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SYNTHESIS OF TETRAHYDRO-1H,7H-BENZO[*ij*]QUINOLIZINE-1,7-DIONE DERIVATIVES

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Tetrahydro-1H,7H-benzo[ij]quinolizine-1,7-diones have been obtained by the cyclization of N-alkoxyphenyl-N-(2-carboxyethyl)-β-alanines. Fission of the ester bond occurs on cyclization of N-(4-ethoxyphenyl)-N-(2-carboxyethyl)-β-alanine, but the cyclization of the 3,4-dialkoxyphenyl derivative leads to the formation of 9-alkoxy-8-hydroxy-2,3,5,7-tetrahydro-1H,7H-benzo[ij]quinolizine-1,7-diones. The corresponding dioximes and diphenylhydrazones were obtained.

Keywords: N-alkoxyphenyl-N-(2-carboxyethyl)-β-alanines, dioximes, diphenylhydrazones, 2,3,5,7-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-diones, cyclization.

The quinolizine system is contained in several alkaloids [1]. Derivatives of benzo[*ij*]quinolizine are used as antibacterial preparations [2]. The preparation of dioxoyulolidines [3-5] by the interaction of acrylic acid or its nitrile with aromatic amines at high temperature in polyphosphoric acid is accompanied by the formation of many side products. A more convenient method of synthesizing benzoquinolizidinediones includes the cyclization of N-aryl-N-carboxyethyl-β-alanines [6].

It seemed of interest to us to obtain benzoquinolizinediones containing alkylenedioxy and alkoxy groups. N-Substituted phenyl-N-(2-carboxyethyl)-β-alanines **2** were obtained by the addition of amines **1** to acrylic acid at a reactant ratio of 1:2. The addition reaction goes at room temperature or on initial heating, and the resulting diacids **2** crystallized out from the reaction mixture. The presence of acetal and ester bonds in **2** caused auxiety that the cyclization of the latter might be accompanied by fission of these bonds. On studying the conditions of forming yulolidine derivatives from the 4-alkoxyphenyl derivatives **2a,b**, it was established that cyclization occurs at 160°C in polyphosphoric acid, and 9-methoxy-2,3,5,7-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione (**3a**) is formed in 11.4% yield. Under the same conditions the ethoxy derivative **2b** undergoes fission of the ether bond and the hydroxy derivative **3b** is isolated from the reaction mixture in 13.5% yield with a method of rapid chromatographic column.

The ^{1}H NMR spectra of compounds **3a,b** show two triplets for the four CH_2 groups of the two heterocycles and also singlets for the two aromatic protons. The signal for the methyl group was missing from the spectrum of **3b** but there was a singlet for the hydroxyl group proton at 9.28 ppm.

Due to the symmetry of compounds **3a,b** relative to the hydroxy or methoxy groups the corresponding lines in the ^{13}C NMR spectra coincided. The signals of both carbon atoms for the carbonyl groups were registered at low field at 192 ppm, and the signal for the methyl group of compound **3a** was observed at

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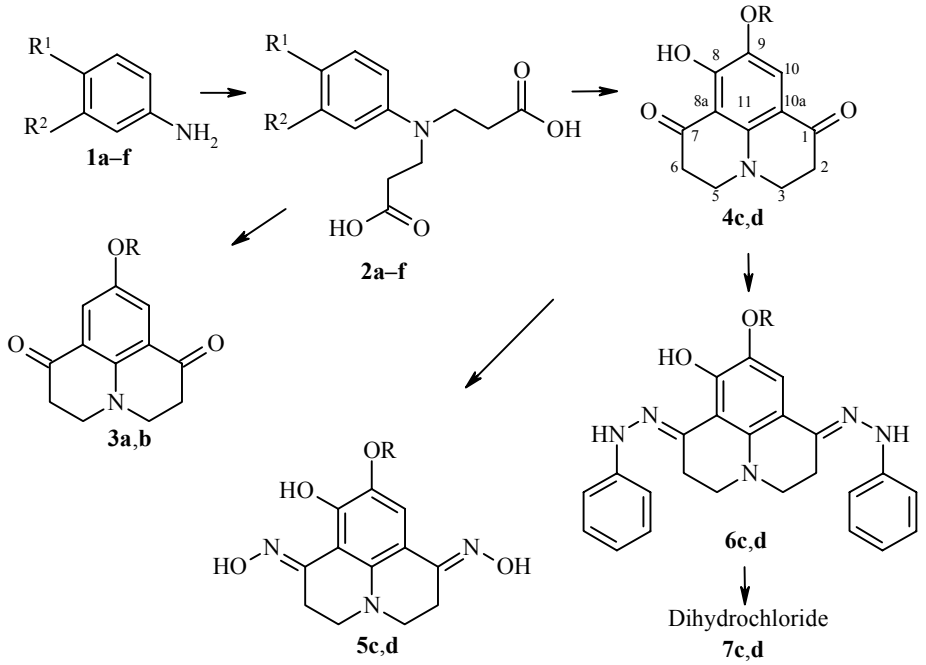
55.8 ppm. The chemical shifts of the $C_{(8)}$, $C_{(8a)}$, $C_{(10)}$, and $C_{(10a)}$ atoms differed by 1 ppm from the corresponding signals for compound **3b**.

It was established by us that the amount of reacting substance proves to have a large effect on the reaction yield. In the cyclization process the yields of **4c** and **4d** were 57 and 47% respectively from 5 mmol of N-(3,4-dimethoxyphenyl)- (**2c**) and N-(3,4-diethoxyphenyl)-N-(2-carboxyethyl)-β-alanines (**2d**) in polyphosphoric acid at 100°C. An increase in the amount of reacting substances or the cyclization temperature did not lead to an increase in yield, at 200°C it did not reach 15%. On refluxing **2c** in $POCl_3$ the yield of **4c** did not exceed 11%.



1, 2 a R^1 = OMe, R^2 = H; **b** R^1 = OEt, R^2 = H; **c** $R^1 = R^2$ = OMe; **d** $R^1 = R^2$ = OEt; **e** $R^1 + R^2$ = O–CH_2–O; **f** $R^1 + R^2$ = O–CH_2–CH_2–O; **3 a** R = Me, **b** R = H; **4-6 c** R = Me, **d** R = Et

It is characteristic that in the cyclization process fission of only one ether bond close to a keto group occurs .

Cyclization of N-(3,4-methylenedioxyphenyl)- and N-(3,4-ethylenedioxyphenyl)-N-(2-carboxyethyl)-β-alanines **2e,f** was unsuccessful. Both in polyphosphoric acid and in $POCl_3$ blackening of the reaction mass occurs even after a few minutes and no products were successfully isolated from it.

The structures of compounds **4** were confirmed by data of elemental analysis and spectral investigations. The ^{1}H NMR spectra taken in DMSO-d_6 show two triplets and a quartet for the two overlapping triplets of CH_2 groups, and in the spectra taken in C_6D_6 all four triplets were observed. As a result of fission of one ether bond the hydroxyl group formed was identified as a singlet at 13.5 ppm with a rather high intensity. According to the data of NOESY spectra of compound **4c** the methoxy group was assigned to position 9, since an interaction was observed for its protons with the $H_{(10)}$ proton of the aromatic ring. This was also confirmed by ^{13}C NMR spectra. Due to the shielding γ-effect of the hydroxyl group the chemical shift of the 7-keto group carbon atom was at 189 ppm, while the signal of the $C_{(1)}$ atom was at lower field at 200 ppm. In the spectrum of compound **4d** deshielding was observed for the $C_{(10)}$ atom, the signal of which was shifted by 1 ppm towards low field. Characteristic lines in the INEPT spectra also confirmed the structure of the benzoquinolizinediones.

TABLE 1. ^{1}H NMR Spectra of Compounds **2c-f** in DMSO-d_6

Compound	Chemical shifts, δ, ppm							J^{HH}, Hz	
	H(5), d	H(2), d	H(6), dd	α-CH_2, t	β-CH_2, t	COOH, s	Other groups	26	56
2c	6.42	6.80	6.22	2.43	3.48	12.08	3.66 (3H, s, 3-CH_3O); 3.74 (3H, s, 4-CH_3O)	2.8	8.7
2d	6.79	6.39	6.21	2.42	3.47	12.04	1.26 (3H, t, 3-$\underline{CH_3}CH_2O$); 1.34 (3H, t, 4-$\underline{CH_3}CH_2O$); 3.91 (2H, q, 3-$CH_3\underline{CH_2}O$); 4.01 (2H, q, 4-$CH_3\underline{CH_2}O$)		8.8
2e	6.74	6.46	6.14	2.41	3.45	12.08	5.87 (2H, s, OCH_2O)	2.8	8.5
2f	6.68	6.22-6.27		2.40	3.43	12.07	4.13 (2H, 2 t, OCH_2CH_2O); 4.18 (2H, 2 t, OCH_2CH_2O)	2.5	8.9

TABLE 2. ^{13}C NMR Spectra of Compounds **2a-f** in DMSO-d_6

Compound	Chemical shifts, δ, ppm									
	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	CO	$C_{(\alpha)}$	$C_{(\beta)}$	$C_{(7)}$; $C_{(8)}$ / $C_{(7')}$; $C_{(8')}$
2a	141.74	114.94	115.26	151.71	115.26	114.94	173.20	32.22	47.27	55.42
2b	142.01	114.61	115.70	150.41	115.70	114.61	174.01	33.14	47.51	63.49; 14.86
2c	142.58	100.42	150.13	141.26	114.71	105.23	173.26	32.29	47.11	55.64; 55.67
2d	142.76	101.75	149.85	140.41	117.10	105.48	173.25	32.29	47.06	64.02; 65.24 / 14.87; 15.07
2e	143.33	96.67	148.31	139.00	108.54	105.61	173.16	32.16	47.37	100.38
2f	142.23	102.27	143.92	135.28	117.39	106.82	173.16	32.21	47.02	63.42; 64.42

Numerous attempts to obtain the 8,9-dimethoxy derivative of benzoquinolizine by alkylation of **4c** with dimethyl sulfate in DMF, with iodomethane in acetone or methyl ethyl ketone in the presence of K_2CO_3, and with iodomethane in methanol in the presence of CH_3ONa did not lead to an appreciable yield of the desired product. Traces of the dimethoxy derivative were detected only by mass spectrometry.

By heating quinolizinediones **4** with hydroxylamine hydrochloride in the presence of pyridine or with phenylhydrazine the dioximes **5** and diphenylhydrazones **6** were obtained. Compounds **5** and **6** were isolated from the reaction mixture in high yield only in those cases when the reaction mixture did not darken initially. In individual cases they began to decompose and darken also when purifying them chromatographically. The hydrochlorides of diphenylhydrazones **7** were obtained by the usual method and were stable substances.

In addition to the signals of to the benzoquinolizinediones the ^1H NMR spectra of oximes **5** show proton signals of the N–OH group at low field at 10.5 and 11.4 ppm. In the ^{13}C NMR spectra the same structural regularities were observed as for compound **4**. Due to the γ-influence of the hydroxyl group at $C_{(8)}$ the signal of the $C_{(7)}$ atom was observed at 150 ppm and of the $C_{(1)}$ atom at 156 ppm. As a result of the deshielding effect of the ethoxy group of compound **5d** the signal for the $C_{(10)}$ atom was shifted by 2 ppm towards low field compared with the analogous atom of compound **5c**.

The molecular weights found for the diphenylhydrazones **6** corresponded to calculated values and the NMR spectra show signals for the two phenyl groups in addition to those characteristic of benzoquinolizinediones.

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Bruker Avance DPX 400 (400 MHz) spectrometer at 46°C. The internal standard for DMSO-d_6 was the residue of DMSO-d_5 (δ_H 2.50 ppm), and for C_6D_6 the residue of C_6D_5H (δ_H 7.16 ppm). The ^{13}C and INEPT NMR spectra were recorded on a Bruker Avance DPX 400 (100.61 MHz) spectrometer. The NOESY spectrum was recorded on Bruker DRX 500 (500 MHz) apparatus. The mass spectra were obtained on a Kratos MS 80 apparatus. Accurate molecular masses were obtained by HRMS. The progress of reactions was followed by TLC using Silufol 254, Silufol UV 254, and Kieselgel 60 F_{254} (Merck 0.25 mm) plates. The ^1H and ^{13}C NMR spectra of compounds **2a-f** are given in Tables 1 and 2.

N-(2-Carboxyethyl)-N-(4-methoxyphenyl)-β-alanine (2a). A mixture of *p*-anisidine **1a** (61.5 g, 0.5 mol) and acrylic acid (72 g, 1 mol) was heated at 50°C for 4 h and left at room temperature for 2 weeks. The resulting crystals were filtered off, and crystallized from ethanol–ether, 1:5. Yield 63.1 g (47.2%); mp 119-120°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.40 (4H, t, α-CH_2); 3.46 (4H, t, β-CH_2); 3.67 (3H, s, CH_3O); 6.71 (2H, d, H_B arom.); 6.81 (2H, d, H_A arom.). Found, %: C 58.44; H 6.41; N 5.24. $C_{13}H_{17}NO_5$. Calculated, %: C 58.42; H 6.41; N 5.24. HRMS (EI): found 267.1076, calculated 267.1107.

N-(2-Carboxyethyl)-N-(4-ethoxyphenyl)-β-alanine (2b) was obtained analogously to **2a** from *p*-phenetidine hydrochloride **1b** (86.75 g, 0.5 mol), AcONa (41 g, 0.5 mol), and acrylic acid (72 g, 1 mol) with a yield of 59 g (42%); mp 96-98°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.27 (3H, t, $\underline{CH_3}CH_2O$); 2.35 (4H, t, α-CH_2); 3.43 (4H, t, β-CH_2); 3.91 (2H, q, $CH_3\underline{CH_2}O$); 6.66 (2H, d, H_B arom.); 6.78 (2H, d, H_A arom.). Found, %: C 59.6; H 6.83; N 4.98. $C_{14}H_{19}NO_5$. Calculated, %: C 59.82; H 6.81; N 4.98. HRMS (EI): found 281.1295, calculated 281.1261.

N-(2-Carboxyethyl)-N-(3,4-dimethoxyphenyl)-β-alanine (2c). 3,4-Dimethoxyaniline **1c** (7.6 g, 50 mmol) and acrylic acid (7.2 g, 0.1 mol) were dissolved in toluene (50 ml). The mixture was stored at room temperature for 1 week. The resulting crystals were filtered off, and crystallized from ethanol. Yield 10.62 g (71.5%); mp 109-110°C. Found, %: C 56.63; H 6.90; N 4.73. $C_{14}H_{19}NO_6$. Calculated, C 56.56; H 6.44; N 4.71. MS FAB (Ar, glycerol): found 298(9), calculated 297.1212.

N-(2-Carboxyethyl)-N-(3,4-diethoxyphenyl)-β-alanine (2d) was obtained from 3,4-diethoxyaniline **1d** (9.1 g, 50 mmol) analogously to **2c**. Yield 11.2 g (69%); mp 92-94°C. Found, %: C 58.63; H 7.51; N 4.42. $C_{16}H_{23}NO_6$. Calculated, %: C 59.06; H 7.13; N 4.31. MS FAB (Ar, glycerol): found 326(100), calculated 325.1525.

N-(2-Carboxyethyl)-N-(3,4-methylenedioxyphenyl)-β-alanine (2e) was obtained from 3,4-methylenedioxyaniline **1e** (6.9 g, 50 mmol) analogously to **2c**. Yield 9.2 g (65.3%); mp 133-134°C (ethanol). Found, %: C 56.11; H 5.71; N 5.15. $C_{13}H_{15}NO_6$. Calculated, %: C 55.51; H 5.38; N 4.98. MS FAB (Ar, NBA): found 282(20), calculated 281.0899.

N-(2-Carboxyethyl)-N-(3,4-ethylenedioxyphenyl)-β-alanine (2f) was obtained from 3,4-ethylenedioxyaniline **1f** (7.6 g, 50 mmol) analogously to compound **2c**. Yield 12.0 g (81.6%); mp 143-144°C. Found, %: C 56.86; H 5.81; N 4.73. $C_{14}H_{17}NO_6$. Calculated, %: C 56.94; H 5.80; N 4.74. MS FAB (Ar, NBA): found 296(100), calculated 295.1056.

9-Methoxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione (3a). A mixture of P_2O_5 (30 g) and H_3PO_4 (10 ml) was refluxed at 160°C for 30 min. Alanine **2a** (1.335 g, 5 mmol) was introduced and the mixture was stirred at the same temperature for 10 min. The reaction mixture was cooled, ice water (100 ml) was poured in, and the mixture was extracted with chloroform (4 x 15 ml). The chloroform was removed on a rotary evaporator, and the residual crystalline substance was purified by rapid column chromatography [Merck kieselgel 60 (0.04-0.063 mm), ethyl acetate–hexane, 3:1]. Yield of **3a** was 0.14 g (11.4%); mp 190°C (decomp.). ^{1}H NMR spectrum, δ, ppm (DMSO-d_6): 2.74 (4H, t, CH_2); 3.42 (4H, t, CH_2); 3.76 (3H, s, CH_3O); 7.50 (2H, s, H arom.); (C_6D_6): 2.39-2.44 (4H, 2t, CH_2); 2.47-2.54 (4H, 2t, CH_2); 3.36 (s, CH_3O); 7.26 (1H, s, H arom.); 8.03 (1H, s, H arom.). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 37.26 ($C_{(2)}$ and $C_{(6)}$); 49.61 ($C_{(3)}$ and $C_{(5)}$); 55.82 (OCH_3); 118.25 ($C_{(8)}$ and $C_{(10)}$); 124.62 ($C_{(8a)}$ and $C_{(10a)}$); 191.79 ($C_{(1)}$ and $C_{(7)}$). Found, %: C 67.43; H 5.91; N 6.23. $C_{13}H_{13}NO_3$. Calculated, %: C 67.52; H 5.67; N 6.06. HRMS (EI): found 231.0889, calculated 231.0895.

9-Hydroxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione (3b) was obtained from **2b** (1.405 g, 5 mmol) analogously to **3a**. Yield 0.15 g (13.5%). The eluent was a mixture of ethyl acetate–hexane–acetone, 3:1:1; mp 95°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.71 (4H, t, CH_2); 3.37 (4H, t, CH_2); 7.41 (2H, s, H arom.); 9.28 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 37.35 ($C_{(2)}$ and $C_{(6)}$); 49.79 ($C_{(3)}$ and $C_{(5)}$); 119.40 and 119.49 ($C_{(8)}$ or $C_{(10)}$); 125.12 ($C_{(8a)}$ and $C_{(10a)}$); 148.67 and 148.85 ($C_{(9)}$ or $C_{(11)}$); 191.91 ($C_{(1)}$ and $C_{(7)}$). Found, %: C 66.31; H 5.08; N 6.47. $C_{12}H_{11}NO_3$. Calculated, %: C 66.35; H 5.10; N 6.45. HRMS (EI): found 217.1067, calculated 217.0739.

8-Hydroxy-9-methoxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione (4c). A mixture of P_2O_5 (30 g) and 85% H_3PO_4 (10 ml) was refluxed at 100°C for 30 min. Compound **2c** (1.485 g, 5 mmol) was added and the mixture was refluxed for 30 min further. The reaction mixture was cooled, ice water (100 ml) was added, and the mixture extracted with chloroform (3 x 50 ml). The chloroform was removed from the extract on a rotary evaporator, and the residual crystals were purified by rapid column chromatography [Merck kieselgel 60 (0.04-0.063 mm), ethyl acetate–hexane–acetone–acetic acid, 30:10:10:5]. Yield 0.71 g (57.5%); mp 144°C (decomp.). ^{1}H NMR spectrum, δ, ppm (DMSO-d_6): 2.63 (2H, t, CH_2); 2.85 (2H, t, CH_2); 3.41-3.46 (4H, 2t, CH_2); 3.74 (3H, s, CH_3O); 7.47 (1H, s, H arom.); 13.56 (1H, s, OH); (C_6D_6): 2.19 (2H, t, CH_2); 2.35 (2H, t, CH_2); 2.42 (2H, t, CH_2); 2.54 (2H, t, CH_2); 3.50 (3H, s, CH_3O); 7.94 (1H, s, H arom.); 14.03 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 36.25 ($C_{(2)}$); 36.34 ($C_{(6)}$); 48.88 ($C_{(3)}$); 49.82 ($C_{(5)}$); 56.50 (OCH_3); 106.09 ($C_{(8a)}$); 110.06 ($C_{(10a)}$); 117.84 ($C_{(10)}$); 139.73 ($C_{(9)}$); 150.66 ($C_{(8)}$); 159.24 ($C_{(11)}$); 189.37 ($C_{(7)}$); 200.11 ($C_{(1)}$). INEPT spectrum (DMSO-d_6), δ, ppm: 37.19 ($C_{(2)}$); 37.28 ($C_{(6)}$); 49.82 ($C_{(3)}$); 50.76 ($C_{(5)}$); 57.30 (OCH_3); 118.40 ($C_{(10)}$). Found, %: C 63.41; H 5.22; N 5.48. $C_{13}H_{13}NO_4$. Calculated, %: C 63.15; H 5.30; N 5.67. HRMS (EI): found 247.0861, calculated 247.0845.

9-Ethoxy-8-hydroxy-2,3,5,6-tetrahydro-1H,7H-benzo[ij]quinolizine-1,7-dione (4d) was obtained from compound **2d** (1.625 g, 5 mmol) analogously to **4c** with a yield of 0.615 g (47.1%); mp 169.5°C (decomp.). ^{1}H NMR spectrum, δ, ppm, *J* (Hz) (DMSO-d_6): 1.29 (3H, t, CH_3); 2.63 (2H, t, CH_2); 2.84 (2H, t,

CH_2); 3.41-3.46 (4H, 2t, CH_2); 3.98 (2H, q, J = 6.9, J = 13.9, $CH_3\underline{CH_2}O$); 7.47 (1H, s, H arom.); 13.55 (1H, s, OH); (C_6D_6): 1.25 (3H, t, CH_3); 2.19 (2H, t, CH_2); 2.34 (2H, t, CH_2); 2.41 (2H, t, CH_2); 2.54 (2H, t, CH_2); 3.82 (2H, q, J = 7.0, J = 13.9, $CH_3\underline{CH_2}O$); 8.01 (1H, s, H arom.); 14.05 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.87 (OCH_2CH_3); 36.46 ($C_{(2)}$); 36.56 ($C_{(6)}$); 49.07 ($C_{(3)}$); 50.00 ($C_{(5)}$); 64.93 ($O\underline{C}H_2CH_3$); 106.34 ($C_{(8a)}$); 110.26 ($C_{(10a)}$); 119.02 ($C_{(10)}$); 138.86 ($C_{(9)}$); 150.99 ($C_{(8)}$); 159.68 ($C_{(11)}$); 189.85 ($C_{(7)}$); 200.54 ($C_{(1)}$). INEPT spectrum (DMSO-d_6), δ, ppm: 15.55 ($OCH_2\underline{C}H_3$); 37.18 ($C_{(2)}$); 37.29 ($C_{(6)}$); 49.81 ($C_{(3)}$); 50.73 ($C_{(5)}$); 65.90 ($O\underline{C}H_2CH_3$); 120.37 ($C_{(10)}$). Found, %: C 64.70; H 6.00; N 5.58. $C_{14}H_{15}NO_4$. Calculated, %: C 64.36; H 5.79; N 5.36. HRMS (EI): found 261.1001, calculated 261.1001.

8-Hydroxy-9-methoxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione Dioxime (5c). A solution of benzoquinolizinedione **4c** (0.99 g, 4 mmol) in methanol (100 ml) was added dropwise to a mixture of hydroxylamine hydrochloride (1.112 g, 16 mmol), pyridine (1.9 g, 24 mmol), methanol (10 ml), and water (0.5 ml). The reaction mixture was refluxed for 4.5 h (TLC), HCl (5 drops) was added, and the light fraction was distilled off on a rotary evaporator. Compound **4c** was purified by rapid column chromatography [Merck kieselgel 60 (0.04-0.063 mm), ethyl acetate–hexane, 3 : 1]. Yield 1.0 g (90.2%), mp 180.8°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.73 (2H, t, CH_2); 2.88 (2H, t, CH_2); 2.97-3.02 (4H, 2t, CH_2); 7.36 (1H, s, H arom.); 12.26 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 22.76 ($C_{(2)}$ and $C_{(6)}$); 48.08 and 49.03 ($C_{(3)}$ or $C_{(5)}$); 56.24 (OCH_3); 104.08 ($C_{(8a)}$); 108.32 ($C_{(10a)}$); 109.42 ($C_{(10)}$); 140.82 ($C_{(9)}$); 141.69 ($C_{(8)}$); 149.22 ($C_{(11)}$); 150.26 ($C_{(7)}$); 155.92 ($C_{(1)}$). Found, %: C 56.18; H 5.67; N 15.34. $C_{13}H_{15}N_3O_4$. Calculated, %: C 56.31; H 5.45; N 15.15. HRMS (EI): found 277.1075, calculated 277.1063.

9-Ethoxy-8-hydroxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione Dioxime (5d) was obtained from **4d** (1.044 g, 4 mmol) analogously to **5c**. Yield 1.0 g (86%), mp 202°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 1.28 (3H, t, CH_3); 2.73 (2H, t, CH_2); 2.88 (2H, t, CH_2); 2.98-3.03 (4H, 2t, CH_2); 3.94 (2H, q, J = 6.9, J = 13.9, $CH_3\underline{CH_2}$); 7.36 (1H, s, H arom.); 10.59 (1H, s, NOH); 11.39 (1H, s, NOH); 12.22 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.91 ($OCH_2\underline{C}H_3$); 22.69 and 22.76 ($C_{(2)}$ or $C_{(6)}$); 48.01 and 48.95 ($C_{(3)}$ or $C_{(5)}$); 64.75 ($O\underline{C}H_2CH_3$); 104.08 ($C_{(8a)}$); 108.34 ($C_{(10a)}$); 111.51 ($C_{(10)}$); 139.62 ($C_{(9)}$); 141.84 ($C_{(8)}$); 149.18 ($C_{(11)}$); 150.75 ($C_{(7)}$); 155.87 ($C_{(1)}$). Found, %: C 57.29; H 6.01; N 14.30. $C_{14}H_{17}N_3O_4$. Calculated, %: C 57.72; H 5.88; N 14.43. HRMS (EI): found 291.1206, calculated 291.1219.

8-Hydroxy-9-methoxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione Diphenylhydrazone (6c). Benzoquinolizinedione **4c** (1.235 g, 5 mmol) was added to a solution of phenylhydrazine (3.24 g, 30 mmol) in 99.5% ethanol (100 ml) and the mixture refluxed for 3 h. On standing the reaction mixture at 4°C crystals formed, were filtered off, and washed with ether. Yield 1.5 g (70.3%), mp 203°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.77 (2H, t, CH_2); 2.94 (2H, t, CH_2); 3.11-3.15 (4H, 2t, CH_2); 3.79 (3H, s, CH_3O); 7.61 (1H, s, H arom.); 6.70-7.36 (10H, m, H arom.); 9.00 (1H, s, NH); 9.46 (1H, s, NH); 13.56 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 24.60 and 25.03 ($C_{(2)}$ or $C_{(6)}$); 48.27 and 49.18 ($C_{(3)}$ or $C_{(5)}$); 56.68 (OCH_3); 105.76 ($C_{(8a)}$); 109.71 ($C_{(10)}$); 111.22 ($C_{(10a)}$); 118.36 and 119.79 ($C_{(4')}$); 112.47 and 112.60 ($C_{(2')}$); 128.43 and 128.97 ($C_{(3')}$); 139.07 ($C_{(8)}$); 141.23 ($C_{(9)}$); 141.42 ($C_{(7)}$); 145.07 and 146.59 ($C_{(1')}$); 147.31 ($C_{(11)}$); 149.65 ($C_{(1)}$). Found, %: C 69.98; H 6.40; N 16.53. $C_{25}H_{25}N_5O_2$. Calculated, %: C 70.22; H 5.88; N 16.39. HRMS (EI): found 427.2019, calculated 427.2008.

9-Ethoxy-8-hydroxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione Diphenylhydrazone (6d) was obtained from **4d** (1.3 g, 5 mmol) analogously to **6c**. Yield 1.8 g, (81.6%), mp 203°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.35 (3H, t, CH_3); 2.77 (2H, t, CH_2); 2.94 (2H, t, CH_2); 3.11-3.15 (4H, 2t, CH_2); 4.03 (2H, q, $CH_3\underline{CH_2}O$); 7.61 (1H, s, H arom.); 6.70-7.32 (10H, m, H arom.); 8.99 (1H, s, NH); 9.45 (1H, s, NH); 13.56 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 15.19 ($CH_3\underline{C}H_2O$); 24.62 and 25.05 ($C_{(2)}$ or $C_{(6)}$); 48.26 and 49.17 ($C_{(3)}$ or $C_{(5)}$); 64.96 ($CH_3\underline{C}H_2O$); 105.80 ($C_{(8a)}$); 111.26 ($C_{(10a)}$); 111.42 ($C_{(10)}$); 112.49 and 112.59 ($C_{(2')}$); 118.36 and 119.77 ($C_{(4')}$); 128.97 and 129.42 ($C_{(3')}$); 139.13 ($C_{(8)}$); 140.18 ($C_{(9)}$); 141.57 ($C_{(7)}$); 145.06 and 146.57 ($C_{(1')}$); 147.37 ($C_{(11)}$); 150.07 ($C_{(1)}$). Found, %:C 69.93; H 6.41; N 15.81. $C_{26}H_{27}N_5O_2$. Calculated, %: C 70.73; H 6.16; N 15.86. HRMS (EI): found 441.2153, calculated 441.2165.

8-Hydroxy-9-methoxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione Diphenylhydrazone Dihydrochloride (7c). Dry HCl was passed through a solution of the diphenylhydrazone **6c** (0.07 g, 0.16 mmol) in dry methanol (20 ml). The solution was filtered into absolute ether. The crystals were filtered off, and dried. Yield 0.08 g (98%), mp 170°C (decomp.).

9-Ethoxy-8-hydroxy-2,3,5,6-tetrahydro-1H,7H-benzo[*ij*]quinolizine-1,7-dione Diphenylhydrazone Dihydrochloride (7d) was obtained from **6d** (0.1 g, 0.23 mmol) analogously to **7c**. Yield 0.1 g (96%), mp 166°C (decomp.).

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