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CONDENSED ISOQUINOLINES. 17*. ENAMINE PROPERTIES OF BENZ-IMIDAZO[1,2-*b*]ISOQUINOLIN-11(5H)-ONE IN ALKYLATION REACTIONS

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The alkylation of benzimidazo[1,2-b]isoquinolin-11(5H)-one has been studied. This occurs at $N_{(5)}$ or $C_{(6)}$ depending on the type of alkylating agent and the reaction conditions. It was shown that $C_{(6)}$ alkylation is effected in reactions with reactive alkyl halides. A repeat alkylation occurs preferentially at the same position. Interaction with o-xylylidene dibromide leads to spiro[benzimidazo[1,2-b]-isoquinolin-6,2'-indan]-11-one and 1,6-dihydro-11H-6a,11b-diazobenzo[b]benzo[5,6]cyclohepta-[1,2,3-l,m]fluoren-11-one, which are derivatives of new heterocyclic systems.

Keywords: heterocyclic enamines, derivatives of 1,6-dihydro-11H-6a,11b-diazabenzo[*b*]benzo[5,6]-cyclohepta[1,2,3-*l,m*]fluoren-11-one and spiro[benzimidazo[1,2-*b*]isoquinolin-6,2'-indan]-11-one, alkylation.

Depending on the nature of the reagent the acylation of benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**1**) leads to the formation of two types of benzimidazoisoquinolines substituted at positions 5 or 6 [1]. These results are in complete agreement with the behavior of secondary enamines [2,3], the structural element of which is present in the compound **1** molecule. However the most characteristic reaction of enamines, alkylation, has not yet been studied among derivatives of **1**. Only two examples of this reaction are known, the $N_{(5)}$-methylation [4,5] and $C_{(6)}$-diallylation of compound **1** [5]. While continuing the investigations of alkylation in the condensed isoquinoline series [6,7] in the present work, we have studied the alkylation of benzimidazoisoquinoline **1** by various alkylating agents under various conditions.

The direction of alkylation in enamines is determined by the nature of the alkylation agent, although on alkylation with phenacyl or benzyl halides attack at the β-carbon is more preferred [2]. In reality, interaction of compound **1** with substituted α-bromoacetophenones takes place extremely vigorously with the formation of a complex mixture of products. Only in the case of reaction with *p*-bromophenacyl bromide was the $C_{(6)}$-alkylation product successfully isolated and characterized, *viz*. 6-[2-(4-bromophenyl)-2-oxoethyl]benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**2**). In the cases of phenacyl and *p*-methoxyphenacyl bromides only compound **3**, the product of oxidative dimerization of compound **1**, was successfully identified in the mixture of products. The ease of formation of compound **3** was noted by us previously [1].

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* For Part 16 see [1].

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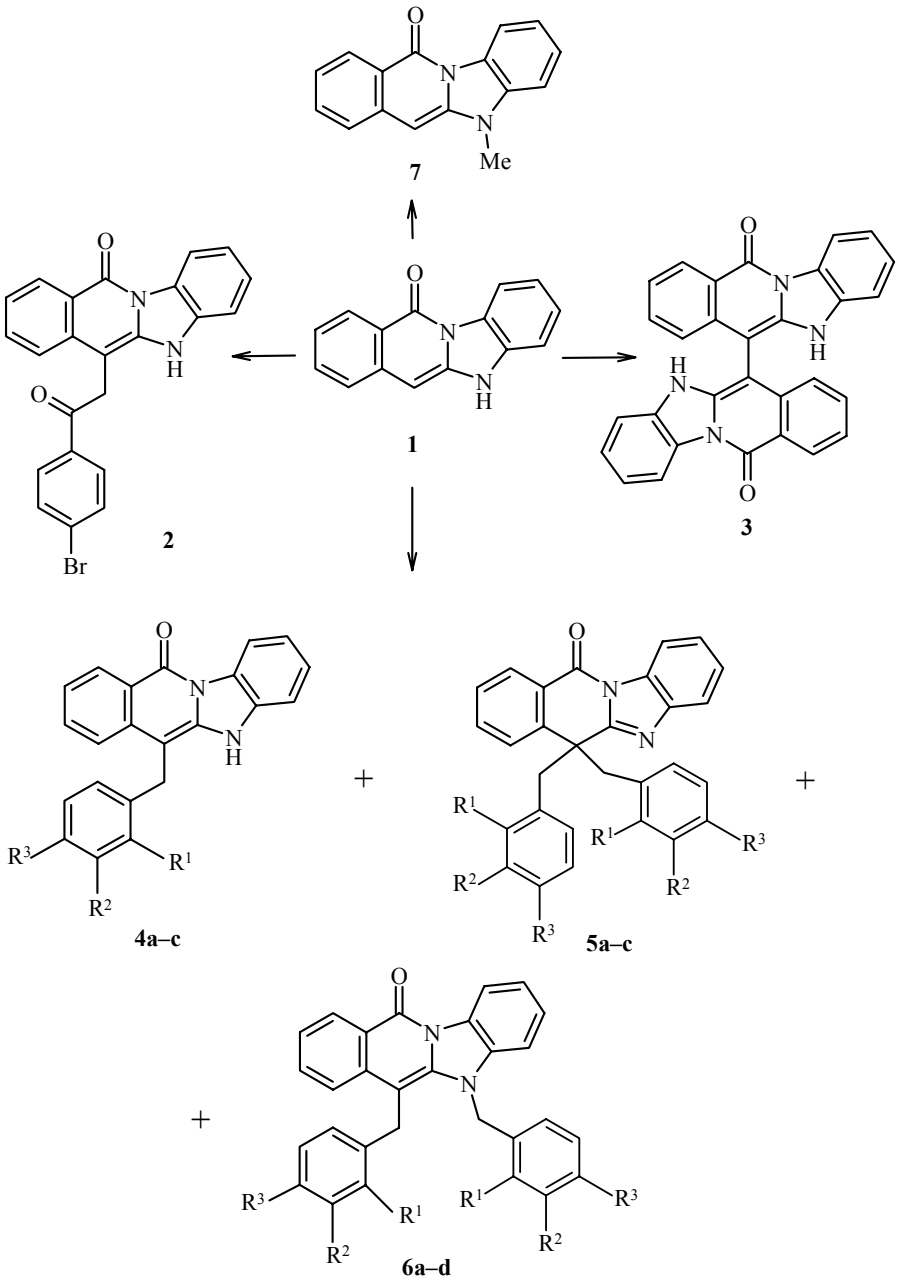


4a, **6b** $R^1 = R^3 = Me$, $R^2 = H$; **4b**, **5b**, **6c** $R^1 = R^3 = H$, $R^2 = NO_2$;
4c, **5c**, **6d** $R^1 = CN$, $R^2 = R^3 = H$, **5a**, **6a** $R^1 = R^2 = R^3 = H$

The main criterion for establishing the direction of alkylation of compound **1** was in all cases the retention or nonappearance of the signals of the $N_{(5)}\underline{H}$ or $C_{(6)}\underline{H}$ protons in the ^1H NMR spectra. For example, the structure of compound **2** as the product of $C_{(6)}$-alkylation is confirmed by the presence of the signal of the $N_{(5)}\underline{H}$ group in the IR and ^1H NMR spectra (Table 1), and also by the absence of resonance at 6.3 ppm for the $C_{(6)}\underline{H}$ observed in the initial compound **1**.

Three types of alkylation product are formed on carrying out the reaction of heterocycle **1** with benzyl halides in 2-propanol in the presence of *i*-PrONa, *viz*. 6-benzylbenzimidoazo[1,2-*b*]isoquinolin-11(5H)-ones (**4a,b**), 6,6-dibenzylbenzimidazo[1,2-*b*]isoquinolin-11(5H)-ones (**5a-c**), and 5,6-dibenzylbenzimidazo[1,2-*b*]-isoquinolin-11(5H)-ones (**6a-d**). The amount of alkyl derivatives **4-6** in the mixture formed depends on the

TABLE 1. Spectral Characteristics of 6-R-benzimidazo[1,2-*b*]isoquinolin-11(5H)-ones

Compound	IR spectrum, ν, cm^{-1}			^{1}H NMR spectrum, δ, ppm (*J*, Hz)											
	Signals of benzimidazo[1,2-*b*]isoquinoline nucleus												Signals of substituent		
	C=O	N–H	Other signals	H-5, s	H-1, d, *J* = 8.0	H-10, d, *J* = 8.0	H-8, t, *J* = 8.0	H-7, d, *J* = 8.0	H-3, t, *J* = 8.0	H-4, d, *J* = 8.0	H-9, t, *J* = 8.0	H-2, t, *J* = 8.0	Ar–H	6-CH_2, 2H, s	Other signals
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
2	1660, 1620	3280		11.72	8.65	8.37	7.60	7.50	7.41	7.31	7.28	7.22	8.12 (2H, d, *J* = 8.0, H-2', H-6'), 7.84 (2H, d, *J* = 8.0, H-3', H-5')	4.76	
4a	1650	3300		11.74	8.67	8.39	7.56	7.33	7.40	7.30	7.27	7.22	7.06 (1H, s, H-3'), 6.70 (1H, d, *J* = 8.0, H-5'), 6.48 (1H, d, *J* = 8.0, H-6')	4.14	2.48 (3H, s, 2'-C<u>H</u>$_3$), 2.19 (3H, s, 4'-C<u>H</u>$_3$)
4b	1650	3200	1560, 1340 ($^{s,as}NO_2$)	11.97	8.65	8.37	7.63-7.57 (2H, m)		7.42	7.35	7.27	7.23	8.16 (1H, s, H-2'), 8.03 (1H, d, *J* = 8.0, H-4'), 7.67 (1H, d, *J* = 8.0, H-6'), 7.52 (1H, t, *J* = 8.0, H-5')	4.46	

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
4c	1655	3180	2200 (CN)	11.92	8.67	8.40	7.59	—*	—*	7.34	7.28	7.24	7.89 (1H, d, *J* = 8.0, H-3', 7.47-7.37 (4H, m, H-3, H-7, H-4', H-5'), 7.03 (1H, d, *J* = 8.0, H-6')	4.52	
8	1650	3200		11.69 (2H)	8.71 (2H)	8.45 (2H)	7.63 (2H)	7.59 (2H)	7.37 (2H)	7.34 (2H)	7.29 (2H)	7.19 (2H)	6.88 (2H, m, H-3', H-4'), 6.75 (2H, m, H-2', H-6')	4.54 (4H)	
11	1655	3180	3280, 3410 ($^{s,as}NH_2$)	12.29	8.63	8.37	7.58	7.47	7.32	7.25-7.12 (5H, m, H-2, H-4, H-9, H-4', H-5')			7.71 (1H, d, *J* = 7.2, H-3'), H-4', H-5'*^{2}, 6.98 (1H, d, *J* = 7.2, H-6')	4.41	8.13 (1H, s, $N\underline{H}_A H_B$), 7.74 (1H, s, $NH_A\underline{H}_B$)
13a	1655	3200	3300, 3410 ($^{s,as}NH_2$)	11.84	8.64	8.37	—*	—*^{2}	7.33	7.27-7.13 (5H, m, H-2, H-4, H-7, H-9, H-4')			7.58-7.54 (2H, m, H-8, H-5'), 7.67 (1H, d, *J* = 8.0, H-3'), H-4'*^{2}, 6.95 (1H, d, *J* = 7.2, H-6')	4.41	10.12 (1H, s, –N'$\underline{H}$N"H–$CONH_2$), 8.11 (1H, s, –N'HN"$\underline{H}$–$CONH_2$), 5.99 (2H, s, $N\underline{H}_2$)
13b	1640, 1710	3050	1230 (C–O)	11.63	8.66	8.39	8.49	—*	7.27-7.21 (4H, m, H-3, H-4, H-9, H-4')			7.15	7.94 (1H, m, H-3'), 7.37-7.30 (2H, m, H-7, H-5'), H-4'*^{2}, 6.90 (1H, m, H-6')	4.62	3.97 (3H, s, $O\underline{CH}_3$)

* Overlap of signals of benzimidazo[1,2-*b*]isoquinoline nucleus and signals of substituent, see column 14.

*^{2} Overlap of signals of benzimidazo[1,2-*b*]isoquinoline.

nature of the substituent in the benzyl radical and on the ratio of the reactants used in the reaction. At an equivalent ratio of reactants (method A) only in the case of 2,4-dimethylbenzyl chloride was a single reaction product, the monobenzyl derivative **4a**, obtained. In the remaining experiments mixtures were formed either of the initial **1** with dibenzyl derivatives (**5a**, **6a**, and **5c**, **6d**), or, as in the case of 3-nitrobenzyl chloride, a mixture of mono- and dibenzyl derivatives (**4b**, **5b**). The use of a twofold excess af alkylating agent (method B) leads to an increase in the overall alkylation yield and a growth in the proportion of dibenzylation products. However in this case also the predominant product with 2,4-dimethylbenzyl chloride (mixture of **4a**, **6b**) remains the 6-benzyl derivative **4a**, probably caused by the reduced reactivity of the reactant itself, and also by steric hindrance from the side of the *ortho* substituent towards a second attack at position 6. The 5,6-dialkyl derivatives **6a-d** are formed in low yield (10-25%). Only the 5,6-dibenzyl derivative **6a** was isolated and characterized, and in the remaining cases the presence of compounds of the type of **6** were recorded in the mixture with the aid of ^{1}H NMR spectra of the unpurified reaction products.

The benzylation of compound **1** by fusion is complicated in many cases by significant resinification. On fusing **1** with benzyl chloride (180°C) the 6,6-dibenzyl derivative **5a** is obtained in low yield (20%), but on using *o*-bromomethylbenzonitrile the monobenzylation product **4c** was isolated successfully. Attempts at a repeat alkylation (without base and on fusing) of the mono-6-benzyl derivatives **4a-c** to the dibenzyl derivatives led to the formation of mixtures of unidentified products. On carrying out the benzylation of heterocycle **1** without base by heating a mixture of the reactants in DMF or MeCN, the formation of dimer **3**, already mentioned above, was observed.

The obtained data indicate the participation of nitrogen analogs of enolate ions in the benzylation in the presence of *i*-PrONa, generated both from the initial benzimidazoisoquinoline **1**, and from compounds **4**. The impossibility of forming such an anion for 5-methylbenzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**7**), obtained previously [4,5], explains the inertness of the latter in this reaction. It may therefore be stated that the main direction of alkylation of compound **1** is at position $C_{(6)}$. The repeat alkylation also takes place predominantly at the same position.

The structure of the benzylation products **4-6** was established by spectral methods (Tables 1, 2). For all three types of benzyl derivatives the signal of the $C_{(6)}\underline{H}$ methine proton observed at 6.3 ppm in the initial compound **1** was absent from the ^{1}H NMR spectra. In the spectra of the monobenzyl derivatives **4a,b** there are signals for the $N_{(5)}\underline{H}$ group (at 11.7-11.9 ppm in the ^{1}H NMR spectrum and at 3100 cm^{-1} in the IR spectrum), which are absent from the spectra of the dibenzyl derivatives **5a-c**, **6a**. The observed differences in signal form and the chemical shifts of the methylene protons of the benzyl substituents of dibenzyl derivatives **5** and **6** also enable their structures to be determined unequivocally. The methylene protons of 5,6-dibenzyl derivatives **6a-d** are observed as two singlets at 3.8-4.4 ($C_{(6)}$–$C\underline{H}_2$) and 5.0-5.6 ppm ($N_{(5)}$–$C\underline{H}_2$), and the signal of the methylene groups in 6,6-dibenzyl derivatives **5a-c** at 3.9-4.2 ppm is observed as an AB spin system with geminal coupling constant 13.2 Hz. The nonequivalence of the methylene group protons at $C_{(6)}$ in compounds **5a-c** is evidently caused by steric hindrance to rotation about the $C_{(6)}$–CH_2–Ar single bonds.

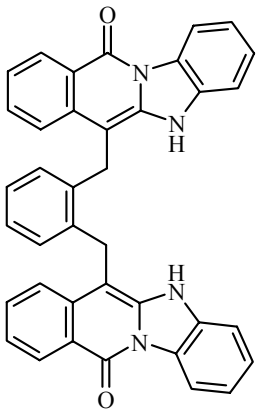
The data on the benzylation of compound **1** and also the possibility of intramolecular alkylation discovered by us previously [1] using 6-(α-halo)acetyl derivatives of **1** as examples enabled us to hope for successful heterocyclization using a reactant with two alkylating functions, *o*-xylylidene dibromide. On carrying out the reaction in the presence of an equivalent quantity of *i*-PrONa we obtained the unusual monoalkylation product 6-{2-[11-oxo-5,11-dihydrobenzo[4,5]imidazo[1,2-*b*]isoquinolin-6-yl)methyl]benzyl}benzo[4,5]imidazo-[1,2-*b*]isoquinolin-11(5H)-one (**8**). The use of a twofold excess of base leads to a mixture of derivatives of two new heterocyclic systems, spiro(benzimidazo[1,2-*b*]isoquinolin-6,2'-indan)-11-one (**9**) and 1,6-dihydro-11H-6a,11*b*-diazabenzo[*b*]benzo[5,6]cyclohepta[1,2,3-*l,m*]fluoren-11-one (**10**) in a 1:5 ratio.

TABLE 2. Spectral Characteristics of 6,6-Dibenzyl Derivatives **5a-c** and Spiro-substituted Compounds **9**, **12**

Compound	IR spectrum, ν, cm^{-1}		^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz)										
			Signals of the benzimidazo[1,2-*b*]isoquinoline nucleus								Signals of substituents		
	C=O	Other signals	H-1, d, *J* = 8.0	H-10, d, *J* = 8.0	H-4, d, *J* = 8.0	H-2, t, *J* = 8.0	H-7, d, *J* = 8.0	H-3, t, *J* = 8.0	H-8, t, *J* = 8.0	H-9, t, *J* = 8.0	Ar–H	6-C$\underline{H}_A$H$_B$, 2H, d	6-CH$_A\underline{H}_B$, 2H, d
1	2	3	4	5	6	7	8	9	10	11	12	13	14
5a	1700		8.31	8.09	7.92	7.90-7.88 (2H, m)		7.48	7.46	7.35	6.86 (2H, t, *J* = 8.0, H-4'), 6.75 (4H, t, *J* = 8.0, H-3', H-5'), 6.39 (4H, d, *J* = 8.0, H-2', H-6')	4.02 (*J* = 13.2)	3.79 (*J* = 13.2)
5b	1700	1510, 1340 ($^{s,as}NO_2$)	8.53		8.07-8.00 (3H, m)		7.95	7.59	7.53	7.42	7.80 (2H, d, *J* = 8.0, H-4'), 7.29 (2H, s, H-2'), 7.15 (2H, t, *J* = 8.0, H-5'), 6.86 (2H, d, *J* = 8.0, H-6')	4.14 (*J* = 13.2)	4.06 (*J* = 13.2)
5c	1700	2210 (CN)	8.22	8.11	8.07	7.84-7.80 (2H, m)		7.56	7.50-7.42 (4H, m, H-8, H-9, H-3')		H-3'*, 7.18 (2H, t, *J* = 8.0, H-5'), 7.08 (2H, t, *J* = 8.0, H-4'), 6.31 (2H, d, *J* = 8.0, H-6')	4.26 (*J* = 13.2)	4.15 (*J* = 13.2)
9	1695		8.38 (m)	8.31	7.64 (2H, m)		7.34	7.55	7.41-7.38 (2H, m)		7.30 (4H, m, H-4' – H-7')	4.11 (*J*= 16.5)	3.58 (*J* = 16.5)
12	1710 (br.)		8.43-8.40 (2H, m)		7.89 (2H, m, H-4, H-7')	7.74-7.61 (4H, m, H-2, H-3, H-7, H-5')			7.44	7.39	H-5', H-7'*[2], 7.58 (1H, t, *J* = 8.0, H-6'), 7.23 (1H, d, *J* = 8.0, H-4')	4.57 (1H, *J* = 18.0)	4.04 (1H, *J* = 18.0)

* Overlap of signals of benzimidazo[1,2-*b*]isoquinoline nucleus and signals of a substituent, see columns 10, 11.

*[2] Overlap of signals of benzimidazo[1,2-*b*]isoquinoline nucleus and signals of a substituent, see columns 6-9.



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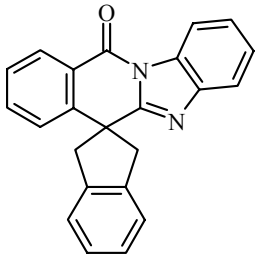

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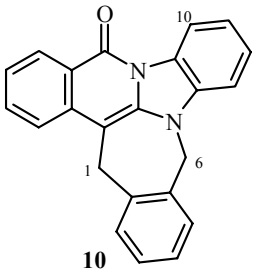

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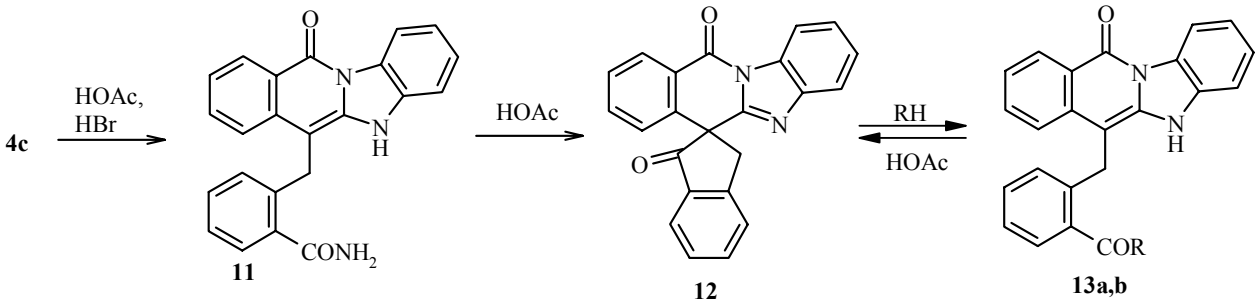
The structures of products **8-10** were confirmed by their spectral data (Tables 1, 2) which were extremely similar to the spectra of benzyl and dibenzyl derivatives **4-6**. Among their special features may be noted the position of the $C_{(7)}\underline{H}$ proton signal in the ^{1}H NMR spectrum of spiro product **9** observed at higher field (7.34 ppm) compared with the corresponding signal of 6,6-dibenzyl derivatives **5a-c** due to shielding of the spiroindane fragment by the benzene ring.

In connection with the ease of acylation of compound **1** it seemed of interest to investigate the problem of the acylation of alkyl-substituted benzimidazoisoquinolines. Experiments on the acylation of compound **7** showed its inertness. The 6-benzyl derivatives **4a,b** in dioxane in the absence of base did not interact with acylating agents, and in pyridine gave a mixture of unidentified products. The conversion of 6-(2-cyanobenzyl)benzimidazoisoquinoline **4c** described above proved to be extremely interesting. On boiling in acetic acid in the presence of HBr this compound is hydrolyzed to amide **11**, but on more extended heating in acetic acid it is possible to obtain the product of intramolecular acylation, spiro(benzimidazo[1,2-*b*]isoquinolin-6(11H),2'-indan)-1',11-dione (**12**).



13 a R = $NHNHCONH_2$, **b** R = OMe

We drew a conclusion on the spiro structure of compound **12** on the basis of data of its ^{1}H NMR spectrum. Apart from the absence from the low field region of signals of exchanging protons of the NH type, which corresponds both to the $C_{(6)}$ acylation product and to the $N_{(5)}$ acylation product, attention is attracted primarily by the position and form of the methylene group proton signal. Two one-proton doublets with J = 18.0 Hz were recorded in the region of 4.0 and 4.5 ppm which correspond in position and form to the

TABLE 3. Physicochemical Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield, % (method)
		C	H	N		
2*[2]	$C_{23}H_{15}BrN_2O_2$	63.96 / 64.05	3.45 / 3.51	6.58 / 6.50	248 (dec.)	65
4a	$C_{24}H_{20}N_2O$	81.69 / 81.79	5.65 / 5.72	8.01 / 7.95	211	57 (A), 45 (B)
4b	$C_{22}H_{15}N_3O_3$	71.50 / 71.54	4.00 / 4.09	11.45 / 11.38	270	31 (A)
4c	$C_{23}H_{15}N_3O$	78.98 / 79.07	4.30 / 4.33	12.10 / 12.03	201	75
5a	$C_{29}H_{22}N_2O$	83.92 / 84.03	5.48 / 5.35	6.86 / 6.76	159	40 (A), 55 (B)
5b	$C_{29}H_{20}N_4O_5$	68.94 / 69.04	3.95 / 4.00	11.19 / 11.11	195	34 (A), 55 (B)
5c	$C_{31}H_{20}N_4O$	80.07 / 80.15	4.26 / 4.34	12.10 / 12.06	134	47 (A), 63 (B)
8	$C_{38}H_{26}N_4O_2$	79.88 / 79.98	4.50 / 4.59	9.85 / 9.82	204	60
9	$C_{23}H_{16}N_2O$	82.10 / 82.12	4.72 / 4.79	8.35 / 8.33	240	18
11	$C_{23}H_{17}N_3O_2$	75.09 / 75.19	4.61 / 4.66	11.47 / 11.44	294	76
12	$C_{23}H_{14}N_2O_2$	78.74 / 78.84	3.95 / 4.03	8.05 / 8.00	282	63
13a	$C_{24}H_{19}N_5O_3$	67.74 / 67.76	5.54 / 5.50	16.43 / 16.46	295	57
13b	$C_{24}H_{18}N_2O_3$	75.30 / 75.38	4.68 / 4.74	7.37 / 7.33	215	75

* Compound **4a** was recrystallized from MeCN, **5a** from EtOH, and the remainder from DMF.

*[2] Analytical data for Br: 18.56% (found), 18.53% (calculated).

protons of the methylene groups of spiro compound **9**, also observed as an AB spin system with J = 16.5 Hz (Table 2). In the ^{13}C NMR spectrum two signals were observed in the region of absorption of aliphatic carbon atoms assigned by us to the resonance of $C_{(spiro)}$ (56.68 ppm) and $C_{(3')}H_2$ (42.55 ppm) and there was a signal for $C_{(1')}$ (199.94 ppm) characteristic of the absorption of carbonyl carbon atoms [8]. In the IR spectrum a broad band was observed at 1710 cm^{-1} corresponding to the vibrations of two carbonyl groups. The formation of the intramolecular acylation product was also confirmed by mass spectral data (350 $[M]^+$, 39%).

Spiroindanone **12**, being fairly stable in acid media, proved to be extremely sensitive to the action of bases. The spiroindanone ring was easily broken with the formation of derivatives of 6-(2-carboxybenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one. On attempting to obtain the semicarbazone we isolated the acylated semicarbazide **13a**, and on boiling in methanol in the presence of Et_3N the methyl ester **13b** was obtained.

EXPERIMENTAL

The melting points of the synthesized compounds were determined on Boetius type heating equipment and are not corrected. The IR spectra (KBr disks) were recorded on a Pye-Unicam SP 3-300 instrument. The ^1H and ^{13}C NMR spectra were obtained on a Varian Mercury 400 instrument (400 MHz for ^1H and 100 MHz for

^{13}C) in DMSO-d_6, internal standard was TMS. The assignment of signals of the aromatic protons was confirmed by data of COSY HH spectra for compounds **2**, **5a**, **6a**, **10**, and **12**. The mass spectra were obtained on a Waters Integrity System instrument, with a Thermabeam detector (mobile phase CH_3CN). A check on the progress of reactions and the purity of the compounds obtained was effected by TLC on Silufol UV-254 plates. The characteristics of the compounds obtained are given in Tables 1-3.

Benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**1**) was obtained by the procedure of [4], and 5-methylbenzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**7**) by the procedure of [5].

6-[2-(4-Bromophenyl)-2-oxoethyl]benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (2). *p*-Bromophenacyl bromide (3.61 g, 13 mmol) was added to a solution of benzimidazoisoquinoline **1** (2.34 g, 10 mmol) in DMF (10 ml) and the mixture boiled for 40 min. After cooling, the precipitated solid was filtered off, and washed with acetone. Recrystallization was from DMF.

Alkylation of Benzimidazo[1,2-*b*]isoquinolin-11(5H)-ones with Benzyl Halides in Solution was carried out using various ratios of reactants calculated on heterocycle **1** (10 mmol). A. Sodium (0.25 g, 11 mmol) and benzyl halide (11 mmol). B. Sodium (0.5 g, 22 mmol) and benzyl halide (22 mmol).

Compound **1** (2.34 g, 10 mmol) was added to a solution of sodium isopropylate in 2-propanol (10 ml) and dissolved on heating. The appropriate benzyl halide was added to the solution obtained and the mixture boiled for 1.5-2 h. After cooling the reaction mixture, the solid formed was filtered off, washed thoroughly with water, and with alcohol, and recrystallized from DMF. Further isolation of products was carried out separately from the solid and the filtrate.

When using benzyl chloride (method A) a solid (0.93 g) was obtained consisting, according to data of the ^1H NMR spectrum*, of compound **6a** and initial **1** in a ratio of 1:1. On alkylation by method B the solid (1.03 g) consisted exclusively of 5,6-dibenzylbenzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**6a**), the yield of which was 25%; mp 242-244°C (DMF). IR spectrum, ν, cm^{-1}: 1650 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.79 (1H, d, *J* = 8.0, $C_{(1)}\underline{H}$); 8.42 (1H, d, *J* = 8.0, $C_{(10)}\underline{H}$); 7.56 (1H, t, *J* = 8.0, $C_{(8)}\underline{H}$); 7.46 (1H, d, *J* = 8.0, $C_{(7)}\underline{H}$); 7.23-7.37 (8H, m, $C_{(2)}\underline{H}$-$C_{(4)}\underline{H}$, $C_{(9)}\underline{H}$, $C_{(3')}\underline{H}$, $C_{(5')}\underline{H}$); 7.19 (2H, m, $C_{(4')}\underline{H}$); 7.10 (4H, m, $C_{(2')}\underline{H}$, $C_{(6')}\underline{H}$; 5.26 (2H, s, 5-$C\underline{H}_2$); 4.18 (2H, s, 6-$C\underline{H}_2$). Found, %: C 83.96; H 5.30; N 6.79. $C_{29}H_{22}N_2O$. Calculated, %: C 84.03; H 5.35; N 6.76.

When alkylating with 2,4-dimethylbenzyl chloride by method A the solid consisted exclusively of NaCl. On alkylating by method B the solid (0.25 g) contained a mixture of **6-(2,4-dimethylbenzyl)benzimidazo-[1,2-*b*]isoquinolin-11(5H)-one (4a) and 5,6-di(2,4-dimethylbenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (6b).** According to the data of the ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.81 (m, ArH); 8.45 (m, ArH); 6.30-7.60 (m, ArH); 5.03 (s, 5-$C\underline{H}_2$, **6b**); 4.15 (s, 6-$C\underline{H}_2$, **4a**); 3.83 (s, 6-$C\underline{H}_2$, **6b**); 2.49 (s, 2'-$C\underline{H}_3$, **4a**); 2.23 (s, 5-[2',4'-$(C\underline{H}_3)_2C_6H_4CH_2$], **6b**); 2.19 (s, 4'-$C\underline{H}_3$, **4a**); 1.96 (s, 6-(2'-$C\underline{H}_3$-4'-CH_3-$C_6H_4CH_2$), **6b**); 1.85 [s, 6-(2'-CH_3-4'-$C\underline{H}_3$-$C_6H_4CH_2$), **6b**], ratio **4a**:**6b**, 5:1.

By method A from 3-nitrobenzyl chloride a mixture (0.22 g) was obtained, consisting, according to data of the ^1H NMR spectrum, of **6-(3-nitrobenzyl)-benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (4b)** and initial **1** in a ratio of 3:2. By method B a mixture (0.3 g) was obtained of the 6-benzyl derivative **4b** and **5,6-di(3-nitrobenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (6c)**. According to data of the ^1H NMR spectrum, δ, ppm (*J*, Hz): 11.96 (br. s, N$\underline{H}$, **4b**); 8.35-8.90 (m, ArH); 7.15-8.19 (m, ArH); 5.65 (s, 5-$C\underline{H}_2$, **6c**); 4.47 (s, 6-$C\underline{H}_2$, **4b** and 6-$C\underline{H}_2$, **6c**), the **4b**:**6c** ratio in the mixture was 5:1.

On using 2-cyanobenzyl bromide (method A) a mixture (0.23 g) was obtained consisting, according to data of the ^1H NMR spectrum, of 5,6-di(2-cyanobenzyl)-benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (**6d**) and initial **1** in a ratio of 1:3. By method B a mixture (0.2 g) was obtained of 6,6-di(2-cyanobenzyl)benzimidazo-[1,2-*b*]isoquinolin-11(5H)-one (**5c**) and the 5,6-dibenzyl derivative **6d**. According to data of the ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.05-8.85 (m, ArH); 7.10-7.90 (m, ArH); 6.30 (m, ArH); 5.46 (s, 5-$C\underline{H}_2$, **6d**); 4.05-4.28 (m, 6-$C\underline{H}_2$, **5c** and 6-$C\underline{H}_2$, **6d**), the ratio of **5c:6d** in the mixture was 1:6.

*Data of the ^1H NMR spectrum of the initial compound **1** are given in [1].

The filtrate was evaporated in vacuum, water (15 ml) was added to the residual oil, and the mixture left for 1 day. The solid formed was filtered off, and washed with a small amount of 2-propanol. On using benzyl chloride by method A 1.65 g (40%) and by method B 2.26 g (55%) of **6,6-dibenzylbenzimidazo[1,2-*b*]-isoquinolin-11(6H)-one (5a)** was obtained.

When using 2,4-dimethylbenzyl chloride by method A 2.0 g (57%) or method B 1.58 g (45%) of **6-(2,4-dimethylbenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (4a)** was obtained (Tables 1 and 3).

When using 3-nitrobenzyl chloride a mixture was obtained (method A) of **6-(3-nitrobenzyl)-benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (4b) and 6,6-di(3-nitrobenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (5b)**, which was separated by recrystallization from DMF (Tables 1-3). The solid precipitated on cooling was filtered off and the monobenzyl derivative **4b** (1.14 g, 31%) was obtained. Water was added to the filtrate and the precipitate of dibenzyl derivative **5b** was filtered off. Yield 1 g (34%). The 6,6-dibenzyl derivative **5b** (1.67 g, 55%) was obtained by method B.

Using *o*-bromomethylbenzonitrile compound **5c** (2.18 g by method A or 2.92 g by method B) was obtained (Tables 2 and 3).

6-(2-Cyanobenzyl)benzo[4,5]imidazo[1,2-*b*]isoquinolin-11(5H)-one (4c) (Tables 1 and 3). A mixture of compound **1** (2.34 g, 10 mmol) and *o*-bromomethylbenzonitrile (2.94 g, 15 mmol) was fused on an oil bath at 135°C for 40 min. The mixture was cooled, and acetone (10 ml) added. The resulting solid was filtered off, washed with acetone, and dissolved with heating in morpholine (5 ml). After cooling, water (20 ml) was added, and the solid formed was filtered off.

6-{2-[(11-Oxo-5,11-dihydrobenzo[4,5]imidazo[1,2-*b*]isoquinol-6-yl)methyl]-benzyl}benzo[4,5]-imidazo[1,2-*b*]isoquinolin-11(5H)-one (8) (Tables 1 and 3). Compound **1** (2.34 g, 10 mmol) was added to a solution of *i*-PrONa (0.9 g, 11 mmol) in 2-propanol (10 ml), and dissolved on heating. *o*-Xylylidene dibromide (3.16 g, 12 mmol) was added and the mixture was boiled for 1.5-2 h. The resulting solid was filtered off, and the filtrate evaporated in vacuum. Water (15 ml) was added to the residual oil, and the mixture was left for 1 day. The solid was filtered off, washed thoroughly with water, and with alcohol, and recrystallized from DMF.

1,6-Dihydro-11H-6*a*,11*b*-diazabenzo[*b*]benzo[5,6]cyclohepta[1,2,3-*l,m*]fluoren-11-one (10). Benz-imidazoisoquinoline **1** (2.34 g, 10 mmol) was added to a solution of sodium (0.5 g, 22 mmol) in 2-propanol (10 ml) and dissolved on heating. *o*-Xylylidene dibromide (3.16 g, 12 mmol) was added to the solution obtained, and the mixture was boiled for 1.5 h. After cooling the solid formed was filtered off. Further isolation of alkylated products was carried out separately for the solid and the filtrate (see below). The solid formed was filtered off, washed thoroughly with water, and recrystallized from DMF. Yield 2.18 g (65%); mp 246-248°C (DMF). IR spectrum, ν, cm^{-1}: 1645 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 8.64 (1H, d, *J* = 8.0, $C_{(10)}\underline{H}$); 8.36 (1H, d, *J* = 8.0, $C_{(12)}\underline{H}$); 8.04 (1H, d, *J* = 8.0, $C_{(15)}\underline{H}$); 7.70 (2H, m, $C_{(7)}\underline{H}$, $C_{(14)}\underline{H}$); 7.54 (1H, dd, J_o = 8.0, J_m = 2.0, $C_{(5)}\underline{H}$); 7.43 (2H, m, $C_{(2)}\underline{H}$, $C_{(8)}\underline{H}$); 7.22-7.30 (3H, m, $C_{(3)}\underline{H}$, $C_{(4)}\underline{H}$, $C_{(13)}\underline{H}$); 7.16 (1H, t, *J* = 8.0, $C_{(9)}\underline{H}$); 5.58 (2H, s, 6-$C\underline{H}_2$); 4.50 (2H, s, 1-$C\underline{H}_2$). Found, %: C 82.09; H 4.70; N 8.32. $C_{23}H_{16}N_2O$. Calculated, %: C 82.12; H 4.79; N 8.33.

Spiro(benzimidazo[1,2-*b*]isoquinolin-6,2'-indan)-11-one (9) (Tables 2 and 3) was isolated from the filtrate remaining after filtering off cycloheptafluorene **10**. The solvent was evaporated in vacuum, water (10 ml) was added to the residual oil, and the mixture left for 1 day. The solid formed was filtered off, washed with water, and with alcohol, and recrystallized from DMF.

6-(Carbamoylbenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (11) (Tables 1 and 3). A mixture of benzimidazoisoquinoline **1** (2.34 g, 10 mmol) and *o*-bromomethylbenzonitrile (2.94 g, 15 mmol) was melted in an oil bath at 135°C for 40 min. The mixture was cooled and acetone (10 ml) was added. The resulting solid was filtered off and washed with acetone. The solid substance obtained was boiled for 3 h in acetic acid (15 ml), during which time the hydrobromide of the 6-(2-cyanobenzyl)-substituted compound **4c** gradually dissolved and the solid benzamide **11** was precipitated. After cooling, the solid was filtered off, washed with AcOH, and with alcohol, and recrystallized from AcOH.

Spiro[benzimidazo[1,2-*b*]isoquinolin-6(11H),2'-indan]-1',11-dione (12) (Tables 2 and 3). A suspension of benzamide **11** (3.67 g, 10 mmol) in AcOH (20 ml) was boiled for 4 h. The initial benzamide gradually dissolved. After cooling, the precipitated solid was filtered off, washed with AcOH, and with alcohol, and recrystallized from DMF. ^{13}C NMR spectrum, δ, ppm: 199.94 (C-1'); 155.29 (C-3'a); 154.13 (C-5a); 142.73 (C-4a); 139.69 (C-6a); 137.33 (C-5'); 135.70 (C-8); 132.32 (C-7'a); 131.69 (C-11b); 129.41, 129.14, 127.75, 126.36, 126.17, 125.94, 125.85, 125.51 (C-2, C-3, C-7, C-9, C-10, C-10a, C-4', C-6', C-7'); 119.99 (C-4); 115.54 (C-1); 56.68 (C-6); 42.55 (C-3'). Mass spectrum, *m/z* (*I*, %): 350 (39) $[M]^+$, 321 (41), 292 (6).

6-(2-Semicarbazidocarbonylbenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (13a) (Tables 1 and 3). A mixture of semicarbazide hydrochloride (2 g) and anhydrous sodium acetate (2 g) in absolute ethanol (20 ml) was boiled and filtered hot. Spiroindanone **12** (0.9 g, 2.6 mmol) was added to the filtrate and the mixture was heated on the water bath for 1.5 h until complete solution of the initial compound. Water (10 ml) was added, and the mixture cooled. The precipitated solid was filtered off, washed with water, and with alcohol, and recrystallized from DMF.

6-(2-Methoxycarbonylbenzyl)benzimidazo[1,2-*b*]isoquinolin-11(5H)-one (13b) (Tables 1 and 3). Triethylamine (2 ml) was added to a suspension of spiroindanone **12** (1.75 g, 5 mmol) in methanol (20 ml) and the mixture was boiled for 4 h. The initial compound gradually dissolved and solid methyl benzoate **13b** was precipitated. After cooling, the solid was filtered off, washed with methanol, and recrystallized from DMF.

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