Synthesis of hexahydroazonino[5,6-*b*]indoles from hexahydroazepino[4,3-*b*]- and -[3,4-*b*]indoles and activated alkynes

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A reaction of substituted hexahydroazepino[4,3-*b*]- and -[3,4-*b*]indoles with activated alkynes was studied. A one-step method for the synthesis of isomeric hexahydroazonino[5,6-*b*]indoles different by positions of the double bond in the azonine ring was developed.

Key words: hexahydroazepino[3,4-*b*]indoles, hexahydroazepino[4,3-*b*]indoles, azonino[5,6-*b*]indoles, ring expansion.

An azonine fragment, annulated with an indole one, is a structural part of such alkaloids, as strychnine, vinblastine, vincristine, ibogaine, and coronaridine, which show various and high biological activities. Only few versions of three- or four-step methods for the synthesis of monocyclic octahydroazonino[5,4-*b*]indoles, which were considered as the dopamine and serotonin receptors antagonists, are described.[1—3] All these versions are based on the transformations of tryptamine. We developed a methodology for the transformation of [*c*]fused tetrahydropyridines to tetrahydroazocines upon treatment with activated alkynes.[4,5] Recently, a possibility for the synthesis by this method of derivatives of a new heterocyclic system, *viz.*, hexahydroazonino[5,6-*b*]indoles isomeric in the position of the double bond in the azonine ring, was shown on a model reaction of hexahydroazepino[4,3-*b*]- and -[3,4-*b*]indoles with methyl propiolate.[6] In the present communication, some characteristics of the reaction of hexahydroazepino[4,3-*b*]- and -[3,4-*b*]indoles with methyl propiolate, acetyl- and tosylacetylenes, as well as with dimethyl acetylenedicarboxylate (DMAD), are considered.

Hexahydroazepino[4,3-*b*]indoles **1—5** were prepared from 1-oxotetrahydrocarbazoles according to the procedure described earlier.[6] Compounds **4** and **5** were synthesized for the first time. Hexahydroazepinoindoles **1—5** quantitatively react with terminal alkynes at 20—25 °C in methanol, giving hexahydroazoninoindoles **6—14** (Scheme 1). 9-Fluorine-substituted azepinoindole **5** reacts slower (4 h) than unsubstituted and 9-methyl-substituted derivatives **1—4** (0.5—2 h), which, apparently, is caused by the electron-withdrawing effect of the fluorine atom, destabilizing the transition zwitterionic state **A**.

Suggested chemistry of the transformation is given in Scheme 1. It includes addition of the amine nitrogen atom at the triple bond of the alkyne to form zwitterion **A**, in which the C(1)—N bond is loosened and polarized. The subsequent nucleophilic assistance of the solvent through the transition state **B** leads to the target products **6—14**. Formation in methanol of only azoninoindoles **6—14** was quite unexpected by us, since their structural analogs, tetrahydro-γ-carbolines, upon treatment with ethyl propiolate in ethanol give a mixture of tetrahydroazocinoindoles and 2-(ethoxycarbonylvinylaminoethyl)-3-ethoxymethylindoles.[5] This distinction is caused, apparently, by the higher strain in the hydrogenated azepine ring in comparison with the piperidine one, which leads to the higher loosening of the C(1)—N bond, resulting in only push-pull assistance of the solvent for the reaction to be finished.

It was experimentally shown that the yield of azoninoindole **14** in the reaction of azepinoindole **3** with methyl propiolate in methanol was 20% higher than in acetonitrile. That is why we used methanol as the solvent for the transformations of other azepinoindoles.

9-Fluorine-substituted tetrahydroazepino[3,4-*b*]indoles **15** and **16**, obtained from 4-oxotetrahydrocarbazoles according to the known procedure,[6] react with tosyl- and acetylacetylenes in methanol at 25 °C as easy as their isomers **1—5** to give products of the azepine ring expansion, hexahydroazoninoindoles **17—20** (Scheme 2).

In the reaction with DMAD in methanol, azepinoindoles **1** and **5** give (Scheme 3) mixtures of azoninoindoles **21**, **23** and the corresponding 3-methoxymethyl-substituted indoles **22**, **24**, which result from the tandem cleavage of the hexahydroazepine ring.

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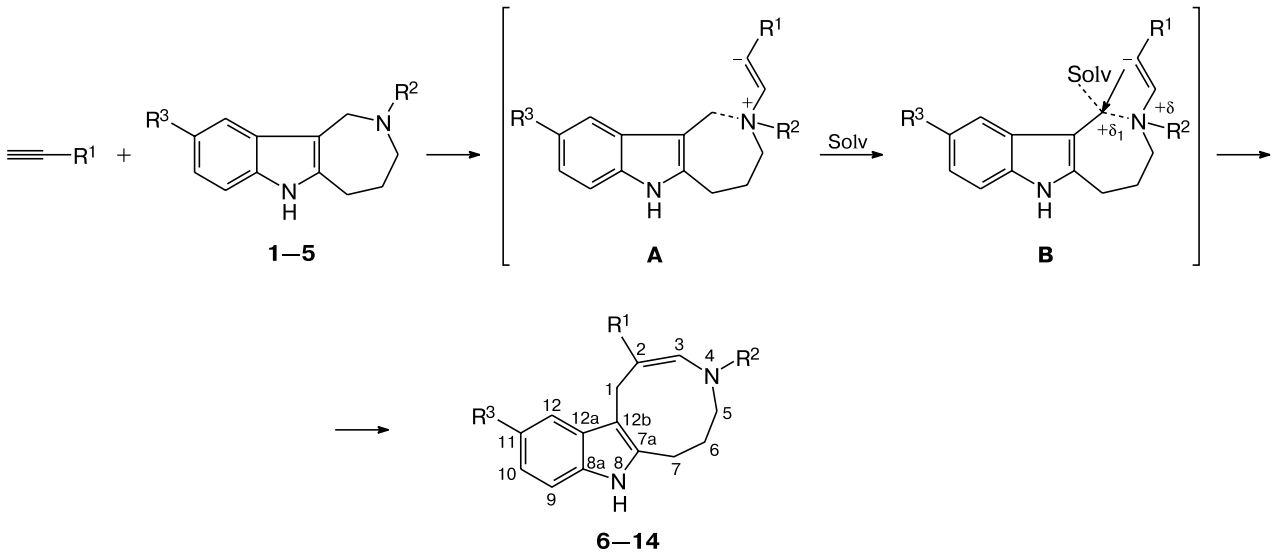
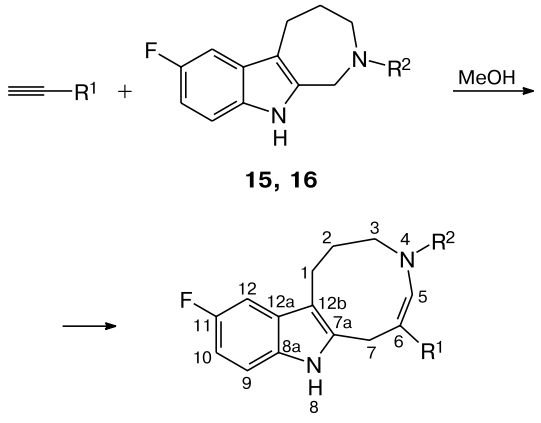
Scheme 1



Solv — solvent

Compound	R^2	R^3	Compound	R^1	R^2	R^3	Compound	R^1	R^2	R^3
1	Et	Me	**6**	Ts	Et	Me	**11**	Ac	Et	H
2	Bn	Me	**7**	Ts	Bn	Me	**12**	COOMe	Bn	H
3	Et	H	**8**	Ts	Et	H	**13**	COOMe	Bn	F
4	Bn	H	**9**	Ac	Et	Me	**14**	COOMe	Et	H
5	Bn	F	**10**	Ac	Bn	Me				

Scheme 2



Com-pound	R^2	Com-pound	R^1	R^2	Com-pound	R^1	R^2
15	Et	**17**	Ts	Et	**19**	Ac	Et
16	Bn	**18**	Ts	Bn	**20**	Ac	Bn

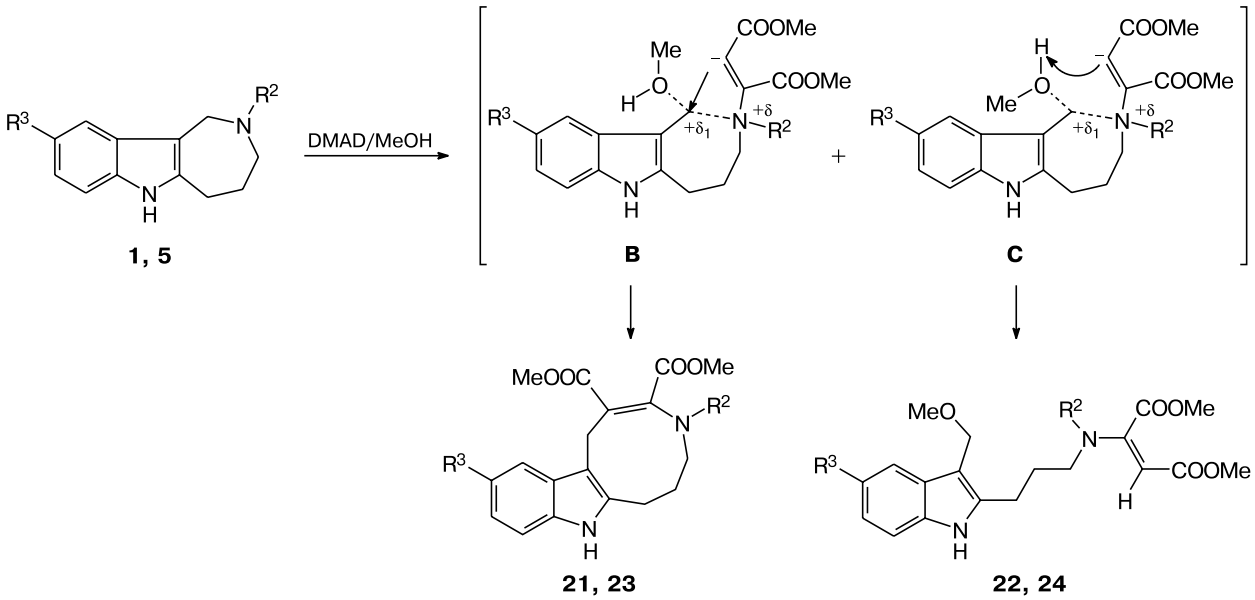
Azepinoindoles **2** and **3** show the similar behavior in the reaction with DMAD.[6] Characteristics of the compounds synthesized are given in Table 1.

Based on the data in Ref. 7 *E*-configuration was ascribed for the enamine fragment of indoles **22** and **24**. Such course of the reaction is caused, apparently, by the lower reactivity (in comparison with terminal alkynes) of the anionic center in the corresponding zwitterion, where the negative charge is spread over the two ester groups. That is why in the reaction process, two transition states are possible: one of type **B**, leading to azoninoindoles, and other of type **C**, resulting in the azepine ring cleavage. During chromatography on silica gel, the substituted indoles **22** and **24** undergo partial cyclization to the corresponding azoninoindoles **21** and **23**, while under MS-GLC conditions, the cyclization proceeds quantitatively.

The structures of azoninoindoles **6—14**, **17—21**, and **23** and indoles **22** and **24** were confirmed by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. In the ^{1}H NMR spectra of the compounds synthesized, signals of all the protons presented in their molecules with chemical shifts and spin-spin coupling constants, corresponding to the positions of these protons, are observed (Tables 2 and 3). The ^{1}H NMR spectra of azoninoindoles **6—14** and **17—20** are characterized by the presence of a singlet signal of H(3) or H(5) protons of the enamine fragment of the molecule in the downfield part of the spectrum in the region δ 7.59—7.87.

In the mass spectra of all the azoninoindoles, the molecular ion peaks of various intensity, corresponding to their molecular weights, are observed. The main directions

Scheme 3



21, 22: R^2 = Et, R^3 = Me
23, 24: R^2 = Bn, R^3 = F

Table 1. Yields, physical and chemical and spectral characteristics of azoninoindoles **6—14**, **17—21**, **23** and 3-methoxymethylindoles **22**, **24**

Compound	Yield (%)	*t**/h	M.p./°C (hexane—AcOEt)	Found / Calculated (%)			Molecular formula	IR (KBr), ν/cm^{-1}	MS, *m*/*z* ([M]$^+$)
				C	H	N			
6	72	0.5	264—265	70.53 70.56	6.92 6.91	6.83 6.86	$C_{24}H_{28}N_2O_2S$	1621, 3312	408
7	74	2	177—178	74.05 74.01	6.42 6.43	5.91 5.95	$C_{29}H_{30}N_2O_2S$	1619, 3319	470
8	72	2	251—253	70.06 70.02	6.61 6.64	7.11 7.10	$C_{23}H_{26}N_2O_2S$	1621, 3326	394
9	64	2	229—231	77.00 76.99	8.14 8.16	9.42 9.45	$C_{19}H_{24}N_2O$	1562, 3245	296
10	68	0.5	109—110	80.44 80.41	7.33 7.31	7.78 7.81	$C_{24}H_{26}N_2O$	1569, 3288	358
11	67	0.5	188—189	76.59 76.56	7.88 7.85	9.91 9.92	$C_{18}H_{22}N_2O$	1558, 3252	282
12	74	2	169—170	76.60 76.64	6.73 6.71	7.74 7.77	$C_{23}H_{24}N_2O_2$	1616, 3401	360
13	73	4	167—169	73.02 73.00	6.12 6.13	7.38 7.40	$C_{23}H_{23}FN_2O_2$	1602, 3299	378
14	70	0.5	179—181	72.46 72.66	7.43 7.21	9.39 9.02	$C_{22}H_{22}N_2O_2$	1658, 3271	298
17	69	2	198—199	67.00 66.97	6.08 6.11	6.74 6.79	$C_{23}H_{25}FN_2O_2S$	1620, 3315	412
18	70	2	186—188	70.84 70.86	5.71 5.73	5.93 5.90	$C_{28}H_{27}FN_2O_2S$	1619, 3348	474
19	69	2	234—235	71.95 71.98	7.04 7.05	9.35 9.33	$C_{18}H_{21}FN_2O$	1572, 3324	300

(*to be continued*)

Table 1 (*continued*)

Compound	Yield (%)	*t**/h	M.p./°C (hexane—AcOEt)	Found / Calculated (%)			Molecular formula	IR (KBr), ν/cm^{-1}	MS, *m/z* ([M]$^+$)
				C	H	N			
20	74	2	142—143	76.24 76.22	6.42 6.40	7.74 7.73	$C_{23}H_{23}FN_2O$	1568, 3297	362
21	23	0.5	179—181	60.06 68.09	7.06 7.07	7.58 7.56	$C_{21}H_{26}N_2O_4$	1658, 3340	370
22	32	0.5	Oil	65.70 65.65	7.54 7.51	6.90 6.96	$C_{22}H_{30}N_2O_5$	—	—
23	22	2	213—215	68.77 68.79	5.78 5.77	6.43 6.42	$C_{25}H_{25}FN_2O_4$	1722, 3368	436
24	24	2	75—76	66.68 66.65	6.26 6.24	5.96 5.98	$C_{26}H_{29}FN_2O_5$	1742, 3367	468

* Reaction time.

Table 2. ^{1}H NMR spectra of hexahydroazoninoindoles **6—14**

Compound	δ (*J*/Hz)									
	C(6)H$_2$	C(7)H$_2$	C(5)H$_2$	C(1)H$_2$ (s)	R^1	R^2	R^3 (s, Me)	H(9)—H(12)	N(8)H (br.s)	H(3) (s)
	m									
6[a]	1.72	2.66	3.49	3.73	2.28 (s, Me); 7.18, 7.52 (both d, *J* = 7.5)	1.19 (t, Me, *J* = 7.2); 3.30—3.35 (m, CH$_2$)	2.35	6.81 (d, *J* = 7.9); 7.05 (s); 7.08 (d, *J* = 7.9)	10.40	7.60
7[a]	1.71	2.69	3.45	3.78	2.30 (s, Me); 7.18, 7.52 (both d, *J* = 7.5)	4.54 (s, CH$_2$); 7.33 (m, Ph)	2.35	6.81 (d, *J* = 7.8); 7.06 (s); 7.08 (d, *J* = 7.8)	10.40	7.73
8[a]	1.73	2.71	3.51	3.76	2.28 (s, Me); 7.18, 7.52 (both d, *J* = 7.5)	1.21 (t, Me, *J* = 7.0); 3.30—3.35 (m, CH$_2$)	—	6.96 (m); 7.20 (d, *J* = 7.7); 7.29 (d *J* = 7.5); 7.08 (d, *J* = 7.7)	10.54	7.62
9[b]	1.82	2.85	3.65	4.00	2.19 (s, Me)	1.25 (t, Me, *J* = 7.2); 3.27 (q, CH$_2$, *J* = 7.2)	2.45	6.93, 7.13 (both d, *J* = 8.1); 7.42 (s)	7.56	7.67
10[b]	1.81	2.87	3.65	4.07	2.21 (s, Me)	4.41 (s, CH$_2$); 7.22—7.42 (m, Ph)	2.46	6.95 (d, *J* = 8.0); 7.15 (m)	7.72	7.73
11[b]	1.80	2.82	3.65	4.04	2.20 (s, Me)	1.24 (t, Me, *J* = 7.2); 3.26 (q, CH$_2$, *J* = 7.2)	—	7.10 (m); 7.25 (s); 7.63 (m)	7.88	7.67
12[a]	1.78	2.86	3.57	3.93	3.52 (s, Me)	4.43 (s, CH$_2$); 7.26, 7.41 (both m, Ph)	—	6.97, 7.09 (both m)	10.60	7.68
13[b]	1.81	2.83	3.61	4.03	3.70 (s, Me)	4.37 (s, CH$_2$); 7.17, 7.28 (both m, Ph)	—	6.87 (s); 7.10 (m)	7.69	7.80
14[a]	1.79	2.82	3.60	3.90	3.52 (s, Me)	1.15 (t, Me, *J* = 7.2); 3.25 (q, CH$_2$, *J* = 7.2)	—	6.98 (m); 7.23, 7.44 (both d, *J* = 7.7)	10.60	7.68

[a] Solvent, DMSO-d$_6$.
[b] Solvent, CDCl$_3$.

of the [M]$^{\bullet+}$ decomposition for compounds **6—14**, **21**, and **23** (Scheme 4, Table 4) are caused by the successive elimination of substituents from the C(2) and nitrogen atoms (fragments A—C), as well as by the cleavage of the azonine fragment of the molecule.

The fragment ions have different intensities due to the different structures of the radicals. When the radical is abstracted from the nitrogen atom, the charge can be localized on both fragments. The cleavage of the azonine fragment in [M]$^{\bullet+}$ is accompanied by elimination of

Table 3. ^{1}H NMR spectra of hexahydroazoninoindoles **17—20** (in DMSO-d_6)

Compound	δ (*J*/Hz)								
	C(2)H$_2$	C(1)H$_2$	C(3)H$_2$	C(7)H$_2$ (s)	R^1	R^2	H(9)—H(12)	H(5) (s)	N(8)H (br.s)
	m								
17	1.62	2.65	3.47	3.89	2.24 (s, Me); 7.16, 7.56 (both d, *J* = 8.1)	1.21 (t, Me, *J* = 7.2); 3.30—3.35 (m, CH$_2$)	6.80, 7.14 (both m)	7.59	10.76
18	1.63	2.68	3.43	3.95	2.24 (s, Me); 7.20, 7.57 (both d, *J* = 8.1)	4.57 (s, CH$_2$); 7.37 (m, Ph)	6.80, 7.13 (both m)	7.81	10.86
19	1.69	2.73	3.61	4.01	2.14 (s, Me)	1.20 (t, Me, *J* = 7.2); 3.70 (q, CH$_2$, *J* = 7.2)	6.78, 7.15 (both m)	7.69	10.85
20	1.70	2.76	3.55	4.06	2.16 (s, Me)	4.59 (s, CH$_2$); 7.32 (m, Ph)	6.77, 7.15 (both m); 7.42 (s)	7.87	10.85

hydrogen and by formation of fragment ions F and G. The loss of H$^\bullet$ and $CH_2{=}CH_2$ is characteristic of fragment F, whereas the cleavage of the C(2)—N and C(3)—C(4) bonds with the formation of $CH_2{=}NR$ and X—C≡C—Y fragments is characteristic of fragment G. Fragmentation of the $[M - X]^+$ ion proceeds with elimination of $^\bullet CH_2CH_2NR$ (*m* = 71 and 133) and $^\bullet CH_2CH_2CH_2NR$ (*m* = 85 and 147) species (cleavage along pathways *b* and *c*). Structures D and E can be suggested for the ions, formed by the cleavage along pathway *b*. Further, the latter loses hydrogen. Under the electron ionization, azoninoindoles **17—20** decompose similarly to their isomers.

In conclusion, an original method for the synthesis of new heterocyclic structures, isomeric hexahydroazonino[5,6-*b*]indoles, differing in the position of the multiple bond, was elaborated. For the first time, it was shown that not only fused tetrahydropyridines, but also fused azepines, can undergo ring expansion upon treatment with alkynes.

Scheme 4

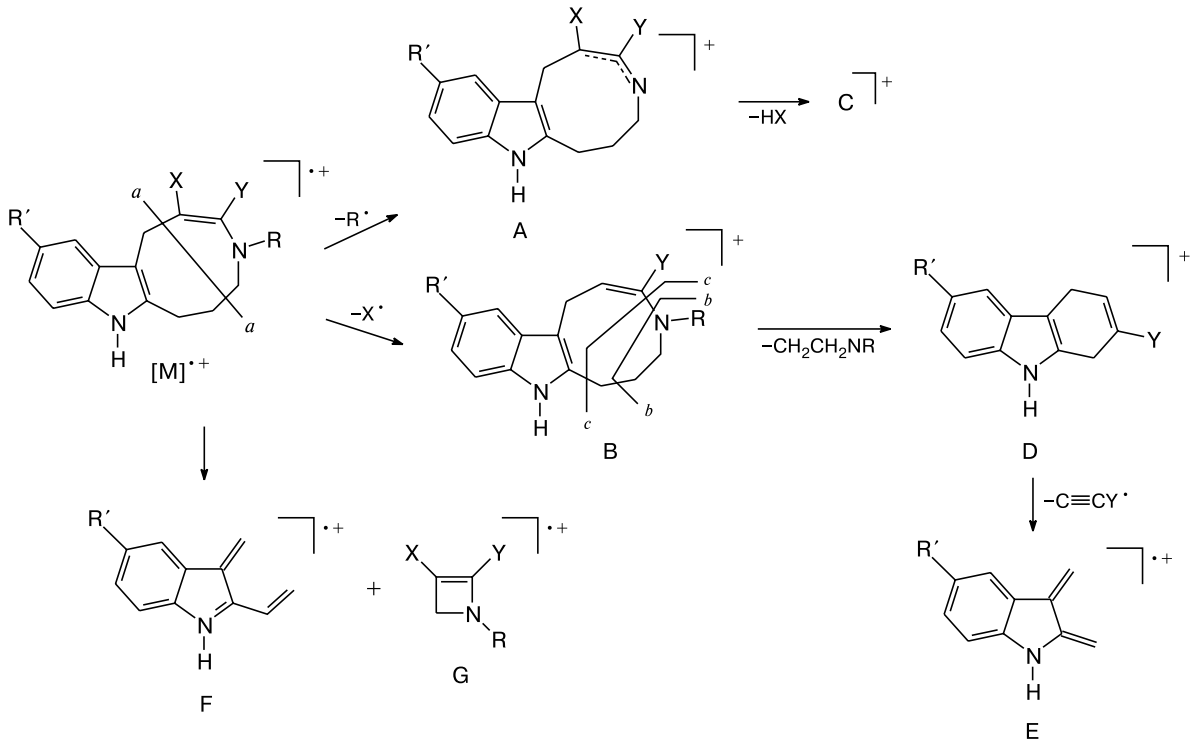


Table 4. Characteristic fragment ions in the mass spectra of azoninoindoles **6—14**, **17—21**, and **23**

Compound	Fragment ion (*I* (%))							
	$[M]^{\bullet+}$	A	B	C	D	E	F	G
6	408 (25)	379 (2)	253 (100)	223 (30)	182 (60)	157 (45)	170 (56)	237 (28)
7	470 (2)	379 (12)	315 (13)	223 (20)	182 (12)	157 (12)	170 (20)	299 (2)
8	394 (25)	365 (2)	239 (90)	209 (30)	168 (90)	143 (45)	156 (83)	237 (62)
9	296 (18)	267 (2)	253 (10)	223 (4)	182 (22)	157 (12)	170 (55)	125 (2)
10	358 (16)	267 (30)	315 (2)	223 (8)	182 (16)	157 (10)	170 (42)	187 (2)
11	282 (88)	253 (16)	239 (48)	209 (20)	168 (66)	143 (32)	156 (100)	125 (2)
12	360 (30)	269 (76)	301 (2)	209 (22)	168 (33)	143 (14)	156 (30)	203 (2)
13	378 (18)	287 (30)	319 (2)	227 (8)	186 (14)	161 (8)	174 (20)	203 (2)
14	298 (82)	269 (15)	239 (16)	209 (12)	168 (70)	143 (28)	156 (38)	141 (2)
17	412 (10)	383 (2)	257 (32)	227 (4)	186 (30)	161 (15)	174 (28)	237 (2)
18	474 (10)	383 (16)	319 (25)	227 (48)	186 (21)	161 (4)	174 (18)	299 (1)
19	300 (100)	271 (8)	257 (35)	227 (22)	186 (70)	161 (22)	174 (45)	126 (40)
20	362 (42)	271 (44)	319 (12)	227 (28)	186 (34)	161 (14)	174 (32)	188 (20)
21	370 (60)	341 (18)	311 (100)	281 (40)	240 (15)	157 (50)	170 (90)	199 (2)
23	436 (12)	345 (100)	377 (12)	285 (35)	244 (2)	161 (5)	174 (18)	261 (2)

Experimental

IR spectra were recorded on a Specord IR-75 spectrometer in KBr pellets (for the crystalline substances) or as neat samples (for oils). Mass spectra were recorded on a Finnigan MAT 95XL and Hewlett—Packard MS-5988 mass-spectrometers with direct inlet of the sample into the source of ions, the ionizing voltage was 70 eV. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 (300.13 and 75 MHz, respectively) and Varian Unity 400 (400 and 100 MHz, respectively) in DMSO-d_6 and $CDCl_3$ with the use of the residual signal of nondeuterated solvent as the internal standard. Silufol UV-254 plates were used for TLC, silica gel from Merck (230—400 mesh) was used for column chromatography. All the solvents were dried and distilled before use. Acetylacetylene, methyl propiolate, and DMAD (Acros Organics) were used without additional purification. Tosylacetylene was synthesized according to the described procedure.[8]

Yields, physical and chemical characteristics, elemental analysis data, and spectral characteristics of the synthesized compounds are given in Tables 1—4.

Hexahydroazepino[4,3-*b*]indoles **1—5** and hexahydroazepino[3,4-*b*]indoles **15** and **16** were synthesized according to the known procedure.[6]

2-Benzyl-1,2,3,4,5,6-hexahydroazepino[4,3-*b*]indole (4). The yield was 55%, m.p. 178—180 °C (AcOEt). Found (%): C, 82.33; H, 7.15; N, 10.05. $C_{19}H_{20}N_2$. Calculated (%): C, 82.57; H, 7.29; N, 10.14. ^{1}H NMR (DMSO-d_6), δ: 1.78 (m, 2 H, C(4)H_2); 2.89, 3.03 (both m, 2 H each, CH_2); 3.62, 3.82 (both s, 2 H each, CH_2); 6.86—6.98 (m, 2 H, Ar); 7.12 (d, 1 H, H(10), $^{1,3}J$ = 7.7 Hz); 7.24—7.33 (m, 6 H, Ar); 10.84 (s, 1 H, N(6)H). MS, *m/z*: 276 $[M]^+$.

2-Benzyl-9-fluoro-1,2,3,4,5,6-hexahydroazepino[4,3-*b*]indole (5). The yield was 58%, m.p. 155—157 °C (AcOEt). Found (%): C, 77.63; H, 6.59; N, 9.51. $C_{19}H_{19}FN_2$. Calculated (%): C, 77.52; H, 6.51; N, 9.52. ^{1}H NMR (DMSO-d_6), δ: 1.75 (m, 2 H, C(4)H_2); 2.87, 2.99 (both m, 2 H each, CH_2); 3.58, 3.77 (both s, 2 H each, CH_2); 6.77 (ddd, 1 H, H(8), $^{1,3}J$ = 9.0 Hz, $^{1,3}J$ = 9.0 Hz, $^{1,4}J$ = 2.3 Hz); 6.85 (dd, 1 H, H(10), $^{1,3}J$ = 9.8 Hz, $^{1,4}J$ = 2.3 Hz); 7.20—7.32 (m, 6 H, Ar); 10.96 (s, 1 H, N(6)H). MS, *m/z*: 294 $[M]^+$.

Reaction of hexahydroazepinoindoles with alkynes in methanol (general procedure). The corresponding alkyne (1.2 mmol) was added to a solution of hexahydroazepinoindole **1—5**, **15**, **16** (1 mmol) in methanol (15 mL). The reaction mixture was stirred for 0.5—4 h at ~20 °C. Monitoring of the course of the reaction was performed by TLC. The solvent was evaporated *in vacuo*, the residue was subjected to chromatography on SiO_2 (with AcOEt—hexane as the eluent) to isolate azonines **6—14**, **17—20**, **21**, and **23** and 3-methoxymethylindoles **22** and **24**.

4-Ethyl-11-methyl-2-[(4-methylphenyl)sulfonyl]-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole (6). ^{13}C NMR (DMSO-d_6), δ: 14.9, 20.8, 21.2 (all CH_3); 21.3, 22.0, 28.9, 44.5, 50.3 (all CH_2); 97.9, 104.9 (both C); 109.9, 116.6, 121.6 (all CH); 126.1 (2 CH); 126.4, 128.8 (both C); 129.1 (2 CH); 132.4, 135.4, 140.7, 141.4 (all C); 148.2 (CH). MS, *m/z* (I_{rel} (%)): 408 $[M]^+$ (25), 379 (2), 253 (100), 237 (28), 223 (30), 208 (50), 195 (80), 170 (56), 157 (45), 144 (30), 115 (10), 91 (70), 65 (20), 58 (50).

4-Benzyl-11-methyl-2-[(4-methylphenyl)sulfonyl]-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole (7). MS, *m/z* (I_{rel} (%)): 470 $[M]^+$ (2), 379 (12), 315 (13), 299 (2), 223 (20), 195 (12), 182 (12), 170 (20), 157 (12), 144 (10), 120 (20), 91 (100), 65 (20).

4-Ethyl-2-[(4-methylphenyl)sulfonyl]-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole (8). ^{13}C NMR (DMSO-d_6), δ: 14.9, 20.8 (both CH_3); 21.2, 21.9, 28.8, 44.5, 50.3 (all CH_2); 97.9, 105.4 (both C); 110.1, 116.8, 118.0, 120.0 (all CH); 126.1 (2 CH); 128.5 (C); 129.0 (2 CH); 134.0, 135.2, 140.5, 141.3 (all C); 148.0 (CH). MS, *m/z* (I_{rel} (%)): 394 $[M]^+$ (25), 365 (2), 239 (90), 223 (30), 209 (30), 195 (64), 182 (70), 168 (90), 156 (83), 130 (40), 108 (10), 91 (100), 77 (10), 65 (30), 58 (50).

1-(4-Ethyl-11-methyl-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indol-2-yl)ethanone (9). MS, *m/z* (I_{rel} (%)): 296 $[M]^+$ (18), 267 (2), 253 (10), 223 (4), 196 (15), 182 (22), 170 (55), 157 (12), 125 (2), 58 (100), 43 (70).

1-(4-Benzyl-11-methyl-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indol-2-yl)ethanone (10). MS, *m/z* (I_{rel} (%)): 358 $[M]^+$

(16), 315 (2), 267 (30), 223 (8), 187 (2), 182 (16), 170 (42), 157 (10), 120 (16), 91 (100), 65 (18), 43 (38).

1-(4-Ethyl-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indol-2-yl)ethanone (11). ^{13}C NMR (DMSO-d_6), δ: 15.5 (CH_3); 20.0, 23.3 (both CH_2); 25.6 (CH_3); 30.1, 45.6, 51.3 (all CH_2); 106.8, 108.2 (both C); 110.7, 118.0, 118.4, 120.5 (all CH); 129.5, 134.7, 135.7 (all C); 153.3 (CH); 193.8 (C). MS, *m/z* (I_{rel} (%)): 282 $[M]^+$ (88), 253 (16), 239 (48), 209 (20), 194 (25), 182 (30), 168 (66), 156 (100), 143 (32), 130 (20), 125 (2), 115 (10), 58 (12), 43 (35).

Methyl 4-benzyl-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole-2-carboxylate (12). ^{13}C NMR (DMSO-d_6), δ: 21.8, 24.1, 29.8, 47.7 (all CH_2); 51.6 (CH_3); 60.2 (CH_2); 94.8, 108.1 (both C); 111.2, 118.4, 118.9, 120.9 (all CH); 128.1 (3 CH); 129.4 (2 CH); 129.7, 135.2, 136.2, 139.4 (all C); 152.1 (CH); 170.6 (C). MS, *m/z* (I_{rel} (%)): 360 $[M]^+$ (30), 301 (2), 269 (76), 237 (25), 209 (22), 203 (2), 195 (10), 181 (22), 168 (33), 156 (30), 143 (14), 130 (10), 91 (100), 65 (12).

Methyl 4-benzyl-11-fluoro-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole-2-carboxylate (13). MS, *m/z* (I_{rel} (%)): 378 $[M]^+$ (18), 319 (2), 287 (30), 227 (8), 203 (2), 199 (10), 186 (14), 174 (20), 161 (8), 91 (100), 65 (20).

Methyl 4-ethyl-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole-2-carboxylate (14). MS, *m/z* (I_{rel} (%)): 298 $[M]^+$ (82), 269 (15), 239 (16), 225 (30), 209 (12), 195 (20), 180 (20), 168 (70), 156 (38), 143 (28), 115 (15), 82 (20), 68 (10), 58 (100), 42 (45).

4-Ethyl-11-fluoro-6-[(4-methylphenyl)sulfonyl]-1,2,3,4,7,8-hexahydroazonino[5,6-*b*]indole (17). ^{13}C NMR (DMSO-d_6), δ: 15.0 (CH_3); 17.9 (CH_2); 20.7 (CH_3); 24.8, 29.0, 44.6, 50.6 (all CH_2); 95.5 (C); 102.2 (d, CH, J = 23 Hz); 108.5 (d, CH, J = 26 Hz); 110.6 (C); 111.3 (d, CH, J = 9 Hz); 126.7 (2 CH); 129.5 (C); 129.6 (2 CH); 131.4, 133.7, 140.7, 142.1 (all C); 149.0 (CH); 157.1 (d, C, J = 230 Hz). MS, *m/z* (I_{rel} (%)): 412 $[M]^+$ (10), 383 (2), 257 (32), 237 (2), 198 (20), 186 (30), 174 (28), 161 (15), 148 (20), 133 (10), 108 (10), 91 (60), 65 (30), 58 (100), 42 (10).

4-Benzyl-11-fluoro-6-[(4-methylphenyl)sulfonyl]-1,2,3,4,7,8-hexahydroazonino[5,6-*b*]indole (18). ^{13}C NMR (DMSO-d_6), δ: 19.0 (CH_2); 21.7 (CH_3); 25.7, 29.4, 46.1, 60.1 (all CH_2); 97.2 (C); 102.6 (d, CH, J = 23 Hz); 108.9 (d, CH, J = 26 Hz); 111.1 (C); 111.8 (d, CH, J = 9 Hz); 127.1 (2 CH); 128.6 (CH); 128.7 (2 CH); 129.6 (2 CH); 130.1 (2 CH + C); 131.9, 134.0, 138.8, 141.1 (C), 142.7 (all C); 150.3 (CH); 157.6 (d, C, J = 230 Hz). MS, *m/z* (I_{rel} (%)): 474 $[M]^+$ (10), 383 (16), 319 (25), 299 (1), 227 (48), 212 (10), 199 (26), 186 (21), 174 (18), 161 (4), 91 (100), 65 (10).

1-(4-Ethyl-11-fluoro-1,2,3,4,7,8-hexahydroazonino[5,6-*b*]indol-6-yl)ethanone (19). ^{13}C NMR (DMSO-d_6), δ: 15.0 (CH_3); 18.3, 23.3 (CH_2); 24.7 (CH_3); 29.7, 45.0, 51.0 (all CH_2); 101.5 (d, CH, J = 22 Hz); 103.3 (C); 107.6 (d, CH, J = 26 Hz); 109.9 (C); 110.7 (d, CH, J = 10 Hz); 129.1 (d, C, J = 10 Hz); 130.9, 135.7 (both C); 153.3 (CH); 156.6 (d, C, J = 230 Hz); 193.1 (C). MS, *m/z* (I_{rel} (%)): 300 $[M]^+$ (100), 271 (8), 257 (35), 227 (22), 212 (50), 200 (40), 186 (70), 174 (45), 148 (30), 126 (40), 84 (20), 58 (20), 43 (50).

1-(4-Benzyl-11-fluoro-1,2,3,4,7,8-hexahydroazonino[5,6-*b*]indol-6-yl)ethanone (20). ^{13}C NMR (DMSO-d_6), δ: 18.6, 23.2 (both CH_2); 24.8 (CH_3); 29.2, 45.8, 59.6 (all CH_2); 101.5 (d, CH, J = 22 Hz); 104.2 (C); 107.6 (d, CH, J = 26 Hz); 109.9 (C); 110.7 (d, CH, J = 10 Hz); 127.4 (CH); 127.6 (2 CH); 128.5 (2 CH); 129.0 (d, C, J = 10 Hz); 131.0, 135.5, 138.0 (all C); 154.2 (CH); 156.6 (d, C, J = 230 Hz); 193.6 (C). MS, *m/z* (I_{rel} (%)): 362 $[M]^+$ (42), 319 (12), 271 (44), 242 (10), 227 (28), 213 (20), 188 (20), 186 (34), 174 (32), 161 (14), 146 (20), 120 (20), 91 (100), 65 (10), 43 (20).

Dimethyl 4-ethyl-11-methyl-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole-2,3-dicarboxylate (21). ^{13}C NMR ($CDCl_3$), δ: 14.7, 21.2 (both CH_3); 22.4, 23.82, 27.0, 44.6 (all CH_2); 51.5, 51.7 (all CH_3); 54.9 (CH_2); 109.1 (C); 109.6, 118.0, 122.2 (all CH); 128.0 (2 C); 128.3, 133.2, 134.0, 150.8, 166.4, 169.2 (all C). MS, *m/z* (I_{rel} (%)): 370 $[M]^+$ (60), 341 (18), 325 (10), 311 (100), 281 (40), 266 (20), 251 (45), 240 (15), 227 (20), 199 (2), 194 (35), 184 (50), 170 (90), 157 (50), 144 (20), 128 (10), 84 (20), 58 (70).

Dimethyl 2-{ethyl[3-(3-methoxymethyl-5-methyl-1*H*-indol-2-yl)propyl]amino}but-2-enedioate (22). ^{1}H NMR ($CDCl_3$), δ: 1.12 (t, 3 H, MeCH_2, J = 7.1 Hz); 1.98 (m, 2 H, C(2)H_2); 2.44 (s, 3 H, C(5)Me); 2.78 (m, 2 H, CH_2); 3.05—3.16 (m, 4 H, CH_2 + CH_2Me); 3.36 (s, 3 H, MeO); 3.62, 3.80 (both s, 3 H each, MeOCO); 4.57 (s, 2 H, CH_2); 4.59 (s, 1 H, =CH); 6.96 (d, 1 H, H(6), J = 8.2 Hz); 7.19 (d, 1 H, H(7), J = 8.2 Hz); 7.38 (s, 1 H, H(4)); 8.16 (s, 1 H, NH).

Dimethyl 4-benzyl-11-fluoro-1,4,5,6,7,8-hexahydroazonino[5,6-*b*]indole-2,3-dicarboxylate (23). MS, *m/z* (I_{rel} (%)): 436 $[M]^+$ (12), 345 (100), 377 (12), 313 (10), 285 (35), 261 (2), 225 (10), 198 (10), 174 (18), 161 (5), 91 (90).

Dimethyl 2-{benzyl[3-(5-fluoro-3-methoxymethyl-1*H*-indol-2-yl)propyl]amino}but-2-enedioate (24). ^{1}H NMR ($CDCl_3$), δ: 1.97 (m, 2 H, C(2)H_2); 2.76, 3.12 (both m, 2 H each, CH_2); 3.34 (s, 3 H, MeO); 3.62, 3.83 (both s, 3 H each, MeOCO); 4.28, 4.50 (both s, 2 H each, CH_2); 4.65 (s, 1 H, =CH); 6.86—7.33 (m, 8 H, Ar); 8.20 (s, 1 H, NH). MS, *m/z* (I_{rel} (%)): 468 $[M]^+$ (15), 436 (52), 405 (12), 345 (42), 285 (28), 225 (5), 198 (8), 174 (25), 161 (16), 91 (100), 65 (14), 45 (12).

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