Synthesis of novel furoquinolines and furobenzodiazepines from tetronic acid

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Condensation of tetronic acid with 2-cyano-, 2-ethoxycarbonyl-, 2-carboxy-, and 2-aminoanilines gave novel furoquinolines and furobenzodiazepines.

Key words: tetronic acid, furoquinolines, furobenzodiazepines.

Tetronic acid (tetrahydrofuran-2,4-dione) attracts the attention of the researchers as a very reactive object for design of various annulated heterocycles.[1—3] In addition, heterocycles containing a fragment of tetronic acid often exhibit biological (*e.g.*, antitumor) activity.[4,5]

The present work is devoted to the study of new possibilities of designing a number of heterotricyclic systems based on tetronic acid.

Earlier,[1] furoquinoline derivatives have been obtained by condensation of tetronic acid with 2-formylaniline and 2-aminobenzophenones. However, those products were 9-unsubstituted or 9-aryl-substituted furoquinolines. At the same time, it is known[6,7] that many natural compounds of the quinoline series and biologically active compounds containing the furoquinoline fragment are functionalized in position 9.

For the synthesis of earlier unknown 9-aminofuroquinolines, we carried out condensation of tetronic acid with 2-aminobenzonitrile or ethyl anthranilate (Scheme 1). The resulting enamine derivatives of tetronic acid, namely, 2-[(5-oxo-2,5-dihydro-3-furyl)amino]benzonitrile (**1**) and ethyl 2-[(5-oxo-2,5-dihydro-3-furyl)amino]benzoate (**2**), were further converted into furoquinolines. The cyclization of compound **1** was carried out in boiling $BF_3 \cdot Et_2O$. It should be noted that this reagent is usually employed as a catalyst for various reactions. The use of $BF_3 \cdot Et_2O$ as both a condensation agent and a solvent led to 9-(ethylamino)furoquinoline **3**; *i.e.*, the cyclization was accompanied by ethylation of the amino group. Decomposition of esters by haloboranes into haloalkanes has been documented.[8]

The cyclization of compound **2** into furoquinolinone **4** was conducted by heating it in an ethanolic solution of sodium ethoxide. Earlier,[9] compound **4** has been obtained by carbonylation of 4-[(2-bromophenyl)amino]furan-2(5*H*)-one under drastic conditions. Conversion of compound **4** into *N*-substituted 9-aminofuroquinolines involved two steps: (1) replacement of the O atom by a Cl atom under the action of the Vilsmeier reagent and (2) reactions of the resulting chloro derivative **5** with amines, yielding 9-(benzylamino)furoquinolinone **6** and 9-morpholinofuroquinolinone **7**. A reaction of compound **5** with 3-aminopyridine gave 3-amino-1-(1-oxo-1,3-dihydrofuro[3,4-*b*]quinolin-9-yl)pyridinium chloride (**8**).

Furoquinolinone **4** reacted with DMF dimethyl acetal to give 3-dimethylaminomethylidene-4-methylfuroquinoline-1,9-dione **9**. In this reaction, DMF acetal acts as both a condensation and *N*-alkylating agent. *N*-Alkylation of pyridones with amide acetals is well documented.[10—12] Because an anion must be initially formed from the substrate during *N*-alkylation, it seems to be highly probable that alkylation precedes condensation at the active methylene unit (see Scheme 1).

To obtain functionalized furoquinolines, we also used 2-[(5-oxo-2,5-dihydro-3-furyl)amino]benzoic acid (**10**) prepared from tetronic and anthranilic acids or by basic hydrolysis of ester **2** (Scheme 2). The Vilsmeier reaction of compound **10** gave 3-(dimethylaminomethylidene)furoquinolinone **11**, which can be easily transaminated into benzylaminomethylidene (**12**) and morpholinomethylidene derivatives (**13**). The ^{1}H NMR spectrum of compound **12** shows signals characteristic of this structure: a doublet for the methylene group of the benzyl substituent (δ 4.68, J = 6.0 Hz), a doublet for the C′H proton (δ 8.31, J = 14.7 Hz), and a signal for

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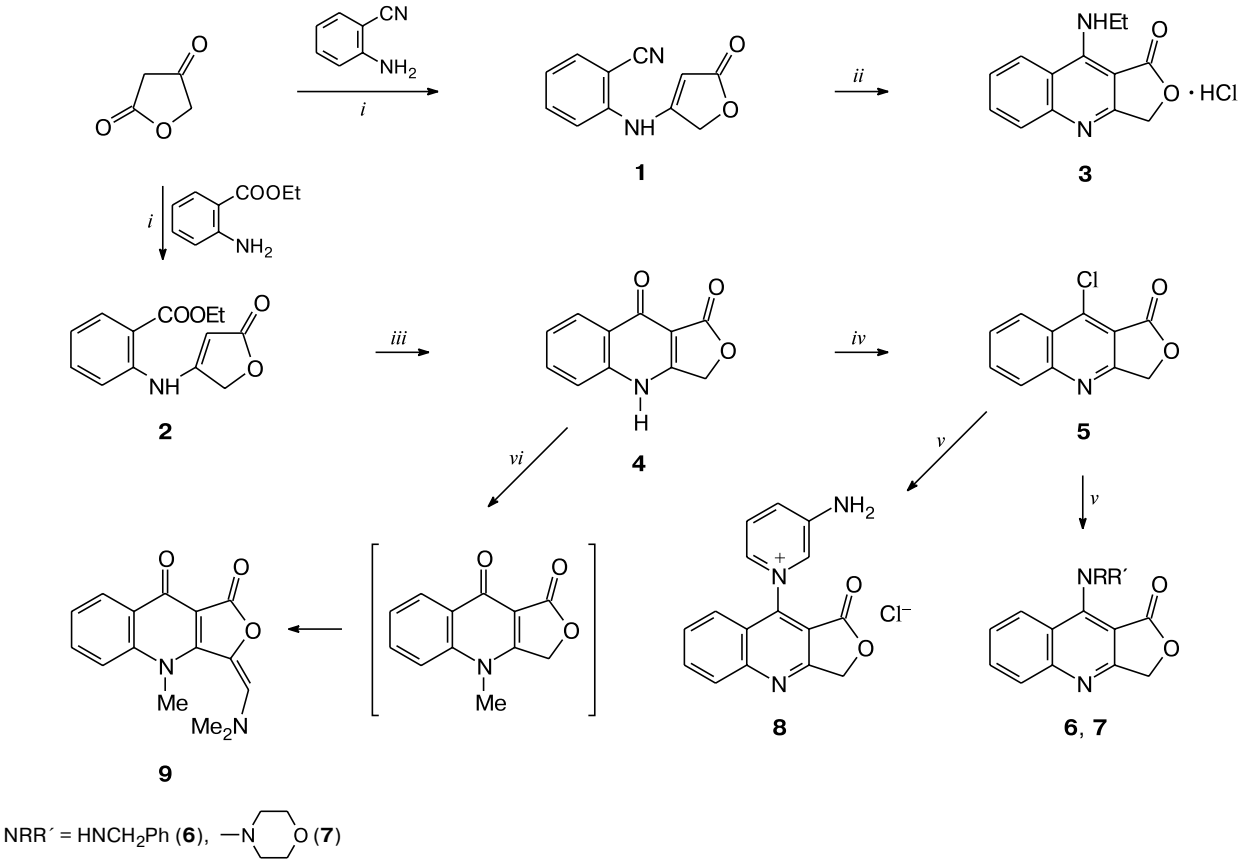
Scheme 1



Reagents and conditions: *i*. MeOH, reflux, 4—8 h. *ii*. $BF_3 \cdot Et_2O$, reflux, 6 h. *iii*. EtONa, EtOH, 40—45 °C, 6 h. *iv*. DMF, $POCl_3$, 20 °C, 4 h. *v*. EtOH, benzylamine (morpholine or 3-aminopyridine), reflux, 1—6 h. *vi*. DMF, DMF acetal, reflux, 3 h.

the NH proton (δ 9.78) that appears as a complex multiplet due to couplings with the H(1′) proton and the CH_2 group.

Under the same conditions, compound **14** was obtained from ester **2** without closing a pyridine ring (see Scheme 2).

The structure of compound **14** was confirmed by NMR spectroscopy. The NOESY NMR spectrum shows the following correlation peaks (δ): 10.30/6.52 (NH/H(2″)), 10.30/7.54 (NH/H(3)), and 6.52/3.07 (H(2″)/NMe_2); the HMBS spectrum shows the following peaks (δ): 9.47/95.4 (CHO/C(4′)), 9.47/154.3 (CHO/C(3′)), 6.52/117.0 (H(2″)/C(2′)), and 6.52/154.3 (H(2″)/C(3′)).

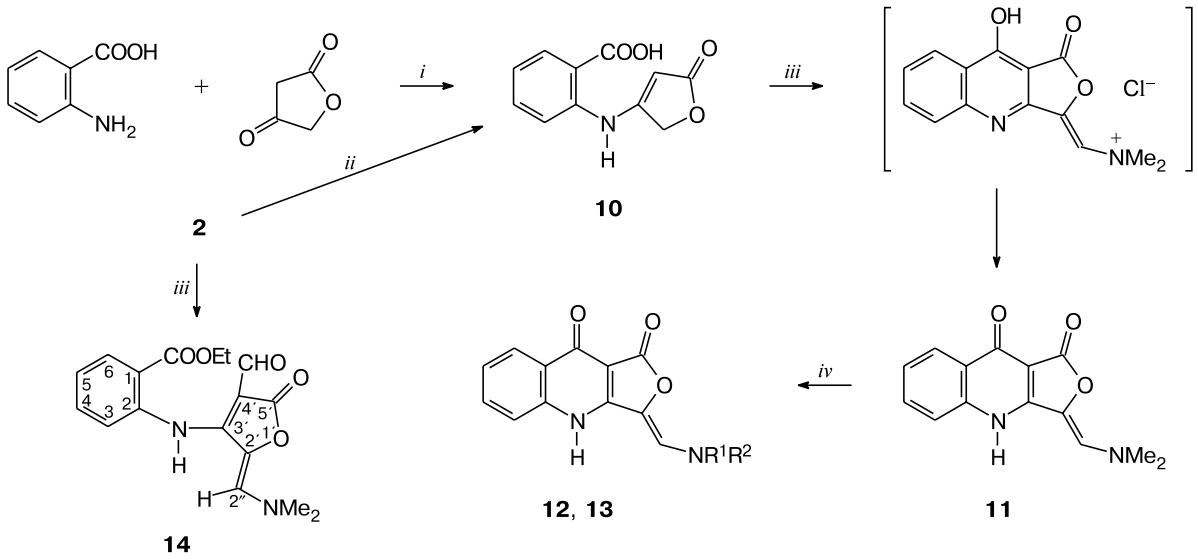
The sole described[13] synthesis of a furobenzodiazepine derivative involves condensation of benzaldehyde with 4-(2-aminoanilino)furan-2(5*H*)-one prepared from tetronic acid and *o*-phenylenediamine. Using this method, we obtained furobenzodiazepines **15**—**17** from other starting aldehydes (3,4-dimethoxybenzaldehyde, 3-phenylpropionaldehyde, and 3-formylpyridine) and studied some of their properties (Scheme 3). Compounds **15**—**17** were characterized by ^{1}H NMR spectroscopy. The spectra of all these furobenzodiazepines contain signals at δ 3.87—5.08 (d, H(10), J = 4.5 Hz), 5.66—6.06 (d, N(9)H, J = 4.5 Hz), and 9.54—9.84 (br.s, N(4)H). Reactions of compounds **15**—**17** with chloroacetyl chloride gave 9-chloroacetyl derivatives **18**—**20**. The acylation at the N(9) atom (rather than N(4)) is evident from ^{1}H NMR data: the spectra of compounds **18**—**20** retain a downfield signal for N(4)H (δ 10.06—10.25), while the signal for N(9)H disappears and the signal for the H(10) proton appears as a singlet* (see Experimental).

Chloroacetylfurobenzodiazepines **18** and **19** were used in reactions with pyrrolidine and piperidine for the synthesis of the corresponding 9-aminoacetyl derivatives **21**—**23** (see Scheme 3).

Thus, we discovered routes to 9-substituted furoquinolines and furobenzodiazepines.

* The exception is the spectrum of compound **19**, in which the signal for the H(10) proton is splitted because of a coupling with the methylene group of the substituent CH_2CH_2Ph.

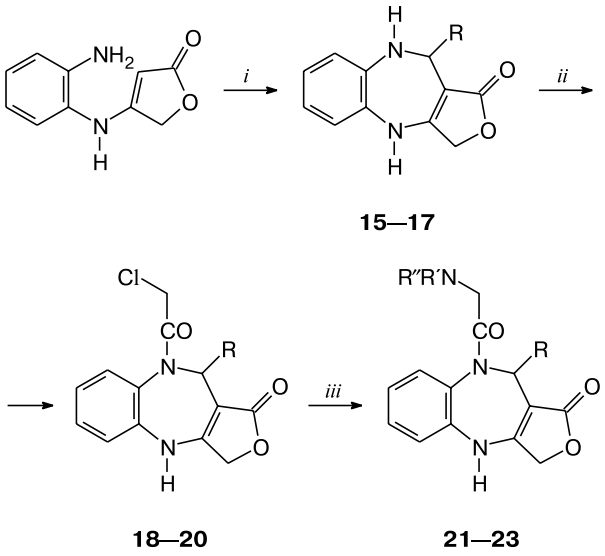
Scheme 2



R^1 = H, R^2 = CH_2Ph (**12**); R^1R^2 = $CH_2CH_2OCH_2CH_2$ (**13**)

Reagents and conditions: *i*. MeOH, reflux, 6 h. *ii*. EtOH, NaOH, reflux, 30 min. *iii*. DMF, $POCl_3$, 20 °C, 4 h, EtOH, NaOH. *iv*. EtOH, benzylamine (morpholine), 20 °C, 4 h.

Scheme 3



R = 3,4-$(OMe)_2C_6H_3$ (**15**, **18**, **21**), CH_2CH_2Ph (**16**, **19**, **22**, **23**),  (**17**, **20**); R′R″ = $(CH_2)_4$ (**21**, **22**), $(CH_2)_5$ (**23**)

Reagents and conditions: *i*. 3,4-Dimethoxybenzaldehyde (3-phenylpropionaldehyde, 3-formylpyridine), EtOH (BuOH), AcOH, reflux, 3 h. *ii*. Chloroacetyl chloride, benzene, reflux, 3 h. *iii*. Pyrrolidine (piperidine), benzene, reflux, 1.5 h.

Experimental

Mass spectra (ESI) were recorded on a Waters ZQ-2000 mass spectrometer (direct inlet probe). ^{1}H NMR spectra were recorded on a Bruker AC-300 spectrometer; 2D NMBC spectra were recorded on a Bruker DRX-500 spectrometer in DMSO-d_6 using a Bruker standard procedure. The course of the reactions was monitored and the purity of the products was checked by TLC on 60 F_{254} plates (Merck). The yields, elemental analysis data, and physicochemical characteristics of the compounds obtained are given in Tables 1—3.

2-[(5-Oxo-2,5-dihydro-3-furyl)amino]benzonitrile (1). A solution of tetronic acid (1.0 g, 10 mmol) and 2-aminobenzonitrile (1.32 g, 11 mmol) in methanol (10 mL) was refluxed with stirring for 8 h. On cooling, the precipitate that formed was filtered off, washed with methanol, and dried. The yield of compound **1** was 1.6 g. ^{1}H NMR (DMSO-d_6), δ: 4.87 (s, 2 H, C(2′)H_2); 5.16 (s, 1 H, H(4′)); 7.30, 7.56, 7.67, 7.70 (all m, 1 H each, H(3)—H(6)); 9.85 (br.s, 1 H, NH).

Ethyl 2-[(5-oxo-2,5-dihydro-3-furyl)amino]benzoate (2). A solution of tetronic acid (4.0 g, 40 mmol) and ethyl anthranilate (6.6 g, 40 mmol) in methanol (40 mL) was refluxed with stirring for 4 h. On cooling, the precipitate that formed was filtered off, washed with methanol, and dried. The yield of compound **2** was 8.34 g. ^{1}H NMR (DMSO-d_6), δ: 1.37 (t, 3 H, C$\underline{H}_3$CH$_2$, J = 7.0 Hz); 4.35 (q, 2 H, CH$_3$C$\underline{H}_2$, J = 7.0 Hz); 4.92 (s, 2 H, C(2′)H_2); 5.38 (s, 1 H, H(4′)); 7.19, 7.53, 7.63, 7.98 (all m, 1 H each, H(3)—H(6)); 9.94 (br.s, 1 H, NH).

9-(Ethylamino)furo[3,4-*b*]quinolin-1(3*H*)-one hydrochloride (3). A mixture of compound **1** (0.5 g, 2.5 mmol) and $BF_3 \cdot Et_2O$

Table 1. Yields, melting points, elemental analysis data, and mass spectra of compounds **1**—**23**

Compound	Yield (%)	M.p./°C (solvent)	Found / Calculated (%)			Molecular formula	MS (ESI), *m/z*
			C	H	N		
1	80.0	197—200 (MeOH)	65.86 / 65.99	4.05 / 4.03	13.85 / 14.00	$C_{11}H_8N_2O_2$	201 $[M + H]^+$, 223 $[M + Na]^+$, 423 $[2 M + Na]^+$
2	84.4	170—171 (EtOH)	63.52 / 63.15	5.26 / 5.30	6.08 / 5.66	$C_{13}H_{13}NO_4$	248 $[M + H]^+$, 270 $[M + Na]^+$, 286 $[M + K]^+$, 517 $[2 M + Na]^+$
3	42.4	255 (decomp.) (EtOH)	59.13 / 58.98	5.38 / 5.30	10.62 / 10.58	$C_{13}H_{13}ClN_2O_2$	173 $[M + H - 56]^+$, 201 $[M + H - 28]^+$, 229 $[M + H]^+$, 267 $[M + K]^+$
4	66.9	308—310 (DMF)	65.91 / 65.67	3.61 / 3.51	7.10 / 6.96	$C_{11}H_7NO_3$	202 $[M + H]^+$, 225 $[M + H + Na]^+$
5	73.0	178 (decomp.) (EtOH)	60.35 / 60.15	2.96 / 2.75	6.60 / 6.38	$C_{11}H_6ClNO_2$	220 $[M + H]^+$, 242 $[M + Na]^+$
6	72.4	190—191 (EtOH)	74.50 / 74.46	4.79 / 4.86	9.60 / 9.65	$C_{18}H_{14}N_2O_2$	291 $[M + H]^+$, 313 $[M + Na]^+$, 329 $[M + K]^+$, 603 $[2 M + Na]^+$
7	74.1	205—207 (MeOH)	66.67 / 66.65	5.15 / 5.22	10.28 / 10.37	$C_{15}H_{14}N_2O_3$	271 $[M + H]^+$, 293 $[M + Na]^+$, 309 $[M + K]^+$, 563 $[2 M + Na]^+$, 579 $[2 M + K]^+$
8	52.6	165—167 (EtOH)	60.83 / 61.25	4.26 / 3.86	12.93 / 13.39	$C_{16}H_{12}ClN_3O_2$	278 $[M + H]^+$, 555 $[2 M + H]^+$
9	25	302—304 (MeOH)	66.42 / 66.65	5.34 / 5.22	10.00 / 10.37	$C_{15}H_{14}N_2O_3$	271 $[M + H]^+$, 293 $[M + Na]^+$, 309 $[M + K]^+$, 563 $[2 M + Na]^+$, 579 $[2 M + K]^+$
10	85.3 (*A*) 67.8 (*B*)	193—195 (EtOH)	59.97 / 60.27	4.15 / 4.14	6.42 / 6.40	$C_{11}H_9NO_4$	220 $[M + H]^+$, 242 $[M + Na]^+$, 258 $[M + K]^+$, 461 $[2 M + Na]^+$, 477 $[2 M + K]^+$, 680 $[3 M + Na]^+$
11	51.9	352 (decomp.) (DMF)	65.33 / 65.61	4.62 / 4.72	11.03 / 10.93	$C_{14}H_{12}N_2O_3$	257 $[M + H]^+$, 279 $[M + Na]^+$, 295 $[M + K]^+$, 513 $[2 M + H]^+$, 535 $[2 M + Na]^+$
12	92.8	312 (decomp.) (DMF)	71.97 / 71.68	3.89 / 4.43	8.85 / 8.80	$C_{19}H_{13}N_2O_3$	319 $[M + H]^+$, 341 $[M + Na]^+$, 357 $[M + K]^+$, 637 $[2 M + H]^+$, 659 $[2 M + Na]^+$, 675 $[2 M + K]^+$
13	68	335—337 (DMF)	64.37 / 64.42	4.55 / 4.73	9.38 / 9.39	$C_{16}H_{14}N_2O_4$	299 $[M + H]^+$, 321 $[M + Na]^+$, 597 $[2 M + H]^+$, 619 $[2 M + Na]^+$, 635 $[2 M + K]^+$
14	27.9	193—195 (EtOH)	62.29 / 61.81	5.50 / 5.49	8.62 / 8.48	$C_{17}H_{18}N_2O_5$	331 $[M + H]^+$, 353 $[M + Na]^+$, 369 $[M + K]^+$, 661 $[2 M + H]^+$, 683 $[2 M + Na]^+$
15	92.2	240—243 (EtOH)	67.44 / 67.45	5.37 / 5.36	8.32 / 8.28	$C_{19}H_{18}N_2O_4$	339 $[M + H]^+$, 361 $[M + Na]^+$, 377 $[M + K]^+$, 677 $[2 M + H]^+$
16	80.5	210—212 (EtOH)	74.38 / 74.49	6.08 / 5.92	9.27 / 9.14	$C_{19}H_{18}N_2O_2$	307 $[M + H]^+$, 329 $[M + Na]^+$, 345 $[M + K]^+$, 613 $[2 M + H]^+$, 635 $[2 M + Na]^+$, 651 $[2 M + K]^+$
17	80.6	299 (decomp.) (EtOH)	68.64 / 68.81	4.68 / 4.69	14.89 / 15.05	$C_{16}H_{13}N_3O_2$	280 $[M + H]^+$, 302 $[M + Na]^+$, 318 $[M + K]^+$
18	96.5	250 (decomp.) (EtOH)	60.85 / 60.80	5.05 / 4.62	6.99 / 6.75	$C_{21}H_{19}ClN_2O_5$	415 $[M + H]^+$, 437 $[M + Na]^+$, 453 $[M + K]^+$, 829 $[2 M + H]^+$
19	97.4	218—220 (EtOH)	65.55 / 65.89	5.24 / 5.00	7.30 / 7.32	$C_{21}H_{19}ClN_2O_3$	383 $[M + H]^+$, 405 $[M + Na]^+$, 421 $[M + K]^+$
20	82.7	297(decomp.) (EtOH)	60.92 / 60.77	4.22 / 3.97	11.87 / 11.81	$C_{18}H_{14}ClN_3O_3$	356 $[M + H]^+$, 378 $[M + Na]^+$, 394 $[M + K]^+$
21	52.8	160—164 (decomp.)	—	—	9.30 / 9.35	$C_{25}H_{27}N_3O_5$	450 $[M + H]^+$, 472 $[M + Na]^+$, 488 $[M + K]^+$
22	83.0	197—200 (MeCN)	72.21 / 71.92	6.41 / 6.52	10.32 / 10.06	$C_{25}H_{27}N_3O_3$	418 $[M + H]^+$, 440 $[M + Na]^+$, 456 $[M + K]^+$
23	65.4	118—121 (toluene)	71.95 / 72.37	6.70 / 6.77	9.90 / 9.74	$C_{26}H_{29}N_3O_3$	432 $[M + H]^+$, 454 $[M + Na]^+$, 470 $[M + K]^+$

(8 mL) was refluxed with stirring for 6 h. On cooling, the precipitate that formed was filtered off, placed in a flask with 4% NaOH (100 mL), stirred for 30 min, and filtered off. The filter cake was washed with water to pH 7, dried, and dissolved in ethanol. The solution was filtered to separate suspended matter and acidified with conc. HCl to pH 5. The resulting hydrochloride was filtered off, washed with ethanol, and dried to give compound **3** (0.25 g).

Table 2. ^{1}H NMR spectra of compounds **3**—**8** (DMSO-d_6)

Compound	δ (*J*/Hz)			
	C(3)H_2 (s, 2 H)	N(4)H	H(5)—H(8) (m)	Substituent at the C(9) atom
3	5.14	—	7.43 (1 H); 7.73 (2 H); 8.39 (1 H)	1.29 (t, 3 H, $CH_2C\underline{H}_3$, *J* = 7.0); 4.05 (m, 2 H, $C\underline{H}_2CH_3$); 8.06 (t, 1 H, NH, *J* = 5.2)
4	5.23	12.70 (br.s)	7.42, 7.57, 7.71, 8.19 (all 1 H each)	—
5	5.48	—	7.86, 8.05, 8.17, 8.45 (all 1 H each)	—
6	5.17	—	7.23—730, 7.48, 7.76, 8.48 (all m, 5 H + 1 H + 2 H + 1 H)*	5.38 (d, 2 H, CH_2, *J* = 6.4); 8.65 (t, 1 H, NH)
7	5.26	—	7.52, 7.79, 7.89, 8.21 (all 1 H each)	3.79—3.89 (m, 8 H, $(CH_2)_4O$)
8	5.67	—	7.76, 7.89, 7.96—8.23, 8.39 (all m, 1 H + 1 H + 3 H + 3 H)*	7.29 (br.s, 2 H, NH_2)

* Overlap with the signals for the substituent at the C(9) atom.

Furo[3,4-*b*]quinoline-1,9(3*H*,4*H*)-dione (4). Compound **2** (7.53 g, 30 mmol) was added at 40 °C to a stirred solution of sodium ethoxide prepared from metallic sodium (1.73 g, 75 mmol) and anhydrous EtOH (80 mL). The reaction mixture was stirred at 40—45 °C for 6 h. On cooling to 20 °C, the precipitate that formed was filtered off and suspended in water (100 mL). The stirred suspension was acidified under cooling with dilute HCl to pH 5. The product was filtered off, washed with water, and dried to give compound **4** (4.1 g).

9-Chlorofuro[3,4-*b*]quinolin-1(3*H*)-one (5). Phosphoryl chloride (6.4 mL) was added dropwise at 5±2 °C for 30 min to stirred DMF (10 mL). The mixture was stirred at this temperature for 10 min. Compound **4** (1.23 g, 6 mmol) was added and the reaction mixture was stirred at 20 °C for 4 h. The precipitate that formed was filtered off, washed with DMF, and suspended in water (100 mL). The suspension was stirred for 30 min and the precipitate was filtered off, washed with water, and dried to give compound **5** (0.95 g).

9-(Benzylamino)furo[3,4-*b*]quinolin-1(3*H*)-one (6). Benzylamine (0.21 g, 2 mmol) was added to a stirred suspension of compound **5** (0.22 g, 1 mmol) in EtOH (10 mL). The mixture was refluxed with stirring for 1 h. On cooling, the precipitate that formed was filtered off, washed with ethanol, and dried to give compound **6** (0.21 g).

9-Morpholinofuro[3,4-*b*]quinolin-1(3*H*)-one (7) and **3-amino-1-(1-oxo-1,3-dihydrofuro[3,4-*b*]quinolin-9-yl)pyridinium chloride (8)** were obtained analogously. In the synthesis of compound **8**, the reaction mixture was refluxed for 6 h.

3-(Dimethylaminomethylidene)-4-methylfuro[3,4-*b*]quinoline-1,9(3*H*,4*H*)-dione (9). Dimethylformamide dimethyl acetal (3.0 g, 25 mmol) was added to a stirred suspension of compound **4** (0.3 g, 1.5 mmol) in DMF (6 mL). The mixture was refluxed with stirring for 3 h. On cooling, the precipitate that formed was filtered off, washed with DMF and water, and dried to give compound **9** (0.1 g). ^{1}H NMR (DMSO-d_6), δ: 3.28 (s, 6 H, NMe_2); 3.84 (s, 3 H, Me); 7.19 (s, 1 H, H(1′)); 7.36, 7.74, 8.18 (all m, 1 H + 2 H + 1 H, H(5)—H(8)).

2-[(5-Oxo-2,5-dihydro-3-furyl)amino]benzoic acid (10). ***A.*** Compound **2** (2.47 g, 10 mmol) was added to a solution of NaOH (0.44 g, 11 mmol) in ethanol (50 mL). The resulting suspension was refluxed with stirring for 30 min. On cooling, the precipitate that formed was filtered off, washed with ethanol, dried, and dissolved in water (25 mL). The solution was acidified with conc. HCl to pH 6—7. The precipitate that formed was filtered off, washed with water, and dried to give compound **10** (1.87 g). ^{1}H NMR (DMSO-d_6), δ: 4.93 (s, 2 H, C(2′)H_2); 5.48 (s, 1 H, H(4′)); 7.14, 7.50, 7.60, 8.00 (all m, 1 H each, H(3)—H(6)); 10.43 (br.s, 1 H, NH); 13.50 (br.s, 1 H, COOH).

B. A mixture of tetronic acid (2.0 g, 20 mmol) and anthranilic acid (2.74 g, 20 mmol) was refluxed in stirred MeOH (20 mL) for 6 h. On cooling, the precipitate that formed was filtered off, washed with methanol, and dried to give compound **10** (2.97 g).

3-(Dimethylaminomethylidene)furo[3,4-*b*]quinoline-1,9(3*H*,4*H*)-dione (11). Phosphoryl chloride (14 mL) was added dropwise at 5±2 °C for 30 min to stirred DMF (45 mL). The mixture was stirred at this temperature for 10 min. Then compound **10** (2.97 g, 13.6 mmol) was added and the reaction mixture was stirred at 20 °C for 4 h. The precipitate was filtered off, washed with DMF, and suspended in water (100 mL). The suspension was stirred for 30 min and the precipitate was filtered off, washed with water, and dried. Then it was suspended in ethanol (200 mL) and the stirred suspension was alkalified with 1 *M* NaOH to pH 7—7.5. On cooling, the precipitate was filtered off, washed with ethanol, and dried to give compound **11** (1.8 g) as a mixture of *E*- and *Z*-isomers (5 : 1). ^{1}H NMR (DMSO-d_6), δ: 3.41, 3.65 (both s, 3 H each, NMe_2); 7.25 and 7.35, 7.48 and 7.52, 7.57 and 7.72, 8.15 and 8.03 (all m, 1 H each, H(5)—H(8)); 8.02, 7.69 (s, 1 H, H(1′)); 11.63, 11.28 (br.s, 1 H, NH).

3-(Benzylaminomethylidene)furo[3,4-*b*]quinoline-1,9(3*H*,4*H*)-dione (12). A suspension of compound **11** (0.13 g, 0.445 mmol) and benzylamine (0.090 g, 0.89 mmol) in ethanol (5 mL) was stirred for 4 h. The precipitate was filtered off, washed with ethanol, dried, and recrystallized from DMF to give compound **12** (0.09 g). ^{1}H NMR (DMSO-d_6), δ: 4.68 (d, 2 H, $C\underline{H}_2$Ph, *J* = 6.0 Hz); 7.21—7.56, 8.15 (both m, 8 H + 1 H, Ph, H(5)—H(8)); 8.31 (d, 1 H, H(1′), *J* = 14.7 Hz); 9.78 (m, 1 H, $N\underline{H}CH_2$Ph); 11.84 (br.s, 1 H, N(4)H).

3-(Morpholinomethylidene)furo[3,4-*b*]quinoline-1,9(3*H*,4*H*)-dione (13) was obtained analogously.

Ethyl 2-{[(2-dimethylaminomethylidene)-4-formyl-5-oxo-2,5-dihydro-3-furyl]amino}benzoate (14). Phosphoryl chloride (9 mL) was added dropwise at 5±2 °C for 30 min to stirred DMF (30 mL). The mixture was stirred at this temperature for 10 min and then compound **2** (2.47 g, 10 mmol) was added. The reac-

Table 3. ^{1}H NMR spectra of compounds **15**—**23** (DMSO-d_6)

Compound	δ (*J*/Hz)						
	C(3)H_2 (s, 2 H, AB system)	H(5)—H(8), Ph	N(4)H (br.s, 1 H)	N(9)H (d, 1 H)	H(10) (1 H)	Substituent at the atom	
						N(9)	C(10)
15	4.82	6.50, 6.65, 6.85 (all m, 1 H + + 4 H + 2 H)	9.66	5.86 (J = 4.5)	4.98 (d, J = 4.5)	—	3.63, 3.66 (both s, 3 H each, OMe)
16	4.69	6.81, 6.96, 7.09, 7.18 (all m, 3 H + 1 H + + 3 H + 2 H)	9.54	5.66 (J = 4.5)	3.87 (m)	—	1.65, 2.55, 2.74 (all m, 2 H + 1 H + + 1 H, C$\underline{H}_2$C$\underline{H}_2$Ph)
17	4.86	6.58, 6.68, 6.74, 6.90 (all m, 1 H each)	9.84	6.06 (J = 4.5)	5.08 (d, J = 4.5)	—	7.15 (dd, 1 H, H(5′), $J_{4',5'}$ = 7.8, $J_{5',6'}$ = 4.7); 7.42 (dt, 1 H, H(4′), $J_{4',5'}$ = 7.8, $J_{4',6'} = J_{2',4'}$ = 1.7); 8.29 (dd, 1 H, H(6′), $J_{4',6'}$ = 1.7, $J_{5',6'}$ = 4.7); 8.36 (d, H(2′), $J_{2',4'}$ = 1.7)
18	4.93	6.39, 6.64, 6.86, 6.96, 7.07, 7.22 (all m, 1 H + + 2 H + 1 H + + 1 H + 1 H + + 1 H)	10.13	—	6.73 (s)	3.69, 4.17 (both d, 1 H each, CH_2Cl, J = 13.8)	3.64, 3.68 (both s, 3 H each, OMe)
19	4.78	7.15, 7.40, 7.59 (all m, 7 H + + 1 H + 1H)	10.06	—	5.53 (dd, J_1 = 5.1, J_2 = 9.2)	3.74, 4.19 (both d, 1 H each, CH_2Cl, J = 13.8)	1.39, 1.57, 2.58, 2.69 (all m, 1 H each, C$\underline{H}_2$C$\underline{H}_2$Ph)
20	4.99	6.87, 6.98, 7.11 (all m, 1 H each)	10.25	—	6.87 (s)	3.78, 4.21 (both d, 1 H each, CH_2Cl, J = 13.8)	7.23 (m, 2 H, H(5′), 1 H from H(5)—H(8)); 7.46 (dt, 1 H, H(4′), $J_{4',5'}$ = 7.8, $J_{4',6'} = J_{2',4'}$ = 1.7); 8.28 (d, H(2′), $J_{2',4'}$ = 1.7); 8.35 (dd, 1 H, H(6′), $J_{5',6'}$ = 4.7, $J_{4',6'}$ = 1.7)
21	4.88	6.79, 7.06, 7.16 (all m, 2 H + + 1 H + 1 H)	10.09	—	6.75 (s)	1.62, 2.35 (both m, 4 H each, $(CH_2)_4$); 2.74, 3.03 (both d, 1 H each, CH_2CO, J = 14.1)	3.66 (s, 6 H, OMe); 6.41, 6.59, 6.62 (dd, d, d, 1 H each, H(2′), H(6′), H(5′), J_o = 8.4, J_m = 1.2)
22	4.73	7.14, 7.43, 7.44 (all m, 7 H + + 1 H + 1 H)	9.90	—	5.54 (dd, J_1 = 5.1, J_2 = 9.2)	2.77, 3.06 (both d, 1 H each, CH_2CO, J = 14.1); 1.32—1.77, 2.34, 2.57, 2.68 (all m, 6 H + 4 H + + 1 H + 1 H, C$\underline{H}_2$C$\underline{H}_2$Ph, $(CH_2)_4$)	
23	4.70	7.12, 7.31, 7.40 (all m, 7 H + + 1 H + 1 H)	9.87	—	5.53 (dd, J_1 = 5.1, J_2 = 9.2)	2.70, 2.82 (both d, 1 H each, CH_2CO, J = 14.1); 1.18—1.71, 2.08, 2.58, 2.70 (all m, 8 H + 4 H + + 1 H + 1 H, C$\underline{H}_2$C$\underline{H}_2$Ph, $(CH_2)_5$)	

tion mixture was stirred at 20 °C for 4 h, diluted with water, and alkalified with 10% NaOH to pH 8. The precipitate that formed was filtered off, washed with water, dried, washed with hot acetone, and recrystallized from ethanol to give compound **14** (0.92 g). ^{1}H NMR (DMSO-d_6), δ: 1.30 (t, 3 H, C$\underline{H}_3$CH$_2$, J = 7 Hz); 4.30 (q, 2 H, CH$_3$C$\underline{H}_2$, J = 7 Hz); 3.07 (s, 6 H, NMe_2); 6.52 (s, 1 H, H(2″)); 7.31, 7.55, 7.94 (all m, 1 H + 2 H + 1 H, H(3)—H(8)); 9.47 (s, 1 H, CHO); 10.30 (br.s, 1 H, NH).

10-(3,4-Dimethoxyphenyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (15). 3,4-Dimethoxybenzaldehyde (0.75 g, 4.5 mmol) and two drops of AcOH were added to a suspension of 4-(2-aminoanilino)furan-2(5*H*)-one (0.82 g, 4.3 mmol)[12] in butanol (40 mL). The mixture was refluxed with stirring for 3 h. On cooling, the precipitate that formed was filtered off, washed with ethanol, and dried to give compound **15** (1.34 g).

10-Phenethyl-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (16) and **10-(3-pyridyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (17)** were obtained analogously. In the synthesis of compound **16**, ethanol was used instead of butanol.

9-(2-Chloroacetyl)-10-(3,4-dimethoxyphenyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (18). Chloroacetyl chloride (0.49 g, 4.4 mmol) was added to a suspension of compound **15** (1.34 g, 4 mmol) in dry benzene (30 mL). The mixture was refluxed with stirring for 3 h. On cooling, the precipitate that formed was filtered off and washed with benzene and ether to give compound **18** (1.6 g).

9-(2-Chloroacetyl)-10-phenethyl-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (19) and **9-(2-chloroacetyl)-10-(3-pyridyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*]-[1,5]benzodiazepin-1-one (20)** were obtained analogously.

10-(3,4-Dimethoxyphenyl)-9-(2-pyrrolidinoacetyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (21). Pyrrolidine (0.35 g, 4.9 mmol) was added to a suspension of compound **18** (0.4 g, 0.97 mmol) in benzene (6 mL). The mixture was refluxed with stirring for 4 h. The solvent was removed and the residue was triturated with water and then with ether. The precipitate was filtered off, washed with ether, dried, and chromatographed on SiO_2 with MeOH as an eluent. The yield of compound **21** was 0.23 g.

10-Phenethyl-9-(2-pyrrolidinoacetyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (22) and **10-phenethyl-9-(2-piperidinoacetyl)-3,4,9,10-tetrahydro-1*H*-furo[3,4-*b*][1,5]benzodiazepin-1-one (23)** were obtained analogously and purified by recrystallization.

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