STRUCTURE AND PROPERTIES OF 2,4a-DIMETHYL-4-PHENYL-3-ETHOXYCARBONYL-5-OXO-4a,5-DIHYDRO-4H-INDENO[1,2-b]PYRIDINE

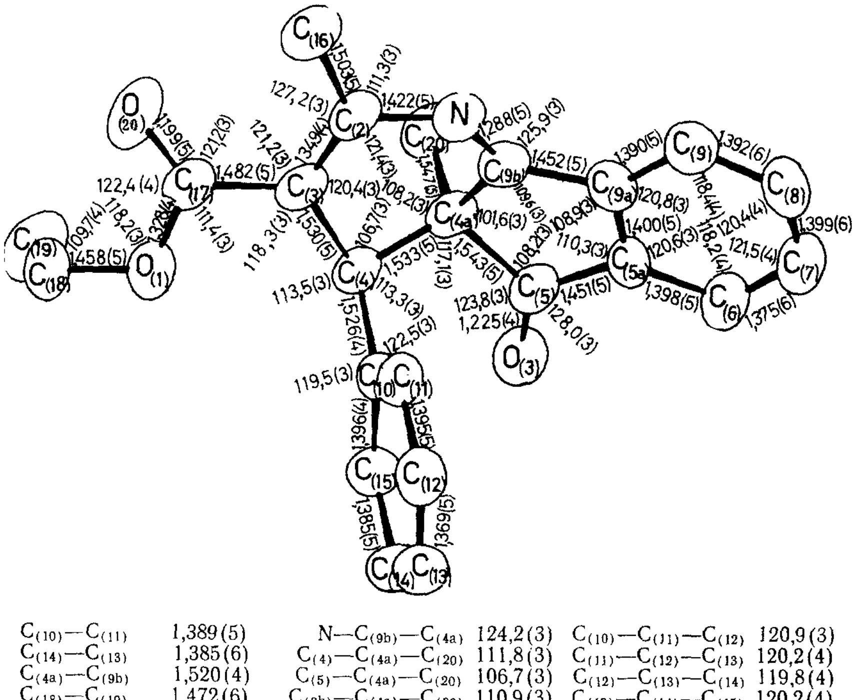
M. F. Bundule, A. F. Mishnev, Ya. Ya. Bleidelis,
V. K. Lusis, D. Kh. Mutsenietse, and G. Ya. Dubur

UDC 548.312.5:547.83'665

The molecular and crystal structure of 2,3a-dimethyl-4-phenyl-3-ethoxycarbony-5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridine has been determined, and its reduction and alkaline and acid hydrolysis reactions have been studied.

The alkylation of derivatives of 4,5-dihydro-1H-indeno[1,2-b]pyridine gives not only N-alkylation products, but also C-alkylated products [1], whose structure was established by comparing data from spectroscopic investigations of the individual compounds. For example, the nature of the PMR spectrum of 2,4a-dimethyl-4-phenyl-5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridine (III) permits the elimination of the alternative C-alkylation products; however, this is impossible for derivatives having substituents at the $C_{(3)}$ atom. The purpose of the present work was to confirm the C-methylation at $C_{(4a)}$ in a number of 3-substituted 5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridines by determining the molecular and crystal structure of 2,4a-dimethyl-4-phenyl-3-ethoxycarbonyl-5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridine (I) and by studying its chemical properties.

Figure 1 presents a spatial model of the molecule of compound I with designations of the atoms and indication of the interatomic distances (Å) and angles (deg.). Table 1 presents the coefficients of the mean planes of the fragments of the molecules, the deviations of the atoms from them, and the dihedral angles between the mean planes of the individual fragments of the molecule.



$C_{(10)}—C_{(11)}$	1,389(5)	$N—C_{(9b)}—C_{(4a)}$	124,2(3)	$C_{(10)}—C_{(11)}—C_{(12)}$	120,9(3)
$C_{(14)}—C_{(13)}$	1,385(6)	$C_{(4)}—C_{(4a)}—C_{(20)}$	111,8(3)	$C_{(11)}—C_{(12)}—C_{(13)}$	120,2(4)
$C_{(4a)}—C_{(9b)}$	1,520(4)	$C_{(5)}—C_{(4a)}—C_{(20)}$	106,7(3)	$C_{(12)}—C_{(13)}—C_{(14)}$	119,8(4)
$C_{(18)}—C_{(19)}$	1,472(6)	$C_{(9b)}—C_{(4a)}—C_{(20)}$	110,9(3)	$C_{(13)}—C_{(14)}—C_{(15)}$	120,2(4)
$C_{(2)}—N—C_{(9b)}$	116,7(3)	$C_{(15)}—C_{(10)}—C_{(11)}$	118,0(3)	$C_{(14)}—C_{(15)}—C_{(10)}$	120,9(3)

Fig. 1

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedineii, No. 10, pp. 1388-1392, October, 1984. Original article submitted January 4, 1984.

0009-3122/84/2010-1145$08.50

TABLE 1. Coefficients of the Equations of the Mean Planes of the Molecular Fragments, Deviations of Atoms from Them, and Dihedral Angles between Mean Planes

Planes	Atoms in plane	Deviation of atoms from plane, Å	Equation of plane $A_x+B_y+C_z-D=0$				Dihedral angle, °
			A	*B*	*C*	*D*	
a	$C_{(2)}$	0,1233	−0,1935	−0,8674	−0,4584	−3,3526	a/b 10,12
	$C_{(3)}$	−0,1163					a/c 39,85
	$C_{(4a)}$	0,1023					a/d 18,78
	$C_{(9b)}$	−0,1093					a/e 17,68
	N^*	−0,1030					a/f 96,29
	$C^*_{(4)}$	−0,5975					
	$C^*_{(20)}$	1,6102					
	$C^*_{(10)}$	−2,1061					
b	N	—	−0,2836	−0,9067	−0,3120	−3,1342	
	$C_{(2)}$	—					
	$C_{(9b)}$	—					
c	$C_{(3)}$	—	−0,0556	−0,3860	−0,9208	−3,0642	
	$C_{(4)}$	—					
	$C_{(4a)}$	—					
d	$C_{(9b)}$	−0,0671	−0,4933	−0,7958	−0,3513	−3,3965	d/e 2,31
	$C_{(4a)}$	0,0703					
	$C_{(5)}$	−0,0526					
	$C_{(5a)}$	0,0135					
	$C_{(9a)}$	0,0358					
	$O^*_{(3)}$	−0,1499					
e	$C_{(5a)}$, $C_{(6)}-C_{(9)}$, $C_{(9a)}$	±0,01	−0,4815	−0,7857	−0,3885	−3,4972	
f	$C_{(10)}-C_{(15)}$	±0,009	0,9158	0,1239	−0,3820	2,3490	
g	$C_{(2)}$	−0,0998	−0,0421	−0,6493	−0,7594	−3,3116	g/h 32,99
	$C_{(3)}$	0,1757					
	$C_{(4)}$	−0,1512					
	$C_{(4a)}$	0,0753					
h	$C_{(2)}$	0,0004	−0,2840	−0,9059	−0,3142	−3,1425	
	N	−0,0009					
	$C_{(4a)}$	−0,0004					
	$C_{(9b)}$	+0,0009					
	$C^*_{(3)}$	−0,4339					
	$C^*_{(4)}$	−0,8896					

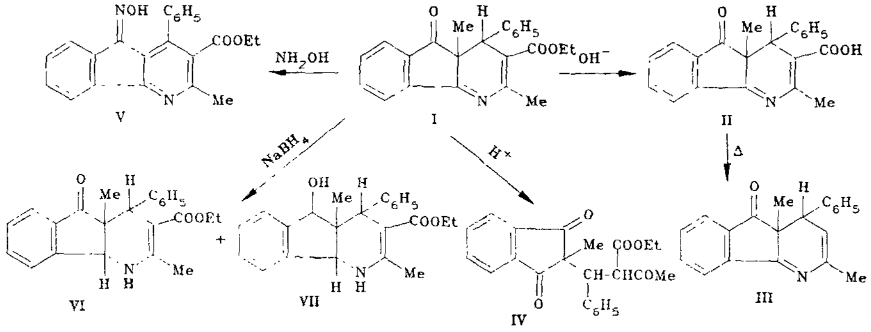
---

*Atoms not taken into account in the calculation of the respective plane.

The 3,4-dihydropyridine structure, i.e., the presence of endocyclic azomethine and carbon–carbon double bonds, as well as the presence of very different and asymmetrically arranged substituents on the carbon atoms of the pyridine ring, cause its distortion. According to the principles in [2], the 3,4-dihydropyridine ring has a distorted eclipsed boat conformation. The ring includes typical C–C single bonds, such as the $C_{(3)}-C_{(4)}$, and $C_{(4a)}-C_{(9b)}$ bonds, and the $C_{(2)}-C_{(3)}$ and $C_{(9b)}-N$ double bonds. The last bond is 0.05 Å shorter than the analogous bond in the pyridine molecule [3]. The mean values of the bonds in phenyl rings e and f are equal to 1.392 and 1.386 Å, respectively. These values practically coincide with the bond lengths in the benzene [4].

The sp^2 hybridization of the $C_{(5)}$, $C_{(5a)}$, $C_{(9a)}$, and $C_{(9b)}$ carbon atoms is confirmed both by the $C_{(5)}-C_{(5a)}$, $C_{(5a)}-C_{(9a)}$, and $C_{(9a)}-C_{(9b)}$ interatomic distances and by the sums of their angles. The $C_{(17)}$ atom also has planar coordination (the sum of the bond angles is 360°C) with $C_{(17)}-O_{(1)}$ and $C_{(17)}-O_{(2)}$ interatomic distances encountered in the molecules of protonated carboxylic acids and esters. The $C_{(20)}$ atom is found in a transoid position with respect to phenyl ring f. The packing of the molecule in a crystal is realized at distances no smaller than the sums of the van der Waals radii of the contacting atoms.

The characteristic reactions of the functional groups in ethyl 2,4a-dimethyl-4-phenyl-5-oxo-4-phenyl-5-oxo-4a,5-dihydroindeno[1,2-b]-pyridine-3-carboxylate (I) are completely consistent with the structure established. The esteric grouping readily undergoes alkaline hydrolysis. This process results in the formation of 2,4a-dimethyl-4-phenyl-5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridine-3-carboxylic acid (II), whose decarboxylation results in the formation of the known compound [1] 2,4a-dimethyl-4-phenyl-5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridine (III). Acid hydrolysis of I results in the splitting of the dihydropyridine ring and the formation of a mixture of products. The structure of ethyl α-acetyl-β-phenyl-β-(2-methylindan-1,3-dion-2-yl)propionate (IV) was provided for one of them, i.e., the product with a peak for its molecular ion at m/z 378, by a back synthesis. The formation of a derivative of 2-methylindan-1,3-dione as a result of the splitting of compound I as well confirms the presence of the $C_{(4a)}$–CH_3 group in the original compound.



When I is reduced by sodium borohydride, the hydrogen is added primarily to the more polar C=N bond, and then the 5-CO keto group is reduced in parallel. Such a reduction sequence is indicated by the composition of the reaction products recovered with different molar ratios between the reducing agent and compound I. For example, when $NaBH_4 : I = 0.25$, 2,4a-dimethyl-3-ethoxycarbonyl-5-oxo-4,4a,5,9b-tetrahydro-1H-indeno[1,2-b]pyridine (VI) is recovered, when there is a fivefold excess of the reducing agent, 2,4a-dimethyl-3-ethoxycarbonyl-5-hydroxy-4-phenyl-4,4a,5,9b-tetrahydro-1H-indeno[1,2-b]pyridine (VII) is recovered almost quantitatively, and when $NaBH_4 : I = 0.5$ to 1, a mixture of compounds VI and VII forms.

The oxidative properties of hydroxylamine are displayed in the conversion of indenopyridine I into an oxime: The 4a-CH_3 group is eliminated during the reaction, and the known 2-methyl-4-phenyl-3-ethoxy-carbonyl-5-oxoindeno[1,2-b]pyridine oxime (V) forms [5].

EXPERIMENTAL

The x-ray diffraction investigation was carried out on a Syntex $P2_1$ diffractometer under the conditions of monochromatic copper radiation (graphite monochromator) with a yellow single crystal measuring 0.35 × 0.25 × 0.25 mm. The crystals with the formula $C_{23}H_{21}NO_3$ are triclinic: $a = 8.4856(5)$, $b = 9.7660(6)$, $c = 12.5959(7)$ Å, $V = 918.24(34)$ Å^3, $M = 359.45$, $d_{cal} = 1.29$ g·cm^3, μ(Cu Kα) = 7.0 cm^{-1}, $Z = 2$, space group P1, $F_{000} = 380$. The intensities of 2880 independent reflections were measured by the θ/2θ scan technique to $2\theta_{max} = 150°$. The calculations were carried out with the use of 2599 reflections with $I \geqslant 2\sigma_I$. The structure was solved by the XTL system for determining structures and refined by the least-squares method in the full-matrix approximation in the anisotropic variant for the nonhydrogen atoms and the isotropic variant for the hydrogen atoms to $R = 0.070$. One hydrogen atom was localized by a difference synthesis in each methyl group ($C_{(16)}$, $C_{(19)}$, and $C_{(20)}$); the coordinates of the remaining hydrogen atoms were obtained on the basis of geometric arguments. The coordinates of the nonhydrogen atoms are given in Table 2.

The PMR spectra were recorded on a Bruker WH-90 spectrometer (the solvent was DMSO-d_6, and the internal reference was TMS), the IR spectra were recorded on a Perkin-Elmer 580B spectrometer in liquid petrolatum, and the mass spectra were recorded on an AEI MS-50 instrument with the direct admission of the sample into the ion source at 70 eV.

2,4a-Dimethyl-4-phenyl-5-oxo-4a,5-dihydro-4H-indeno[1,2-b]pyridine-3-carboxylic Acid (II). A 1-g portion (3 mmole) of I and 0.3 g (5 mmole) of KOH in 30 ml of ethanol are boiled for 4 h. The solvent is evaporated, the residue is treated with 50 ml of water, cooled, and acidified, and the yellow precipitate is filtered out. The yield is 0.9 g (98%). After recrystallization from methanol, the compound decomposes at 243-273°C. IR spectrum: ($CDCl_3$): 3515 (OH), 1728 cm^{-1} (5-CO). PMR spectrum: 0.63 (s, 3H, 4a-CH_3), 1.93 (s, 3H, 2-CH_3), 4.14 (s, 1H, 4-H), 6.74-6.90 (m, 2H, arom.), 6.96-7.12 (m, 3H, arom.), 7.62-8.18 (m, 4H, arom. in indene fragment), 12.43 ppm (br. s, 1H, 3-COOH). Found: C, 76.4; H, 5.6; N, 4.4%. Calculated from $C_{21}H_{17}NO_3$: C, 76.1; H, 5.2; N, 4.2%.

When II is heated with copper powder in quinoline, it undergoes decarboxylation, and the physicochemical characteristics of the product obtained correspond to the data in [1] for 2,4a-dimethyl-4-phenyl-5-oxo-4a,5-dihydroindeno[1,2-b]pyridine.

TABLE 2. Coordinates of Nonhydrogen Atoms ($\times 10^4$)

Atom	x	y	z	Atom	x	y	z
$O_{(1)}$	4606	3162	0432	$C_{(9a)}$	−2113	2571	3742
$O_{(2)}$	6117	1183	1135	$C_{(9b)}$	−0246	2173	3121
$O_{(3)}$	−2470	4344	1299	$C_{(10)}$	0577	4926	2175
N	1067	1665	3527	$C_{(11)}$	0587	5231	3243
$C_{(2)}$	2772	1518	2803	$C_{(12)}$	−0140	6683	3731
$C_{(3)}$	2945	2311	1913	$C_{(13)}$	−0912	7831	3169
$C_{(4)}$	1297	3351	1629	$C_{(14)}$	−0921	7552	2099
$C_{(4a)}$	−0073	2618	1939	$C_{(15)}$	−0181	6114	1606
$C_{(5)}$	−2020	3603	2037	$C_{(16)}$	4239	0489	3217
$C_{(5a)}$	−3152	3442	3108	$C_{(17)}$	4723	2134	1149
$C_{(6)}$	−5010	4024	3533	$C_{(18)}$	6193	2999	−0493
$C_{(7)}$	−5783	3734	4592	$C_{(19)}$	6058	2433	−1521
$C_{(8)}$	−4756	2845	5224	$C_{(20)}$	0454	1263	1114
$C_{(9)}$	−2906	2262	4804				

Hydrolysis of Indenopyridine I. A 0.7-g portion (2 mmole) of I is boiled in a mixture of 40 ml of ethanol, 10 ml of water, and 0.5 ml of conc. HCl. The alcohol is evaporated, the water is decanted, and the oily residue is treated with methanol. A colorless product with mp 163-165°C (methanol) is obtained. The yield is 30%. The substance does not cause melting-point depression with ethyl α-acetyl-β-phenyl-β-(2-methylindan-1,3-dion-2-yl)propionate (IV) obtained by a back synthesis, i.e., by alkylation of ethyl α-acetyl-β-phenyl-β-(indan-1,3-dion-2-yl)propionate [6] according to the method in [7]. IR spectrum: 1745, 1732, 1705 cm^{-1} (CO). PMR spectrum: 1.04 (s, 3H, 2-CH_3), 1.08 (t, 3H, $OCH_2C\underline{H}_3$), 1.86 (s, 3H, $COCH_3$), 3.96 (q, 2H, $OC\underline{H}_2CH_3$), 4.07 (d, 1H, β-H), 4.67 (d, 1H, α-H; $J_{CH—CH} = 11.50$ Hz), 7.09 (s, 5H, arom.), 7.78-7.94 ppm (m, 4H, arom. of indene fragment). Mass spectrum: $M^{\ddagger}$ 378 (2), $[C_6H_4COCH_3]^+$ 131 (100). Found: C, 72.6; H, 6.0%. Calculated for $C_{23}H_{22}O_5$: C, 73.0; H, 5.9%, M 378.

Oxime Formation from Indenopyridine I. A mixture of 0.3 g of I and 0.3 g of $NH_2OH \cdot HCl$ in 10 ml of pyridine is heated in a water bath for 3 h and diluted with water. Colorless crystals with mp 285-287°C (ethanol), which are identical to a known specimen [5] of 2-methyl-3-ethoxycarbonyl-4-phenyl-5-oxoindeno[1,2-b]pyridine oxime (V), are obtained. IR spectrum: 0.86(t, 3H, $OCH_2C\underline{H}_3$), 2.59 (s, 3H, 2-CH_3), 3.97 (q, 2H, $OC\underline{H}_2CH_3$), 7.27-7.89 (m, 1H), and 8.33-8.51 (m, 1H) (aromatic protons), 11.50 ppm (s, 1H, $\overline{O}H$). Mass spectrum: $M^{\ddagger}$ 358 (29), $[M - OH]^+$ 341 (100).

Reduction of Indenopyridine I. A. 2,4a-Dimethyl-3-ethoxycarbonyl-4-phenyl-5-oxo-4,4a,5,9b-tetrahydro-1H-indeno[1,2-b]pyridine (VI). A mixture of 0.7 g (2 mmole) of I and 0.02 g (0.5 mmole) of $NaBH_4$ in 30 ml of acetonitrile is stirred for 20 min, evaporated to a volume of 5 ml, and chromatographed in a column with silica gel (L160/100). The eluent is a 9:7:1 chloroform—hexane—acetone mixture. The original compound I (∿50%) is recovered from the yellow fraction of the eluent, and colorless crystals of VI with mp 211-213°C (methanol) are recovered from the next fraction. IR spectrum: 3340 (NH), 1717, 1660 cm^{-1} (CO). PMR spectrum: 0.99 (t, 3H, $OCH_2C\underline{H}_3$), 1.34 (s, 3H, 4a-CH_3), 2.44 (s, 3H, 2-CH_3), 3.80 (q, 2H, $OC\underline{H}_2CH_3$), 3.86 (s, 1H, 4-H), 4.60 (d, 1H, 9b-H, $J_{CH—NH} = 3.75$ Hz), 6.40-6.73 (m, 5H, 4-C_6H_5), 6.80-7.18 and 7.38-7.67 (m, 2H, arom. of indene fragment), 7.84 ppm (d, 1H, NH). Mass spectrum: $[M]^{\ddagger}$ 361 (28), $[M - COOC_2H_5]^+$ 288 (100). Found: C, 76.3; H, 6.6; N, 4.0%. Calculated for $C_{23}H_{23}NO_3$: C, 76.4; H, 6.4; N, 3.9%; M 361.

B. 2,4-a-Dimethyl-3-ethoxycarbonyl-5-hydroxy-4-phenyl-4,4a-5,9b-tetrahydro-1H-indeno[1,2-b]pyridine (VII). A 0.7-g portion (2 mmole) of compound I in a mixture of 50 ml of acetonitrile and 5 ml of methanol is stirred for 20 min with 0.4 g (10 mmole) of $NaBH_4$. The mixture is evaporated, treated with 20 ml of water, and extracted by ether (three 25-ml portions), the ether is evaporated, and the colorless residue is recrystallized from methanol. The mp is 166-168°C (at 90-95°C the substances loses methanol without melting). IR spectrum: 3320, 3375, 3425 (OH, NH), 1655 cm^{-1} (CO). PMR spectrum: 0.94 (t, 3H, $OCH_2C\underline{H}_3$), 1.34 (s, 3H, 4a-CH_3), 2.34 (s, 3H, 2-CH_3), 3.74 (q, 2H $OC\underline{H}_2CH_3$), 3.79 (s, 1H, 4-H), 4.31 (d, 1H, 9b-H), 4.91 (d, 1H, 5-H), 5.37 (d, 1H, OH, $J_{CH—OH} = 5.37$ Hz), 6.40-7.27 (m, 4H, arom. of indene fragment), 6.54 (s, 5H, 4-C_6H_5), 7.61 ppm (d, 1H, NM, $J_{CH—NH} = 4.00$ Hz). The protons of the 5-OH group undergo deuterium exchange with D_2O. The relative positions of the 5-OH and 5-CH and of the 9b-CH and N—H protons was also revealed by double resonance. Mass spectrum: $[M]^{\ddagger}$ 363 (30), $[M - COOC_2H_5]^+$ 290 (100). Found: C, 72.7; H, 7.6; N, 3.5%. Calculated for $C_{23}H_{25}NO_3 \cdot CH_3OH$: C, 72.9; H, 7.4; N, 3.5%; M 363.

LITERATURE CITED

1. V. K. Lusis, D. Kh. Mutsenietse, A. Z. Zandersons, I. B. Mazheika, and G. Ya. Dubur, Khim., Geterotsikl. Soedin., No. 3, 393 (1984).
2. D. Cremer and J. A. Pople, J. Am. Chem. Soc., 97, 1354 (1975).
3. Tables of Interatomic Distances and Configuration in Molecules and Ions, Special Publication No. 18, London (1965).
4. E. G. Cox, D. W. J. Cruickshann, and J. A. S. Smith, Proc. Soc. London, A247, 1 (1958).
5. V. Petrow, J. Saper, and B. Sturgeon, J. Chem. Soc., No. 9, 2134 (1949).
6. L. P. Zalukaev and I. K. Anokhina, Zh. Obshch. Khim., 34, 840 (1964).
7. P. Hrnčiar and F. Szemes, Coll., 36, 1843 (1971).

ARYLIDENEHYDROACRIDINES FROM DI(3-ARYLIDENE-2-OXOCYCLOHEXYL)-METHANES

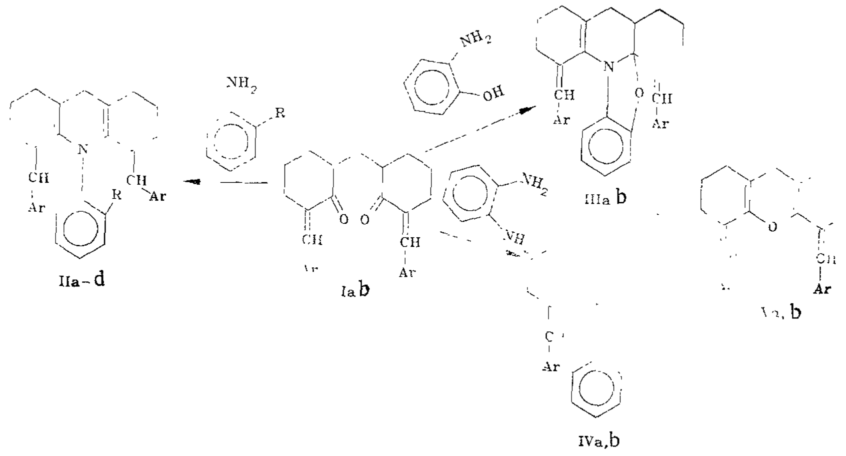
N. N. Minaeva, V. A. Kaminskii, and M. N. Tilichenko

UDC 547.835.9'572:542.953.2

The reaction of di(3-benzylidene-2-oxocyclohexyl)methane and its p-methoxy analog with primary amines results in the formation of derivatives of 4,5-diarylidenehydroacridines, whereas the reaction with o-phenylenediamine is accompanied by the elimination of one arylidene group and gives derivatives of 4-arylidenehydroacridines.

The investigation of α,α'-diarylidene 1,5-diketones [1] is of interest for the synthesis of heterocyclic compounds containing arylidene groups, which have useful, in particular, fluorescence properties [2].

We studied the reaction of di(3-benzylidene-2-oxocyclohexyl)methane (Ia) and its-p-substituted analog Ib with several aromatic amines, which takes place at the carbonyl groups. In all cases, the reaction proceeds with greater difficulty than in the case of diketones without arylidene groups [3, 4] and, as a rule, does not go to completion. Di(3-cyclohexylidene-2-oxocyclohexyl)methane [5], in which the degree of conjugation is smaller and the shielding of the carbonyl group is greater than in diketones Ia and b, according to our data, scarcely reacts with aniline and o-phenylenediamine.



I, III—V a $Ar=C_6H_5$; b $Ar=C_6H_4OCH_3$-*p*; II a R=H, $Ar=C_6H_5$; b R=H, $Ar=C_6H_4OCH_3$-*p*; c $R=OCH_3$, $Ar=C_6H_5$; d $R=OCH_3$, $Ar=C_6H_4OCH_3$-*p*

The products of the reactions of diketones Ia and b with aniline and o-anisidine are

---

Far-Eastern State University, Vladivostok 690600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1393-1395, October, 1984. Original article submitted December 14, 1983.

0009-3122/84/2010-1149$08.50