazine; the stereoisomeric 3-R-3-(2-phenyl-3-indolyl)-1-phenyl-1-propanols (the α- and β-isomeric forms **16b** and **16c** respectively) by treatment of the ketones with sodium borohydride (see Scheme 3). The isomers **16b** and **16c** were separated by high-pressure HPLC on a column of Silasorb. The IR spectra of the phenylhydrazones **15b**,**c** do not contain absorption bands for the carbonyl group, but there are bands at 3450 and 3330 cm^{-1}, corresponding to the absorption of the NH group in the indole and hydrazone fragments. In the IR spectra of the stereoisomeric alcohols **16b**,**c** instead of the absorption band of the carbonyl group there is an absorption band for the OH group at 3597 cm^{-1}. Their structure is also confirmed by the ^1H NMR spectra (Table 2).

Scheme 3

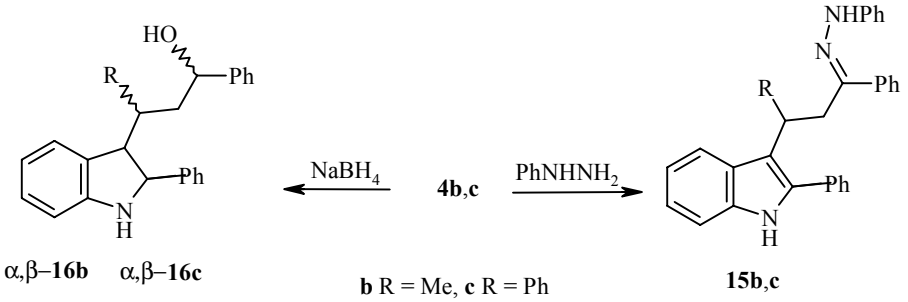


TABLE 1. The Characteristics of Mono- and Bisphenylhydrazones **2a-c** and **3a**,**c**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	R_f*	IR spectrum, ν, cm^{-1}	Mass spectrum, M^+, *m/z*	^{1}H NMR spectrum ($CDCl_3$), δ, ppm,*[2] SSCC (*J*), Hz	Yield, %
		C	H	N						
2a	$C_{23}H_{22}N_2O$	80.70 / 80.70	6.25 / 6.43	8.35 / 8.19	108-109 (decomp.)	0.39	3298 (NH), 1675 (CO), 1602 (C=N)	342	2.05 (2H, m, β-CH_2); 2.70 (2H, m, γ-CH_2); 3.20 (2H, m, α-CH_2.); 6.70 (1H, t, *J* = 7.5, *p*-H_{PhNH}); 7.00-8.00 (14H, m, H_{Ph}); 9.45 (1H, s, NH)	82
2b	$C_{24}H_{24}N_2O$	80.75 / 80.90	6.92 / 6.74	8.00 / 7.86	132-133	0.45	3293 (NH), 1676 (CO), 1602 (C=N)	356	1.00 (3H, d, *J* = 7.0, CH_3); 2.85 (2H, m, γ-CH_2); 3.25 (3H, m, α-CH_2 and β-CH); 6.80 (1H, t, *J* = 7.5, *p*-H_{PhNH}); 7.20-8.00 (14H, m, H_{Ph}); 9.50 (1H, s, NH)	85
2c	$C_{29}H_{26}N_2O$	83.50 / 83.25	6.37 / 6.22	6.90 / 6.70	151-153	0.43	3294 (NH), 1676 (CO), 1602 (C=N)	418	3.65 (1H, m, β-CH); 3.20 (2H m, 2α-CH_2); 2.50 (2H, m, γ-CH_2); 6.80 (1H, t, *J* = 7.5, *p*-H_{PhNH}); 7.00-8.00 (19H, m, H_{Ph}); 9.40 (1H, s, NH)	88
3a	$C_{29}H_{28}N_4$	80.75 / 80.55	6.30 / 6.48	13.10 / 12.96	114-116 (decomp.)	0.30	3359 (NH), 1602 (C=N)	432	2.00 (2H, m, β-CH_2), 2.60-3.30 (4H, m, 2α-CH_2); 6.70-8.10 (20H, m, H_{Ph}); 9.40 (1H, s, NH)	70
3c	$C_{35}H_{32}N_4$	82.48 / 82.68	6.20 / 6.30	10.85 / 11.02	118-120 (decomp.)	0.27	3343 (NH), 1602 (C=N)	508	3.05 (2H, dd, J_1 = 8.0, J_2 = 14.0, H_A ABX-system); 3.28 (2H, dd, J_1 = 6.0, J_2 = 14.0, H_B); 3.40 (1H, m, H_X); 6.60-7.00 (25H, H_{Ph}); 9.65 (2H, s, NH)	75

* On plates with Sorbfil, petroleum ether–ethyl acetate, 5:1.

*[2] The signals were assigned on the basis of comparison with the ^{1}H NMR spectra of the initial diketones.

TABLE 2. The Characteristics of β-(3-Indolyl) Ketones **4b**,**c** and Their Derivatives: Phenylhydrazones **15a-c** and Alcohols **16b**,**c**

Com-pound	Empirical formula	Found, % / Calculated, %			mp, °C	R_f*	Mass spectrum, *m/z*	IR spectrum ($CHCl_3$), ν, cm^{-1}	^1H NMR spectrum ($CDCl_3$), δ, ppm, SSCS, (*J*), Hz	Yield, % (method)
		C	H	N						
1	2	3	4	5	6	7	8	9	10	11
4b	$C_{24}H_{21}NO$	85.10 / 84.95	6.30 / 6.19	4.30 / 4.13	146-147	0.35	339	3455(NH); 1685(C=O)	1.55 (3H, d, *J* = 7.0, CH_3,); 3.45 (1H, dd, J_1 = 7.0, J_2 = 16.0, H_A ABX-system); 3.65 (1H, dd, J_1 = 7.0, J_2 = 16.0, H_B); 4.00 (1H, m, H_X); 7.10-7.90 (14H, m, H arom); 7.95 (1H, s, NH)	30 (A); 20 (B); 18 (C); 10 (D)
4c	$C_{29}H_{23}NO$	86.90 / 86.78	5.60 / 5.73	3.60 / 3.49	112-114	0.44	401	3454 (NH); 1687 (C=O)	3.85 (1H, dd, J_1 = 7.0, J_2 = 18.0, H_A ABX-system), 3.95 (1H, dd, J_1 = 7.0, J_2 = 18.0, H_B); 5.30 (1H, t, *J* = 7.0, H_X); 7.10-7.80 (19H, m, H arom); 8.0 (1H, s, NH)	36 (A); 24 (B); 20 (C); 8 (D)
15a	$C_{29}H_{25}N_3$	84.05 / 83.85	6.11 / 6.02	10.30 / 10.12	166-167	0.40	415	3480 (NH indole); 3350 (NH hydrazole)	3.07 (2H, m, CH_2); 3.21 (2H, m, CH_2); 6.55-7.80 (19H, m, H arom); 7.90 (2H, br. s, NH)	70 (F)
15b	$C_{30}H_{27}N_3$	83.80 / 83.91	6.40 / 6.29	9.95 / 9.79	176-178	0.42	429	3451 (NH indole); 3333 (NH hydrazole)	1.67 (3H, d, *J* = 7.0, CH_3); 3. 07 (1H, dd, J_1 = 9.5, J_2 = 19.0, H_A ABX-system); 3.55 (1H, m, H_B); 3.55 (1H, m, H_X); 6.16-8.10 (19H, m, H arom); 7.90 (2H, br. s, NH)	93
15c	$C_{35}H_{29}N_3$	85.30 / 85.54	6.10 / 5.90	8.70 / 8.55	210-211	0.55	491	3453 (NH indole); 3330 (NH hydrazole)	3.64 (1H, dd, J_1 = 3.5, J_2 = 14.0, H_A ABX-system); 3.82 (1H, dd, J_1 = 12.5, J_2 = 14.0, H_B); 4.72 (1H, dd, J_1 = 3.5, J_2 = 12.0, H_X); 6.85-7.65 (24H, m, H arom); 7.96 (2H, br. s, NH)	90

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11
α-16b	$C_{24}H_{23}NO$				54-56	0.17	341	3450 (NH indole); 3596 (OH)	1.48 (3H, d, J = 7.1, CH_3); 2.09 and 2.39 (1H, m and 1H, m, CH_2); 3.50 (1H, m, C<u>H</u>CH_3); 4.43 (1H, m, CHOH); 7.10-7.52 (14H, m, H arom); 7.94 (1H, br. s, NH)	50
β-16b	$C_{24}H_{23}NO$				144-146	0.19	341	3450 NH indole); 3596 (OH)	1.47 (3H, d, J = 7.1, CH_3); 2.12 and 2.56 (1H, ddd, J_1 = 6.0, J_2 = 7.0, J_3 = 14.4 and 1H, ddd, J_1 = 6.8, J_2 = 9.1, J_3 = 14.4, CH_2); 3.17 (1H, m, C<u>H</u>CH_3); 4.47 (1H, t, J = 6.9, C<u>H</u>OH); 7.00-7.72 (14H, m, H arom); 8.05 (1H, br. s, NH)	17
α-16c	$C_{29}H_{25}NO$	<u>86.20</u> 86.35	<u>6.40</u> 6.20	<u>3.60</u> 3.47	70-72	0.28	403	3454 (NH indole); 3597 (OH)	2.65 and 2.91 (1H, ddd, J_1 = 6.0, J_2 = 7.4, J_3 = 13.5 and 1H, ddd, J_1 = 13.5, J_2 = 6.4, J_3 = 9.4, CH_2); 4.30 (1H, dd, J_1 = 6.0, J_2 = 9.4, C<u>H</u>OH); 4.49 (1H, t, J = 7.0, C<u>H</u>Ph); 6.60-7.75 (19H, m, H arom); 8.10 (1H, br. s, NH)	45
β-16c	$C_{29}H_{25}NO$	<u>86.12</u> 86.35	<u>6.06</u> 6.20	<u>3.30</u> 3.47	197-198	0.32	403	3450 (NH indole); 3597 (OH)	2.56 and 2.71 (1H, ddd, J_1 = 5.4, J_2 = 9.7, J_3 = 14.2 and 1H, ddd, J_1 = 3.5, J_2 = 10.8, J_3 = 14.2, C<u>H</u>$_2$); 4.46 (1H, dd, J_1 = 3.5, J_2 = 9.7, C<u>H</u>OH); 4.79 (1H, dd, J_1 = 5.4, J_2 = 10.8, C<u>H</u>Ph); 7.05-7.67 (19H, m, H arom); 8.10 (1H , br. s, NH)	15

* On plates with Sorbfil, petroleum ether–ethyl acetate, 3:1.

TABLE 3. The Characteristics of Side Processes Accompanying the Indolization of Phenylhydrazones **2a-c** and **3a**,**c**

Com-pound	mp, °C	mp, °C [publ.]	IR spectrum, ν,cm^{-1}	Mass spectrum, M^+, *m/z*	^{1}H NMR spectrum ($CDCl_3$), δ, ppm, CCSS, (*J*), Hz	Yield, % (method)
5a	79-80	80-81 [10]	1598; 1489	231	—	12 (A); 15 (B); 11 (C); 8 (D)
5b	80-82	81-82 [11]	1596; 1502	245	—	10 (A); 13 (B); 5 (C); 6 (D)
5c	134-136	136-137 [12, 13]	1596; 1500	307	—	12 (A); 9 (B); 10 (C); 5 (D)
12	188-189	188-189 [14]	3463; 1606	193	6.82 (1H, s, H-3); 6.98-7.80 (9H, m, H arom); 8.35 (1H, br. s, NH)	5-7* (from **2a**); 10-12* (from **2b**); 15-20* (from **2c**)
13a	154-156	158 [15, 16]	—	222	—	5-7*
13b	103-105	104-106 [17]	1596; 1504; 1494	236	1.35 (3H, d, J = 6.6; CH_3); 2.90 (1H, dd, J_1 = 18.0, J_2 = 5.0, H_A ABX-system); 3.55 (1H, dd, J_1 = 18.0, J_2 = 11.5, H_B); 4.50 (1H, m, H_X); 6.85 (1H, t, J_1 = 7.0, *p*-H_{PhN}); 7.20-7.80 (9H, m, H_{Ph})	5-7*
13c	134-136	134-135 [18]	1598; 1504; 1496	298	3.15 (1H, dd, J_1 = 18.0, J_2 = 7.0, H_A ABX-system); 3.85 (1H, dd, J_1 = 18.0. J_2 = 13.0, H_B); 5.30 (1H, dd, J_1 = 13.0, J_2 = 7.0, H_X); 6.80 (1H, t, J = 7.0, *p*-H_{PhN}); 7.00-7.80 (14H, m, H_{Ph})	10-14*

* In all the investigated cases.

We also investigated the transformations of the bishydrazones **3a**,**c** under the conditions of the Fischer indole synthesis (methods A-D) and with heating in ethylene glycol (method E). According to theoretical ideas the formation of the respective derivatives of 3,3'-bisindolylmethane (analogs of certain marine antibiotics) was expected from these compounds. However, analysis of the obtained reaction mixtures by chromato-mass spectrometry showed that they are hardly formed at all under the indicated conditions. The pyridines **5a**,**c** (probably through the intermediates **17a**,**c** and **7a**,**c**), 2-phenylindole **12**, and Δ^2-pyrazolines **13a**,**c** were obtained by methods A-D, and the phenylhydrazone **15a** and the ketone derivative **4a** were obtained by heating the bishydrazone in ethylene glycol (Scheme 2). All these compounds were isolated from the reaction mixture and identified by direct comparison with authentic samples (TLC, mixed melting tests, comparison of the spectra). According to the obtained data, the bisphenylhydrazones **3a**,**c** are transformed in an acidic medium like the corresponding monophenylhydrazones **2a**,**c** (scheme 2). They undergo retro-Michael dissociation and conversion to pyridines extremely readily (paths 2 and 3 in the scheme). Indolization usually stops at the formation of one indole ring and takes place more effectively not in an acidic medium (A-D) but under the conditions of the thermal indole synthesis (E). Partial transformation of the diphenylhydrazones into the initial 1,5-diketones was observed on heating in acetic acid.

The obtained data show that the phenylhydrazones of the various types of 1,5-diketones differ appreciably from each other in their behavior under the conditions of the Fischer reaction. Thus, for the above-mentioned derivatives of aliphatic-aromatic 1,5-diketones, in contrast to their alicyclic and semicyclic analogs, cyclodehydration of the indolization products formed from them was not observed, but a significant tendency toward retro-Michael dissociation in an acidic medium was detected. At the same time partial pyridinization was characteristic of hydrazones of all types.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker WM-250 instrument (250 MHz) in deuterochloroform with the subsequent addition of deuteromethanol and with TMS as internal standard. The IR spectra were recorded on a Spectrum BX-II FT-IR System spectrophotometer (Perkin-Elmer) in chloroform, vaseline oil, and tablets with potassium bromide. The mass spectra were obtained on an LKB 9000s instrument with direct injection into the ion source at 70 eV. In individual cases the reaction mixtures were analyzed by chromato-mass spectrometry on an HP 5972 MSD/HP 5890 series II GC instrument (Hewlett-Packard); CPB-5 column, 140→280°C, 5 deg/min, carrier gas helium, ionizing potential 70 eV.

The melting points were determined on a Boetius bench. Silica gel L (Chemapol, former Czechoslovakia) was used for low-pressure column chromatography. The reactions and the separation of the reaction mixtures were monitored by TLC with detection of the spots with iodine vapor. To separate the stereoisomeric alcohols we used high-pressure HPLC on an Ultrasphere-Si column (25 cm × 10 mm) in 7:1 petroleum ether–ethyl acetate; Du Pont 8800 chromatograph, RIDK-2 refractometric detector.

Monophenylhydrazones of 1,5-Diketones 1a-c (2a-c). To a solution of phenylhydrazine (20 mmol) in a 5:4 mixture of acetic acid and ethanol (2.2 ml) we added a solution of the diketone **1a-c** (10 mmol) in acetic acid (10 ml). The reaction mixture was kept at room temperature for 2-4 h. The precipitated product **2a-c** was filtered off, washed on the filtered with alcohol, and dried under vacuum.

Bisphenylhydrazones of 1,5-Diketones 1a,c (3a,c). To a solution of phenylhydrazine (40 mmol) in a 5:4 mixture of acetic acid and ethanol (4.4 ml) while stirring we added a solution of the diketone **1a**,**c** (10 mmol) in acetic acid (5 ml). The reaction mixture was kept at room temperature for 3-5 h until a precipitate of the product **3a**,**c** had formed. The precipitate was filtered off, washed with alcohol, and recrystallized from alcohol.

Heterocyclization of Monophenylhydrazones 2a-c. A. The compound **2a-c** (10 mmol) was boiled in absolute methanol (30 ml) saturated with hydrogen chloride for 1.5-2 h. The solution was yellow and then became dark-green. The precipitated ammonium chloride was filtered off. The methanol was distilled from the filtrate, and water (20 ml) and ethyl acetate (20 ml) were added to the oily residue. The ethyl acetate extract was washed with water and saturated sodium bicarbonate solution, dried over magnesium sulfate, and evaporated. A mixture of reaction products was obtained (TLC) in the form of a thick oil, which was stirred with ether (20 ml). After 2-3 h the precipitated chromatographically individual ketone **4b** (0.7 g, 20%) or **4c** (1.0 g, 25%) was filtered off. The filtrate was evaporated, and the residue was separated by column chromatography with silica gel. The substances were eluted with petroleum ether and a mixture of petroleum ether and ethyl acetate (100:1 → 100:7). Here the Δ^2-pyrazoline **13a-c** (fraction with violet fluorescence), pyridine **5a-c**, 2-phenylindole **12**, and further amounts of the ketone **4b**,**c** were isolated in succession. The total yield amounted to 30% of **4b** and 36% of **4c**. Compounds **4b**,**c** were washed with ether and recrystallized from alcohol.

B. A mixture of the compound **2a-c** (10 mmol) and polyphosphoric acid (2 g) was heated to 180°C for 1 h. It was then kept at this temperature for 15 min and cooled to room temperature. To the reaction mass we added a 5% solution of sodium hydroxide to pH 8. The product was extracted with ethyl acetate (3 × 10 ml), and the extract was dried over magnesium sulfate and evaporated. The reaction products were isolated from the residue as described in method A.

C. The compound **2a-c** (10 mmol) was heated in acetic acid (10 ml) to boiling point for 30 min and kept at this temperature for 2.5 h. The reaction mixture was cooled to room temperature, neutralized with a saturated solution of sodium carbonate, and extracted with ethyl acetate (3 × 10 ml). The extract was dried over magnesium sulfate and evaporated. The reaction products were isolated from the residue as described in method A.

D. A mixture of the compound **2a-c** (10 mmol) and boron trifluoride etherate (2 ml) in benzene (10 ml) was boiled for 3 h. The benzene was then distilled from the reaction mixture, a saturated solution of sodium bicarbonate (25 ml) was added to the residue, and the product was extracted with ethyl acetate (3 × 10 ml). The extract was dried over magnesium sulfate and evaporated. The reaction products were extracted from the residue (method A).

Heterocyclization of Bisphenylhydrazones 3a,c. A-D. The products **5a**,**c**, **12**, **13a**,**c** were obtained as a result of treatment of compounds **3a**,**c** by methods A-D described above and were identified by comparison with authentic samples.

E. The bisphenylhydrazone **3a** (1 mmol) was kept in freshly distilled ethylene glycol (10 ml) at 190°C for 6 h. After the reaction mixture had cooled the precipitate was filtered off and washed with ethanol, and 0.29 g (70%) of β-(2-phenyl-3-indolyl)propiophenone phenylhydrazone (**15a**) was obtained.

Phenylhydrazones of β-Indolylpropiophenones 4b,c (15b,c). A mixture of **4b**,**c** (1 mmol) with phenylhydrazine (2 mmol) was boiled in ethanol (10 ml) for 4-6 h. After the reaction mass had cooled the precipitate of the respective phenylhydrazone **15b**,**c** was filtered off and recrystallized from alcohol.

The α and β Stereoisomers of 3-Methyl-1-phenyl-3-(2-phenyl-3-indolyl)-1-propanol (16b) and 1,3-Diphenyl-3-(2-phenyl-3-indolyl)-1-propanol (16c). A mixture of the ketone **4b**,**c** (1 mmol) and sodium borohydride (0.2 g) in THF (15 ml) and water (2 ml) was stirred at room temperature for 2 h. The organic layer was separated, washed to a neutral reaction with water, and dried over magnesium sulfate. The solvent was distilled, and 0.30 and 0.35 g respectively of a caramel-like mass was obtained. Analysis of the reaction products by chromato-mass spectrometry showed the presence of two substances with identical molecular mass equal to 341 (in the case of **16b**) and 403 (in the case of **16c**). The individual α- and β-diastereoisomers **16b** or **16c** (in a ratio of ~1:3) were isolated by HPLC on a column of Silasorb and were recrystallized from hexane.

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REFERENCES

1. T. V. Moskovkina and M. N. Tilichenko, *Khim. Geterotsikl. Soedin.*, 46 (1986).
2. T. V. Moskovkina and M. N. Tilichenko, *Khim. Geterotsikl. Soedin.*, 645 (1976).
3. T. V. Moskovkina and V. A. Kaminskii, *Khim. Geterotsikl. Soedin.*, 1002 (1999).
4. M. N. Tilichenko, *Zh. Obshch. Khim.*, **25**, 2503 (1955).
5. S. Kostanetski and V. Rossbach, *Berichte*, **29**, 1448 (1896).
6. N. I. Aboskalova, V. M. Berestovitskaya, G. A. Berkova, and A. V. Fel'gendler, *Zh. Org. Khim.*, **35**, 156 (1999).
7. K. I. Kuchkova, A. A. Semenov, and I. V. Terent'eva, *Khim. Geterotsikl. Soedin.*, 197 (1965).
8. E. Hardegger and H. Corrodi, *Helv. Chim. Acta*, **39**, 514 (1956).
9. D. O. Holland and J. H. K. Nayler, *J. Chem. Soc.*, 280 (1953).
10. D. Bruce-Smith and A. C. Skinner, *J. Chem. Soc.*, 577 (1963).
11. T. Kobayashi, Y. Iiino, and M. Nitta, *Chem. Lett.*, 1549 (1986).
12. F. Chabb, A. S. Hay, and R. B. Sandin, *J. Am. Chem. Soc.*, **75**, 6042 (1953).
13. *Methods for the Production of Chemical Reagents and Products* [in Russian], No. 17, IREA (1967), p. 152.
14. K. Weygand and G. Hilgetag, *Experimental Methods in Organic Chemistry* [Russian translation], Khimiya, Moscow (1968), p. 866.
15. K. Von Auwers, *Berichte*, **65**, 832 (1932); *Beilstein*, **23**, 153.
16. C. F. H. Allen, *Can. J. Chem.*, **53**, 865 (1975).
17. K. Von Auwers and A. Lammerhirt, *Berichte*, **54**, 1011 (1921); *Beilstein*, **23**, 168.
18. K. Von Auwers and F. Voss, *Berichte*, **42**, 4422 (1909); *Beilstein*, **23**, 245.