Chemistry of Heterocyclic Compounds, Vol. 40, No. 10, 2004

[3 + 3] CYCLOCONDENSATION OF 1-ALKYL-3,4-DIHYDROISOQUINOLINES WITH β-KETO ESTERS. NEW ANNELATION REACTION IN A SERIES OF CYCLIC SCHIFF'S BASES

O. V. Gulyakevich[1], A. A. Govorova[1], P. V. Kurman[2], A. S. Lyakhov[3], and A. L. Mikhal'chuk[1]

A new annelation reaction in a series of cyclic Schiff's bases is described with examples of [3 + 3] cyclocondensation of 1-alkyl-3,4-dihydroquinolines and acetoacetic esters.

Keywords: azomethines, benzo[*a*]quinolizines, 3,4-dihydroisoquinolines, ketimines, β-keto esters, Schiff's bases, pyrido[2,1-*a*]isoquinolines, annelation, heterocyclization, cyclocondensation.

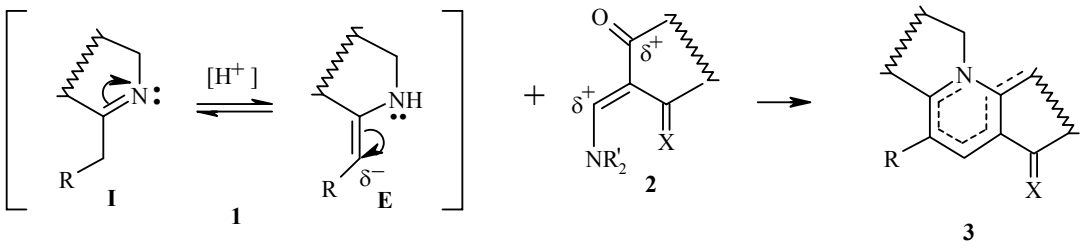
The multifunctionality of cyclic ketimines and derivatives of carbonyl compounds permits exceptionally wide possibilities for the synthesis of condensed nitrogen-containing heterocycles with an angular nitrogen atom [1-5], particularly alkaloids [6,7], and heterocyclic analogs of steroids (azasteroids) [3-5].

We previously studied the reaction of azomethines **1** with aminovinylcarbonyl (**2**, X = 2H) and dicarbonyl (**2**, X = O) compounds, leading to the condensed system **3** (Scheme 1) [5].

It seemed of interest to extend this reaction to other carbonyl compounds, particularly to β-keto esters.

An additional stimulus for studying such reactions were the numerous data on the interaction of β-dicarbonyl compounds (1,3-dielectrophiles) with bifunctional nitrogen bases, such as hydrazine [8], hydroxylamine [9], and others [10].

Scheme 1

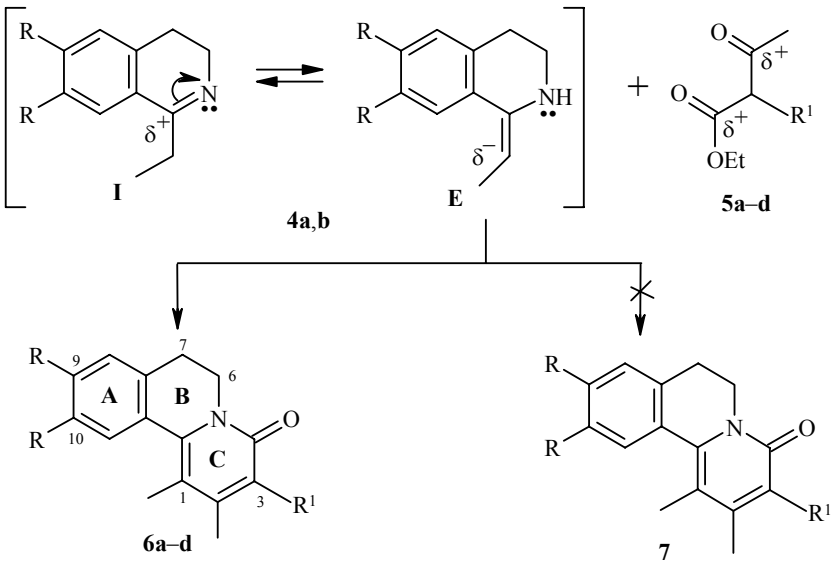


R = H, Alk; R' = Alk, $(CH_2)_n$; X = 2H, O

[1] Institute of Bioorganic Chemistry, National Academy of Sciences of the Republic of Belarus, Minsk 220141; e-mail: mikhalch@imaph.bas-net.by. [2] EKOMIR Center, National Academy of Sciences of the Republic of Belarus, Minsk 220012. [3] Research Institute for Physicochemical Problems, Belarussian F. Scorina State University, Minsk 220050. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1492-1500, October, 2004. Original article submitted August 5, 2002.

In contemporary theory and practice of organic chemistry the enamine tautomers of Schiff's bases are usually considered as C-nucleophiles [11-15]. However the results of theoretical investigations [16] and experimental data [5] enable these compounds to be considered as 1,3-dinucleophiles, capable of interacting with dielectrophiles. Paying attention to the results of the previous investigations [17,18], and also to the ability of 1-alkyl substituted 3,4-dihydroisoquinolines (cyclic ketimines) to act both as imine (**4I**) and as enamine (**4E**) tautomers [19], and the 1,3-dielectrophilic nature of β-keto esters, we have studied the interaction of 3,4-dihydroisoquinolines **4a,b** with acetoacetic esters **5a-d.** It was discovered that, as a result of these interactions, a previously unknown heterocyclization reaction is effected, leading to pyrido[2,1-*a*]isoquinolines (benzo[*a*]quinolizines, **6a-d**). As a result of the interaction of the indicated substrates it is theoretically possible to expect the formation of both derivatives **6a-d** and derivatives **7** isomeric with them. However the sole products of the interaction studied proved to be derivatives **6a-d**.

Scheme 2



4a, **6c**,**d** R = H, **4b**, **6a**,**b** R = OMe, **5a**, **6a** R^1 = Me, **5b**, **6c** R^1 = *i*-Bu,
5c, **6d** R^1 = CH_2CH_2COMe, **5d**, **6b** R^1 = CH_2Ph

The condensation of 3,4-dihydroquinolines **4a,b** with acetoacetic esters **5a-d** was effected by heating mixtures of them at 140-220°C. The reaction products were isolated after cooling and were purified by crystallization. In individual cases flash chromatography (Silica gel L 40/5 μ from Chemapol, eluent chloroform) was used for isolation and purification of the product [20].

The enhanced tendency of derivatives **6a-d** to form crystal hydrates should be noted. These are extremely stable and lose the water of crystallization with difficulty even on heating under reduced pressure over phosphoric anhydride. On the strength of this it is necessary to use anhydrous solvents to obtain samples without solvated water.

The structure ascribed to the product of interaction of 3,4-dihydroisoquinolines **4a,b** with acetoacetic esters **5a-d** was confirmed by data of physicochemical investigations, and for compound **6a** also by data of X-ray structural analysis.

In the IR spectra of derivatives **6a-d** intense broadened and asymmetric absorption bands (AB) were observed at 1590-1620, 1570-1585, and 1485-1550 cm^{-1} caused by C=O and C=C stretching vibrations of the γ-pyridone **C** rings and the benzene **A** rings [21], and also AB at 1440-1470 cm^{-1} which are caused by the C–H deformation vibrations of methylene and methyl groups [22].

Interesting regularities were traced in the electronic absorption spectra of derivatives **6a-d**. In the spectra of derivatives **6a,b,** characterizing the presence in their structure of methoxy substituents at positions 9 and 10, about three AB were observed in the 235-310 nm region at λ ~240, 260, and 308 nm, while for derivatives **6c,d** (9,10-desmethoxy derivatives) only two AB were observed in the indicated region of the spectrum at λ ~255 and 286 nm. Proceeding from the indicated differences of derivatives **6a,b** and **6c,d** and in accordance with the data of [23], the AB of derivatives **6a,b** displayed at ~240 nm should be assigned to an electronic transition of the methoxy-substituted benzene rings **A**. The AB located in the long wave region of the spectrum (250-310 nm) are caused by the electronic transitions of the γ-pyridone rings **C** linked by the $C_{(11a)}$–$C_{(11b)}$ bond with the benzene rings **A**. The AB displayed in the region below 220 nm are caused by electronic transitions of rings **A** [23].

In the ^{1}H NMR spectra of derivatives **6a-d** the signals of the methylene groups $C_{(6)}H_2$ and $C_{(7)}H_2$ and the methyl groups at atoms $C_{(1)}$ and $C_{(4)}$ were common for all the described compounds. These were displayed as characteristic two-proton triplets (J = 6-7 Hz) at δ 3.95-4.00 and 2.90-2.96 ppm and three-proton singlets at δ ~2.36 and 2.46 respectively.

The presence of a γ-pyridone ring **C** (**6a-d**) in the obtained compounds and not the α-pyridone ring (**7**) isomeric with it was finally established from the X-ray structural analysis of compound **6a**. Compound **6a** crystallizes as a molecular complex with a molecule of water. The bond lengths and valence angles (Tables 1 and 2) are in good agreement with the corresponding values in the molecular compounds containing analogous fragments [24]. The structure of the pyrido[2,1-*a*]isoquinoline **6a** molecule and the numbering of the atoms are shown in Figure 1.

TABLE 1. Bond Lengths (*d*) in the Compound **6a** Molecule

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
$C_{(1)}$–$C_{(11b)}$	1.3731(18)	$C_{(4)}$–$C_{(14)}$	1.5055(19)	$C_{(9)}$–$O_{(9)}$	1.3633(18)
$C_{(1)}$–$C_{(2)}$	1.4345(19)	$N_{(5)}$–$C_{(11b)}$	1.3836(17)	$C_{(9)}$–$C_{(10)}$	1.4059(19)
$C_{(1)}$–$C_{(12)}$	1.5012(18)	$N_{(5)}$–$C_{(6)}$	1.4882(16)	$C_{(10)}$–$O_{(10)}$	1.3675(17)
$C_{(2)}$–$O_{(2)}$	1.2680(16)	$C_{(6)}$–$C_{(7)}$	1.511(2)	$C_{(10)}$–$C_{(11)}$	1.3799(19)
$C_{(2)}$–$C_{(3)}$	1.4327(19)	$C_{(7)}$–$C_{(7a)}$	1.4972(19)	$C_{(11)}$–$C_{(11a)}$	1.4012(19)
$C_{(3)}$–$C_{(4)}$	1.3682(19)	$C_{(7a)}$–$C_{(11a)}$	1.3888(18)	$C_{(11a)}$–$C_{(11b)}$	1.4852(19)
$C_{(3)}$–$C_{(13)}$	1.5086(19)	$C_{(7a)}$–$C_{(8)}$	1.393(2)	$C_{(15)}$–$O_{(9)}$	1.425(2)
$C_{(4)}$–$N_{(5)}$	1.3733(18)	$C_{(8)}$–$C_{(9)}$	1.382(2)	$C_{(16)}$–$O_{(10)}$	1.4168(18)

TABLE 2. Valence Angles (ω) in the Compound **6a** Molecule

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
$C_{(11b)}$–$C_{(1)}$–$C_{(2)}$	119.97(12)	$C_{(4)}$–$N_{(5)}$–$C_{(11b)}$	121.04(11)	$O_{(10)}$–$C_{(10)}$–$C_{(11)}$	124.26(13)
$C_{(11b)}$–$C_{(1)}$–$C_{(12)}$	123.92(12)	$C_{(4)}$–$N_{(5)}$–$C_{(6)}$	119.97(11)	$O_{(10)}$–$C_{(10)}$–$C_{(9)}$	116.08(12)
$C_{(2)}$–$C_{(1)}$–$C_{(12)}$	116.06(11)	$C_{(11b)}$–$N_{(5)}$–$C_{(6)}$	118.89(11)	$C_{(11)}$–$C_{(10)}$–$C_{(9)}$	119.65(13)
$O_{(2)}$–$C_{(2)}$–$C_{(1)}$	120.61(12)	$N_{(5)}$–$C_{(6)}$–$C_{(7)}$	110.73(11)	$C_{(10)}$–$C_{(11)}$–$C_{(11a)}$	121.01(12)
$O_{(2)}$–$C_{(2)}$–$C_{(3)}$	121.70(12)	$C_{(7a)}$–$C_{(7)}$–$C_{(6)}$	108.37(12)	$C_{(7a)}$–$C_{(11a)}$–$C_{(11)}$	119.07(12)
$C_{(1)}$–$C_{(2)}$–$C_{(3)}$	117.67(12)	$C_{(11a)}$–$C_{(7a)}$–$C_{(8)}$	119.96(13)	$C_{(7a)}$–$C_{(11a)}$–$C_{(11b)}$	119.53(12)
$C_{(4)}$–$C_{(3)}$–$C_{(2)}$	120.02(12)	$C_{(11a)}$–$C_{(7a)}$–$C_{(7)}$	116.28(12)	$C_{(11)}$–$C_{(11a)}$–$C_{(11b)}$	121.31(11)
$C_{(4)}$–$C_{(3)}$–$C_{(13)}$	122.75(13)	$C_{(8)}$–$C_{(7a)}$–$C_{(7)}$	123.62(12)	$C_{(1)}$–$C_{(11b)}$–$N_{(5)}$	120.07(12)
$C_{(2)}$–$C_{(3)}$–$C_{(13)}$	117.21(12)	$C_{(9)}$–$C_{(8)}$–$C_{(7a)}$	120.93(13)	$C_{(1)}$–$C_{(11b)}$–$C_{(11a)}$	124.21(12)
$C_{(3)}$–$C_{(4)}$–$N_{(5)}$	120.65(12)	$O_{(9)}$–$C_{(9)}$–$C_{(8)}$	125.19(13)	$N_{(5)}$–$C_{(11b)}$–$C_{(11a)}$	115.68(11)
$C_{(3)}$–$C_{(4)}$–$C_{(14)}$	122.56(13)	$O_{(9)}$–$C_{(9)}$–$C_{(10)}$	115.43(13)	$C_{(9)}$–$O_{(9)}$–$C_{(15)}$	117.66(13)
$N_{(5)}$–$C_{(4)}$–$C_{(14)}$	116.74(12)	$C_{(8)}$–$C_{(9)}$–$C_{(10)}$	119.35(13)	$C_{(10)}$–$O_{(10)}$–$C_{(16)}$	117.23(11)

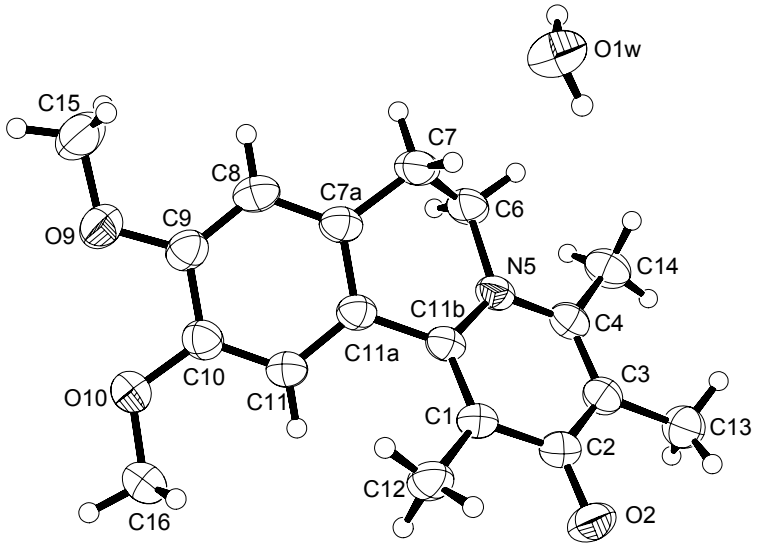
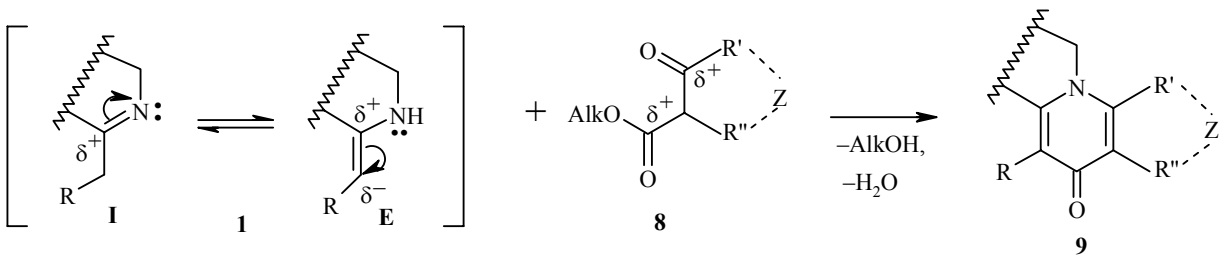


Fig. 1. Structure of the compound **6a** molecule.

Analysis of the bond lengths in the γ-pyridone ring **C** shows the presence of significant conjugation in the ring. Rings **A** and **C** in the pyrido[2,1-*a*]isoquinoline **6a** molecule are planar, the deviation of individual atoms from the mean square planarity of the rings was 0.008(1) Å for ring **A** and 0.029(1) Å for ring **C**. Since these rings are separated by the $C_{(11a)}$–$C_{(11b)}$ bond it might be right to expect interaction or interference between them. However, as in the case of the 8-azasteroid derivatives with γ-pyridone rings **C** studied previously [25,26], the planes of rings **A** and **C** for derivative **6a** are tilted relative to one another by 36.46(4)°. It is evident that such a relative disposition of these rings excludes interaction (overlap) of their π-electron clouds. This is confirmed by the fact that the $C_{(11a)}$–$C_{(11b)}$ bond is only 0.012 Å shorter than the $C_{(7)}$–$C_{(7a)}$ bond. Ring **B** has the conformation of a strongly distorted boat since the $C_{(7)}$, $C_{(7a)}$, $C_{(11a)}$, and $C_{(11b)}$ atoms lie practically in one plane [the deviations of the atoms from mean square planarity are 0.0099(8) Å], and the $C_{(6)}$ and $N_{(5)}$ atoms emerge from it by 1.002(3) and 0.644(2) Å.

In a generalized form the reaction discovered by us may be represented by Scheme 3 and is a convenient method of forming a γ-pyridone ring by the heterocyclization of azomethines **1** with β-keto esters **8** with the formation of condensed nitrogen-containing heterocycles containing a γ-pyridone structural fragment of type **9**. No close analogies to this reaction were found in the accessible periodical [11-15], monograph [27], or reference literature (*Chemical Abstracts*). This enables us to affirm that the new reaction is straightforward, probably has a general character, and enables the synthesis in one step of condensed nitrogen-containing

Scheme 3



heterocycles with an angular nitrogen atom. One of the most obvious applications of it may be the synthesis of alkaloids and heterocyclic analogs of steroids by annelation of 1-alkyl-3,4-dihydroisoquinolines of type **4** or 1-alkyl-3,4-dihydro-β-carbolines with alkoxycarbonyl derivatives of cycloalkanones and heterocyclic ketones, such as pyranones, thiopyranones, piperidones, etc.

EXPERIMENTAL

The 3,4-dihydroisoquinolines **4a,b** used in the work were obtained by the cyclodehydration of the corresponding phenylethylamides under the action of polyphosphoric acid (**4a**) and phosphorus oxychloride (**4b**) under the conditions of the Bischler–Napieralski reaction [28]. A check on the progress of reactions and the purity of products was effected by TLC on Silufol UV 254 plates, eluent was chloroform–methanol, 9:1, visualizing in UV light or iodine vapor with subsequent roasting at 250-350°C. Melting points were determined on a Boetius heating block. The IR spectra were obtained on a UR 20 instrument in KBr disks. The UV spectra were taken on a Specord M 400 spectrophotometer in ethanol. The ^{1}H NMR spectra were obtained on a Bruker AC 200 (200 MHz) radiospectrometer in $CDCl_3$, internal standard was TMS. The mass spectra of derivatives **6a-d** were measured on a HP 5890/5972 GC/MS chromato-mass spectrometer (quartz capillary column HP 5MS, 30 m × 0.25 mm × 0.25 μm, carrier gas helium at 0.7-1 μl/min, evaporator temperature 250°C, temperature program 40-300°C, 6°C/min), energy of ionizing electrons 70eV.

X-Ray Structural Investigation of Compound 6a. A prismatic crystal of dimensions 0.74 × 0.40 × 0.36 mm was selected for the analysis. A three-dimensional set of X-ray diffraction data was obtained on a Nicolet R3m automatic four-circle diffractometer, Mo$K\alpha$ radiation, graphite monochromator, θ/2θ scanning, $2\theta_{max}$ = 55°. The total number of reflections measured was 4183, 3755 were independent (R_{int} = 0.0147). The crystal was triclinic, space group $P\bar{1}$. Parameters of the unit cell were a = 7.566(2), b = 8.899(1), c = 12.397(3) Å; α = 88.52(2), β = 81.94(2), γ = 80.06(2)°; V = 814.0(3) Å^3; Z = 2; $d_{X\text{-}ray}$ = 1.295 g/cm^3; μ = 0.91 cm^{-1}. The structure of the compound was solved by the direct method (SIR97 [29]). The positions of the hydrogen atoms were calculated geometrically, except for the hydrogen atoms of the water molecule, the positions of which were determined by a Fourier difference synthesis. Refinement (SHELXL-97 [30]) was carried out by the full-matrix least squares method allowing for the anisotropy of the thermal vibrations of the nonhydrogen atoms. The hydrogen atoms were refined with a rider model (protons of the water molecule were refined isotropically). Final values of the uncertainty factors were R_1 = 0.0429, wR_2 = 0.1241 [$I > 2\sigma(I)$]; R_1 = 0.0562, wR_2 = 0.1380 (all data); goodness of fit $GOOF$ = 1.055. The coordinates and equivalent isotropic parameters of the displacement of atoms may be obtained from the authors.

9,10-Dimethoxy-1,3,4-trimethyl-6,7-dihydro-2H-pyrido[2,1-*a*]isoquinolin-2-one (6a). A mixture of isoquinoline **4b** (1.1 g, 5 mmol) and ester **5a** (0.79 ml, 5.5 mmol) was heated for 6 h at 140-160°C. The reaction mixture was then diluted with alcohol and left at +5°C overnight. The separated substance was filtered off and recrystallized from alcohol–ether. Pyridoisoquinoline **6a** (1.16 g, 73%) was obtained as colorless prismatic crystals; mp 186-188°C. IR spectrum, ν, cm^{-1}: 3250-3350, 2820-3050, 1612, 1585, 1500-1540, 1470, 1448, 1376, 1350, 1275, 1260, 1235, 1228, 1205, 1150, 1105, 1040, 1012, 880, 842, 822, 780, 768. UV spectrum, λ_{max}, nm (ε): 215 (20680), 238.8 (23880), 260 (21635), 307.1 (17358); λ_{min}, nm (ε): 205 (19265), 225 (17510), 249.4 (16690), 274.1 (11165). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.20 (3H, s, $C_{(3)}CH_3$); 2.38 (3H, s, $C_{(1)}CH_3$); 2.42 (3H, s, $C_{(4)}CH_3$); 2.90 (2H, t, J = 6.0, $C_{(7)}H_2$); 3.62 (2H, s, H_2O); 3.92 (3H, s, OCH_3); 3.96 (3H, s, OCH_3); 4.00 (2H, t, J = 6.0, $C_{(6)}H_2$); 6.79 (1H, s, $C_{(8)}H$); 7.16 (1H, s, $C_{(11)}H$). Mass spectrum, m/z (I_{rel}, %): 300 (13.4) $[M+1]^{+\cdot}$; 299 (79.6) $[M]^{+\cdot}$; 298 (100) $[M-1]^{+\cdot}$; 285 (11.0); 284 (60.7); 282 (16.1); 271 (10.7); 256 (42.2); 254 (15.6); 253 (15.1); 227 (10.1); 226 (10.9); 213 (19.1); 212 (16.5); 184 (13.5); 127 (10.1); 120 (14.5); 115 (12.2); 105 (10.7). Found, %: C 68.00; H 7.32; N 4.31. $C_{18}H_{21}NO_3.H_2O$. Calculated, %: C 68.12; H 7.30; N 4.41. M 317.38.

3-Benzyl-9,10-dimethoxy-1,4-dimethyl-6,7-dihydro-2H-pyrido[2,1-*a*]isoquinolin-2-one (6b). A mixture of isoquinoline **4b** (1.65 g, 7.5 mmol) and ester **5d** (2.7 ml, 11.3 mmol) was heated for 9 h at 140-160°C. The excess of β-keto ester was distilled off, the residue was dissolved in alcohol, and the mixture left to crystallize at +5°C. The separated crystals were filtered off, washed on the filter with cold 70% alcohol, and recrystallized from 70% alcohol. Pyridoisoquinoline **6b** (1.9 g, 64.4%) was obtained as white flaky crystals; mp 168.5-170.5°C. IR spectrum, ν, cm^{-1}: 3280, 2800-3100, 1595-1620, 1585, 1490-1545, 1440-1465, 1384, 1352, 1344, 1319, 1255-1285, 1232, 1225, 1138, 1075, 1044, 1025, 882, 840, 780, 733, 702. UV spectrum, λ_{max}, nm (ε): 240 (39850), 262.4 (36325), 308.8 (28160); λ_{min}, nm (ε): 228 (31080), 250 (27250), 286.2 (20170). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.36 (3H, s, $C_{(1)}CH_3$); 2.42 (3H, s, $C_{(4)}CH_3$); 2.51 (2H, s, H_2O); 2.90 (2H, t, $J_{1,2}$ = 6.0, $C_{(7)}H_2$); 3.92 (3H, s, OCH_3); 3.95 (2H, t, $J_{1,2}$ = 6.0, $C_{(6)}H_2$); 3.97 (3H, s, CH_3); 4.14 (2H, s, $C_{(14)}H_2$); 6.78 (1H, s, $C_{(8)}H$); 7.18 (1H, s, $C_{(11)}H$); 7.10-7.36 (5H, m, $C_{(2')}H$, $C_{(3')}H$, $C_{(4')}H$, $C_{(5')}H$, $C_{(6')}H$). Mass spectrum, *m/z* (I_{rel}, %): 375 (100) $[M]^{+\cdot}$; 374 (83.2) $[M-1]^{+\cdot}$; 360 (30.1); 358 (14.9); 285 (11.9); 284 (62.8); 207 (19.1); 187 (48.4); 180 (14.2); 165 (13.7); 157 (13.1); 142 (13.7); 141 (10.2); 135 (12.3); 129 (13.9); 128 (26.7); 127 (20.3); 115 (22.9); 102 (10.6); 91 (27.9); 78 (11.8); 77 (18.8). Found, %: C 73.19; H 6.95; N 3.45. $C_{24}H_{25}NO_3.H_2O$. Calculated, %: C 73.26; H 6.92; N 3.45. M 393.48.

3-Isobutyl-1,4-dimethyl-6,7-dihydro-2H-pyrido[2,1-*a*]isoquinolin-2-one (6c). A mixture of isoquinoline **4a** (1.19 g, 7.5 mmol) and ester **5b** (1.58 g, 8.5 mmol) was heated in a stream of argon at 160-180°C for 12 h. The reaction mixture was then diluted with ether, and after rubbing with a glass rod, was left to crystallize. The substance which separated was filtered off, washed with ether, and recrystallized from an alcohol–ether mixture. Pyridoisoquinoline **6c** (1.6 g, 74.9%) was obtained as white flaky crystals; mp 169-171°C. IR spectrum, ν, cm^{-1}: 3250-3300, 2830-3100, 1590-1620, 1570, 1520-1550, 1485, 1450, 1429, 1380, 1365, 1283, 1252, 1230, 1077, 768, 752. UV spectrum, λ_{max}, nm (ε): 208.7 (20100), 256.7 (28475), 291.5 (10050); λ_{min}, nm (ε): 228.6 (7370), 271.7 (9380). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.96 (6H, d, *J* = 7.0, $C_{(14)}H_3$, $C_{(15)}H_3$); 1.95 (1H, m, $C_{(13)}H$); 2.13 (1H, br s, $0.5H_2O$); 2.34 (3H, s, $C_{(1)}CH_3$); 2.42 (3H, s, $C_{(4)}CH_3$); 2.58 (2H, d, *J* = 7.0, $C_{(12)}H_2$); 2.95 (2H, t, *J* = 7.0, $C_{(7)}H_2$); 3.95 (2H, t, *J* = 7.0, $C_{(6)}H_2$); 7.28 (1H, m, $C_{(8)}H$); 7.34 (2H, m, $C_{(9)}H$, $C_{(10)}H$); 7.63 (1H, m, $C_{(11)}H$). Mass spectrum, *m/z* (I_{rel}, %): 281 (21.69) $[M\}^{+\cdot}$; 280 (14.2) $[M-1]^{+\cdot}$; 267 (13.7); 266 (68.9); 240 (16.7); 239 (100); 238 (71.5); 236 (14.4); 225 (11.5); 224 (27.0); 210 (18.6); 194 (13.8); 128 (15.2); 115 (12.1). Found, %: C 78.29; H 8.68; N 4.66. $C_{19}H_{23}NO.0.5H_2O$. Calculated, %: C 68.12; H 7.30; N 4.41. M 290.

1,4-Dimethyl-3-(3-oxobutyl)-6,7-dihydro-2H-pyrido[2,1-*a*]isoquinolin-2-one (6d). A mixture of isoquinoline **4a** (1.19 g, 7.5 mmol) and ester **5c** (1.18 g, 9 mmol) was heated in a stream of argon for 15 h at 200-220°C. The reaction mixture was then evaporated, the residue dissolved in chloroform, washed with potassium carbonate solution, with water, dried over magnesium sulfate, and filtered through silica gel (5 g). The solution obtained was evaporated under reduced pressure, and the dry residue crystallized from a chloroform–hexane mixture. Pyridoisoquinoline **6d** (1.29 g, 58%) was obtained as colorless finely prismatic crystals; mp 191-194°C (decomp.). IR spectrum, ν, cm^{-1}: 2830-3100, 1715, 1610, 1575, 1530-1550, 1486, 1455, 1435, 1404, 1355-1385, 1286, 1251, 1163, 1074, 785, 774, 754. UV spectrum, λ_{max}, nm (ε): 205 (33075), 254.6 (35035), 281.9 (12960); λ_{min}, nm (ε): 229.6 (11700), 271.9 (12330). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.19 (3H, s, $C_{(15)}H_3$); 2.34 (3H, s, $C_{(1)}CH_3$); 2.48 (3H, s, $C_{(4)}CH_3$); 2.77 (2H, m, $C_{(12)}H_2$); 2.92 (2H, m, $C_{(13)}H_2$); 2.96 (2H, t, *J* = 6.5, $C_{(7)}H_2$). 3.96 (2H, t, *J* = 6.5, $C_{(6)}H_2$); 7.26-7.43 (3H, m, $C_{(8)}H$, $C_{(9)}H$, $C_{(10)}H$); 7.62 (1H, m, $C_{(11)}H$). Mass spectrum, *m/z* (I_{rel}, %): 295 (11.0) $[M]^{+\cdot}$; 253 (20.3); 252 (100); 236 (15.2). Found, %: C 77.20; H 7.15; N 4.65. $C_{19}H_{21}NO_2$. Calculated, %: C 77.26; H 7.17; N 4.74. M 295.38.

The authors are grateful to Academician Afanasii Andreevich Akhrem for his interest in the investigation in progress, for fruitful discussions, and helpful comments when discussing the experimental data and the theoretical research.

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