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SPECIAL FEATURES OF THE ALKYLATION OF 7-BROMO-5-(2-CHLOROPHENYL)-3-HYDROXY-1,2-DIHYDRO-3H-1,4-BENZODIAZEPIN-2-ONE WITH ALKYL TOSYLATES

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On interacting 7-bromo-5-(2-chlorophenyl)-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin-2-one with methyl, hexyl, dodecyl, and cetyl tosylates, 1-alkyl-7-bromo-5-(2-chlorophenyl)-1,2,4,5-tetrahydro-3H-1,4-benzodiazepin-2,3-diones, and 1-alkyl-7-bromo-5-(2-chlorophenyl)-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin- 2-ones were obtained. Only the dione was formed in the case of hexyl tosylate. On alkylating with methyl tosylate only the 3-hydroxy derivative was formed. It was shown that at pH 14 the 1-cetyl and 1-dodecyl-3-hydroxy derivatives were completely converted into the corresponding diones. The molecular and crystal structures of the compounds were established by X-ray structural analysis.

Keywords: 1,4-benzodiazepine, molecular and crystal structure, prototropic migration, synthesis.

Derivatives of 1,2-dihydro-3H-1,4-benzodiazepine possess valuable pharmacological properties. Among them such preparations as *diazepam*, *lorazepam*, *nitrazepam*, *phenazepam*, and *hydazepam*, etc. are widely known [1-3]. The effect of substituents in position 1 on the geometric parameters and antispasmodic properties of 1,2-dihydro-3H-1,4-benzodiazepin-2-ones was shown by us previously in [4].

In investigations of the link of structure and properties of 1-substituted 1,2-dihydro-3H-1,4-benzodiazepin-2-ones, we have in the present work studied the alkylation of 7-bromo-5-(2-chlorophenyl)-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin-2-one (**1**) with methyl, hexyl, dodecyl, and cetyl tosylates in anhydrous dioxane. On alkylating compound **1** with methyl tosylate 7-bromo-5-(2-chlorophenyl)-3-hydroxy-1-methyl-1,2-dihydro-3H-1,4-benzodiazepin-2-one (**4a**) was obtained, and in the case of hexyl tosylate 7-bromo-5-(2-

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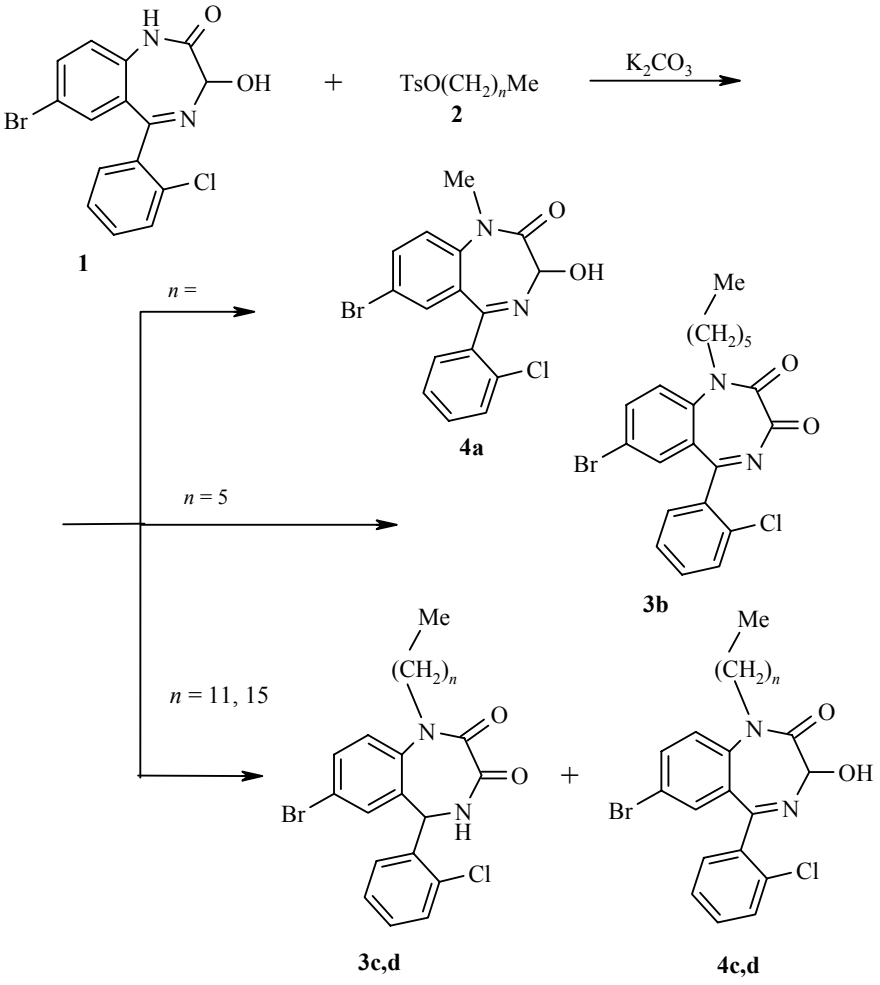
chlorophenyl)-1,2,4,5-tetrahydro-3H-1,4-benzodiazepine-2,3-dione (**3b**). Alkylation of compound **1** with dodecyl and cetyl tosylates led to the formation of a mixture of 7-bromo-1-dodecyl- and 7-bromo-1-cetyl-5-(2-chlorophenyl)-1,2,4,5-tetrahydro-3H-1,4-benzodiazepine-2,3-diones **3c,d** and 7-bromo-5-(2-chlorophenyl)-1-dodecyl- and 7-bromo-1-cetyl-5-(2-chlorophenyl)-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin-2-ones **4c,d**.

It is known that 3-hydroxy derivatives of 1,4-benzodiazepin-2-one undergo a prototropic migration with conversion into the corresponding 1,2,4,5-tetrahydro-1,4-benzodiazepin-2,3-diones [5-7].



3, 4 c n = 11, **d** n = 15

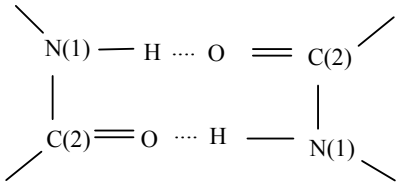
We have studied the possibility of prototropic migration in the case of compounds **4c,d** under the conditions of carrying out the reaction. However even on extended heating no formation of products **3c,d** was observed.

The formation of compounds **3c,d** was observed when using aqueous alcoholic solutions of bases (NaOH). If the solution pH is 10 then conversion of **4c,d** to **3c,d** occurs by 10% after 7 days at 20-25°C, but at pH 14 prototropic migration occurs to 100% after 2.5 h. Conversion of **3c,d** into **4c,d** was not observed on varying the pH value within the limits 1-14.

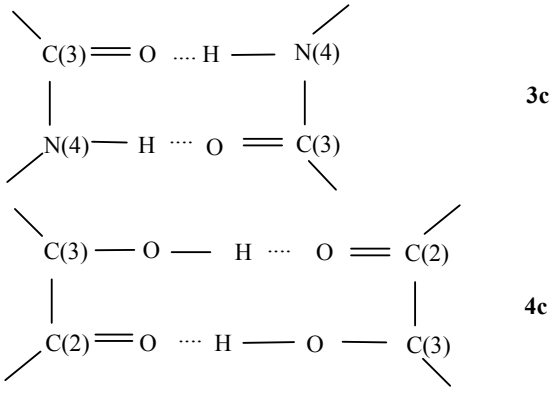
4c,d $\underset{\text{pH 1–14}}{\overset{\text{pH 14}}{\rightleftharpoons}}$ **3c,d** 95%

Monocrystals of **3c** and **4c** were grown from hexane and their molecular and crystal structures were established by X-ray analysis.

The molecular structures of compounds **3c** and **4c** are shown in Fig. 1. Analysis of the molecular structure showed that these compounds are structural isomers. Redistribution of the hydrogen atoms in the framework of the molecule leads to a different character of intermolecular hydrogen bonds in the crystals of compounds **3c** and **4c**. In both cases dimeric associates are formed (Fig. 2). It is known that in the absence of a substituent at position 1 (*fenazepam* [8], *nitrazepam* [9]) dimerization occurs as a result of the formation of hydrogen bonds between the amide groups. In this way a dimeric associate of dimension R^2_8 is formed [10].



A substituent in position 1 makes dimerization similar to this impossible. Dimeric associates of different sizes are formed in the crystals of compounds **3c** and **4c**, R^2_8 in **3c** and R^2_{10} in **4c**.



The parameters of the hydrogen bonds are given in Table 1, and the redistribution of the bond character in compounds **3c** and **4c** in Table 2.

The geometric parameters of the heterocycles **3c** and **4c** are different. The bond lengths of N(1)–C(2) and C(2)–C(3) are close to those found in 7-bromo-3-hydroxy-1-methyl-5-phenyl- and 7-bromo-5-(2-chlorophenyl)-3-hydroxy-1-methyl-1,2-dihydro-3H-1,4-benzodiazepin-2-ones [11], where they are on average equal to 1.372 and 1.534 Å respectively. The C(3)–N(4) distances differ significantly at 1.341(3) in compound **3c** and 1.468(4) Å in compound **4c**. These values correspond to a single bond and are close to those found in [11] in the range 1.454-1.460 Å. The N(4)–C(5) bond in compound **3c** is single [1.469(3) Å], but in compound **4c** is double [1.280(4) Å]. The remaining distances in the **3c** and **4c** molecules are analogous to the corresponding distances in other compounds of this class [8, 11, 12].

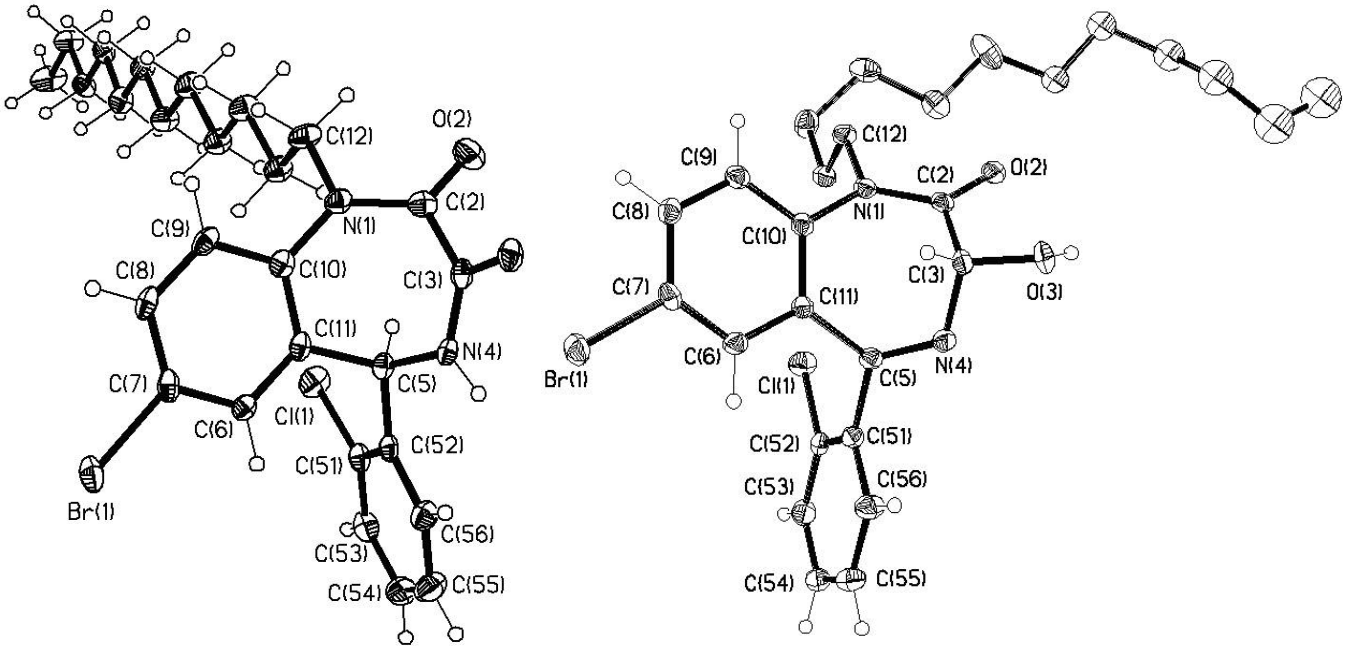
TABLE 1. Hydrogen bonds and DHA angles in compounds **3c** and **4c**

Com-pound	D–H···A*	*d*, Å			DHA angle, deg
		D–H	H...A	D...A	
3c	N(4)–H(4)···O(3)*^{2}	0.88	2.32	2.956(3)	129
4c	O(3)–H(3A) ···O(2)*^{3}	0.84	2.07	2.824(3)	148

*Transformations of symmetry of equivalent atoms.

*^{2} $-x + 1, -y + 2, -z + 2$.

*^{3} $-x + 2, -y, -z + 1$.



3c **4c**

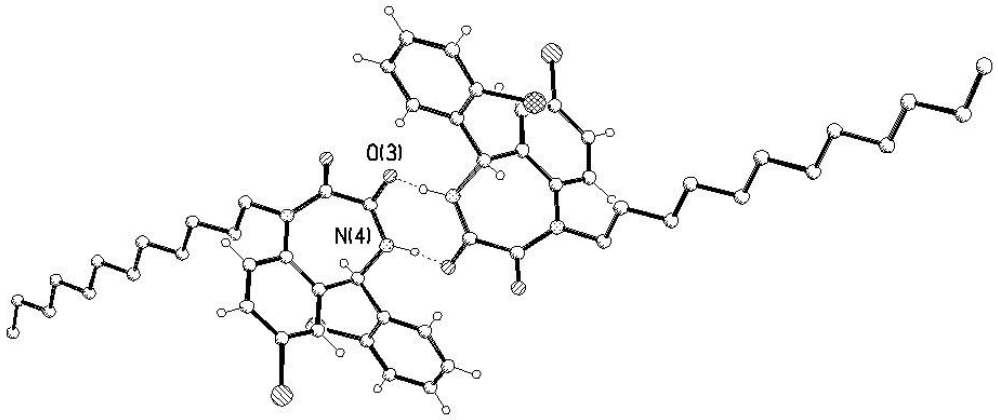
Fig. 1. Molecular structure of compounds **3c** and **4c** (the second position for the disordered fragment of **4c** is not shown).

Table 2. Selected Bonds (*d*) in the Seven-membered Heterocycles of Compounds **3c** and **4c**

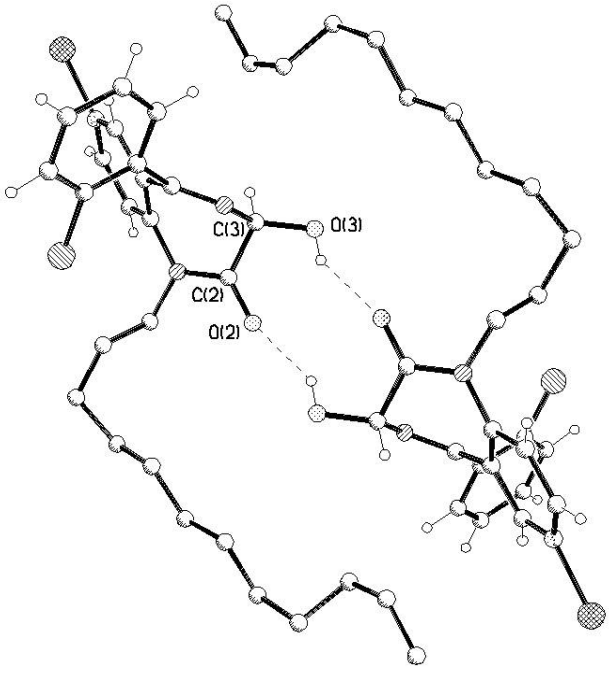
Bond	*d*, Å		Bond	*d*, Å	
	3c	**4c**		**3c**	**4c**
N(1)–C(2)	1.370(3)	1.358(4)	N(4)–C(5)	1.469(3)	1.280(4)
C(2)–C(3)	1.538(3)	1.533(4)	C(5)–C(11)	1.520(3)	1.488(4)
C(2)–O(2)	1.218(3)	1.235(4)	C(11)–C(10)	1.394(3)	1.403(4)
C(3)–N(4)	1.341(3)	1.468(4)	N(1)–C(10)	1.430(3)	1.435(4)
C(3)–O(3)	1.224(3)	1.395(4)			

TABLE 3. Selected Valence Angles (ω) in the Seven-membered Heterocycles of Compounds **3c** and **4c**

Angle	ω, deg	
	3c	**4c**
C(2)–N(1)–C(10)	124.0(2)	122.6(3)
N(1)–C(2)–C(3)	119.0(2)	115.8(3)
O(2)–C(2)–N(1)	123.3(2)	123.3(3)
O(2)–C(2)–C(3)	117.7(2)	120.8(3)
N(4)–C(3)–C(2)	117.0(2)	106.5(2)
O(3)–C(3)–C(2)	119.1(2)	111.6(3)
O(3)–C(3)–N(4)	123.7(2)	110.9(3)
C(3)–N(4)–C(5)	120.0(2)	117.2(3)
N(4)–C(5)–C(11)	106.7(2)	124.3(3)
C(10)–C(11)–C(5)	118.0(2)	123.1(3)
C(11)–C(10)–N(1)	120.8(2)	121.1(3)



3c



4c

Fig. 2. Dimerization of the **3c** and **4c** molecules in the crystal through hydrogen bonds (hydrogen atoms are omitted from the aliphatic chains).

TABLE 4. Torsion Angles (θ) in the Heterocycles of Compounds **3c** and **4c**

Angle	θ, deg	
	3c	**4c**
N(4)C(3)C(2)N(1)	61.1(3)	75.5(3)
C(3)C(2)N(1)C(10)	-8.1(3)	0.9(4)
C(2)N(1)C(10)C(11)	-44.4(3)	-47.5(4)
N(1)C(10)C(11)C(5)	4.5(3)	7.4(5)
C(10)C(11)C(5)N(4)	70.4(3)	41.2(5)
C(11)C(5)N(4)C(3)	-65.3(3)	-1.7(5)
C(5)N(4)C(3)C(2)	-14.4(3)	-72.5(3)

The valence angles also undergo some changes. The total angle at the N(1) atoms are 359.6(2) in **3c** and 360.1° in **4c**, which indicates the low pyramidicity of the nitrogen atom. The angles at atoms C(3) of 117.0(2)° (**3c**), 106.5(2)° (**4c**) and at atom C(5) at 106.7(2)° (**3c**), and 124.3(3)° (**4c**) are subject to a larger change (Tables 3 and 4). This indicates once again the change in character of the hybridization of the C(3) and C(5) atoms.

The conformation of the 7-membered ring is a *pseudoboat* with angles θ_1 (angle between the aromatic rings), θ_2 (angle between N(1)C(2)N(4)C(5) and N(1)C(10)N(11)C(5)) and θ_3 (N(1)C(2)N(4)C(5) and C(10)C(3)N(4)), given in Table 5. Compound **4c** is close in its conformational parameters (Table 6) to *phenazepam* [8]. The parameters of compound **3c** are significantly different. In compound **3c** the torsion angles at

TABLE 5. Some Geometric Characteristics of 7-Membered Heterocycles

Compound	θ, deg		
	θ_1	θ_2	θ_3
3c	86.1	52.9	149.8
4c	85.3	36.6	118.3
Phenazepam	75.4	33.8	59.8

TABLE 6. Crystallographic Data and Parameters of X-ray Structural Experiments

	3c	**4c**
Empirical formula	$C_{27}H_{34}BrClN_2O_2$	$C_{27}H_{34}BrClN_2O_2$
Molecular mass	533.92	533.92
T, K	100(2)	100(2)
Wavelength, Å	0.71073	0.71073
System	Triclinic	Triclinic
Space group	*P*-1	*P*-1
a, Å	8.5262(5)	8.4950(2)
b, Å	10.7145(7)	10.8270(4)
c, Å	14.2342(9)	14.2250(5)
α, deg	85.567(5)	96.187(1)
β, deg	84.041(5)	102.417(2)
γ, deg	89.785(5)	92.140(2)
V, Å^3	1289.44(14)	1267.83(7)
Z	2	2
ρ_{calc} g/cm^3	1.375	1.399
μ, mm^{-1}	1.724	1.753
F(000)	556	556
Crystal parameters, mm	0.4×0.4×0.05	0.3×0.3×0.1
Range of θ for data selected, deg	4.14-26.37	2.46-27.53
Range of indices	$-10 \le h \le 10$ $-13 \le k \le 11$ $-17 \le l \le 17$	$-11 \le h \le 9$ $-14 \le k \le 14$ $-18 \le l \le 18$
Number of reflections		
measured	17 686	10 023
independent	5255 [R_{int} = 0.0363]	5552 [R_{int} = 0.0310]
Number of parameters refined	298	293
GOOF	1.054	1.005
R factor ($I>2\sigma(I)$)	R_1 = 0.0401 wR_2 = 0.1029	R_1 = 0.0507 wR_2 = 0.1286
R factor (for the whole mass)	R_1 = 0.0471 wR_2 = 0.1086	R_1 = 0.0610 wR_2 = 0.1345
$\Delta\rho_{max}$, eÅ^{-3}	0.827	1.208
$\Delta\rho_{min}$, eÅ^{-3}	-0.713	-0.550

the C–C bond in the aliphatic chain are close to 180° (*trans* conformation). In compound **4c** a portion of the angles turn into a *gauche* conformation. Analysis of the packing in compound **3c** showed that adjoining dimers are joined in bands as a result of π-π interactions, effected between the bromo-substituted aromatic rings with a distance between centers of 3.34 Å. Adjacent bands interact through hydrogen bonds C-H···O, in which a CH_2 group of the aliphatic chain and the carbonyl oxygen atom in position 2 of the 7-membered ring of the heterocycle participate. In compound **4c** adjacent dimers are linked with one another basically by van der Waals forces.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR 75 in chloroform solution, and the ^{1}H NMR spectra on a Varian WXP 300 instrument (299 MHz) in $CDCl_3$, internal standard was TMS, at 25 °C. Mass spectra were recorded by electron impact on a MX 1321 mass spectrometer (ionizing voltage 70 eV, temperature of ionization chamber 200°C). The purity of compounds was checked by HPLC, Shimadzu chromatograph LC 8A, analytical column Zorbax C 18, mobile phase, methanol + 2% TFA : water + 2% TFA, 9:1. The progress of reactions was checked by TLC. Thin layer chromatography was carried out on Silufol UV 254 plates in acetonitrile–chloroform—hexane, 1:1:3, visualization was with UV light at λ 254 nm.

X-ray Structural Investigation. The main parameters of the experiment and the interpretation of structures are given in Table 6. Monocrystals of compound **3c** were colorless plates. The experimental material was obtained on a KUMA CCD-4 diffractometer with monochromatized (graphite monochromator) MoKα radiation at 100 K. Overall 17686 refections were recorded of which 5255 were used for determining and refining the structure. The data obtained were processed with the aid of the Kuma Diffraction (Wroclaw, Poland) set of programs.

The structure was solved by the direct method and was refined by the full-matrix least-squares method in an anisotropic approximation for the non-hydrogen atoms with the SHELX-97 set of programs [13]. The coordinates of the H atoms were found objectively from Fourier difference syntheses and were refined in a rigid body model.

Crystals of compound **4c** were close in appearance to crystals of compound **3c**. The experimental material was obtained on a Nonius Kappa diffractometer at 100K with monochromatized MoKα-radiation by φ-ω scanning. Parameters of the unit cell were refined from the overall mass of experimental data. The framework was integrated and Lorenz and polarization factors were introduced into the intensities with the DENZO program [14]. Scaling and refining of the cell parameters was carried out with the SCALEPACK program [14]. No correction for absorption was considered. The methods for solving the structure and refinement were similar to those given for compound **3c.** In the refinement process it was established that the alkyl radical was randomized at two positions with a population probability of 3:1. The hydrogen atoms in the framework of the molecule were found objectively and were refined in a rigid body model, in the randomized aliphatic chain they were not determined. The coordinates of the main atoms were deposited in the Cambridge Crystallographic Data Collection, Nos. 630346 and 630347.

7-Bromo-5-(2-chlorophenyl)-1-dodecyl-1,2,4,5-tetrahydro-3H-1,4-benzodiazepine-2,3-dione (3c) and 7-Bromo-5-(2-chlorophenyl)-1-dodecyl-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin-2-one (4c). Potassium carbonate (0.52 g, 3.7 mmol) was added to a suspension of compound **1** (0.5 g, 1.38 mmol) and dodecyl tosylate **2c** (0.58 g, 1.8 mmol) in anhydrous dioxane (10 ml), and the mixture was stirred at 40-50°C for 10 h. Chloroform (30 ml) was added to the reaction mixture, which was washed with water (4×20 ml). The solvent was evaporated on a rotary evaporator at reduced pressure. The residue obtained was recrystallized from chloroform and colorless crystals of compounds **3c** and **4c** were obtained by fractional crystallization.

Compound 3c. Yield 0.28 g (38%); mp 135-140°C, R_f 0.4. IR spectrum, ν, cm^{-1}: 3360 (N–H free), 3180 (N–H assoc.), 1675 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.72 (1H, d, *J* = 7.8, H-4); 6.64-7.24 (7H, m,

H-6,8,9, H-3′,4′,5′, 6′); 6.16 (1H, d, J = 7.8, H-5); 4.6 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{10}$CH$_3$); 3.6 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{10}$CH$_3$); 1.24 (20H, m, CH$_2$(C<u>H</u>$_2$)$_{10}$CH$_3$); 0.88 (3H, t, J = 6.7, CH$_3$). Mass spectrum, *m/z* (I_{rel}, %): 532 (20) [M]$^+$, 503 (6) [M-CHO]$^+$, 489 (32) [M-NH–C=O]$^+$, 364 (100) [M-$C_{12}H_{24}$]$^+$. Found, %: C 60.82; H 6.37; N 5.16. $C_{27}H_{34}BrClN_2O_2$. Calculated, %: C 60.74; H 6.42; N 5.25.

Compound 4c. Yield 0.095 g (11%); mp 97-100°C, R_f 0.54. IR spectrum, ν, cm^{-1}: 3440 (O–H), 1655 (C=O). ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.24-7.71 (7H, m, H-6,8,9, H-3′,4′,5′,6′); 4.96 (1H, d, J = 9.3, H-3); 4.81 (1H, d, J = 9.3, OH); 4.32 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{10}$CH$_3$); 3.75 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{10}$CH$_3$); 1.24 (20H, m, CH$_2$(C<u>H</u>$_2$)$_{10}$CH$_3$); 0.88 (3H, t, J = 6.8, CH$_3$). Mass spectrum, *m/z* (I_{rel}, %): 532 (14) [M]$^+$, 503 (100) [M-CHO]$^+$, 335 (49) [M-CHO–$C_{12}H_{24}$]$^+$. Found, %: C 60.67; H 6.33; N 5.43. $C_{27}H_{34}BrClN_2O_2$. Calculated, %: C 60.74; H 6.42; N 5.25.

7-Bromo-1-cetyl-5-(2-chlorophenyl-1,2,4,5-tetrahydro-3H-1,4-benzodiazepine-2,3-dione (3d) and 7-Bromo-1-cetyl-5-(2-chlorophenyl)-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin-2-one (4d) were obtained analogously to compounds **3c** and **4c** from compound **1** (1 g, 2.76 mol) as colorless crystals.

Compound 3d. Yield 0.65 g (40%); mp 97-99°C, R_f 0.48. IR spectrum, ν, cm^{-1}: 3340 (N–H free), 3175 (N–H assoc.), 1685 (C=O). ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.83 (1H, d, J = 7.8, H-4); 6.64-7.23 (7H, m, H-6,8,9, H-3′,4′,5′,6′); 6.15 (1H, d, J = 7.8, H-5); 4.57 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$); 3.58 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$); 1.24 (28H, m, CH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$); 0.86 (3H, t, J = 6.7, CH$_3$). Mass spectrum, *m/z* (I_{rel}): 588 (35) [M]$^+$, 559 (9) [M-CHO]$^+$, 545 (38) [M-NH–C=O]$^+$, 364 (69) [M-$C_{16}H_{32}$]$^+$. Found, %: C 62.93; H 7.26; N 5.02. $C_{31}H_{42}BrClN_2O_2$. Calculated, %: C 63.10; H 7.17; N 4.75.

Compound 4d. Yield 0.25 g (14%); mp 87-89°C, R_f 0.63. IR spectrum, ν, cm^{-1}: 3465 (O–H), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.21-7.70 (7H, m, H-6,8,9, H-3′,4′,5′,6′); 4.95 (1H, d, J = 9.4, H-3); 4.81 (1H, d, J = 9.3, OH); 4.31 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$); 3.73 (1H, m, C<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$); 1.23 (28H, m, CH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$); 0.86 (3H, t, J = 6.7, CH$_3$). Mass spectrum, *m/z* (I_{rel}, %): 588 (23) [M]$^+$, 559 (100) [M-CHO]$^+$, 545 (8) [M-NH–C=O]$^+$, 364 (28) [M-$C_{16}H_{32}$]$^+$, 335 (80) [M-CHO-$C_{16}H_{32}$]$^+$. Found, %: C 63.16; H 7.25; N 4.83. $C_{31}H_{42}BrClN_2O_2$. Calculated. %: C 63.10; H 7.17; N 4.75.

7-Bromo-5-(2-chlorophenyl)-1-hexyl-1,2,4,5-tetrahydro-3H-1,4-benzodiazepine-2,3-dione (3b) was obtained analogously to compound **3c** from compound **1** (1 g, 2.76 mmol). After recrystallization from benzene the product (0.47 g) was isolated as colorless crystals. Yield 38%; mp 196-199°C, R_f 0.3. IR spectrum, ν, cm^{-1}: 3360 (N–H free), 3186 (N–H assoc.), 1673 br (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz): 7.32-7.68 (7H, m, H-6,8,9, H-3′,4′,5′,6′); 6.45 (1H, s, H-5); 5.95 (1H, s, H-4); 4.37-4.47 (1H, m, C<u>H</u>$_2$(CH$_2$)$_4$CH$_3$); 4.69-4.75 (1H, m, C<u>H</u>$_2$(CH$_2$)$_4$CH$_3$); 1.23-1.50 (8H, m, CH$_2$(C<u>H</u>$_2$)$_4$CH$_3$); 0.83 (3H, t, J = 7.0, CH$_3$). Mass spectrum, *m/z* (I_{rel}, %): 448 (34) [M]$^+$, 405 (28) [M-NH-C=O]$^+$, 377 (8) [M-C_5H_{11}]$^+$, 364 (52) [M-C_6H_{12}]$^+$. Found, %: C 55.32; H 4.56; N 6.51. $C_{20}H_{19}BrClN_2O_2$. Calculated, %: C 55.26; H 4.41; N 6.44.

7-Bromo-5-(2-chlorophenyl)-3-hydroxy-1-methyl-1,2-dihydro-3H-1,4-benzodiazepin-2-one (4a) was obtained analogously to compound **4c** from compound **1** (1 g, 2.76 mmol). Product (0.53 g) was isolated as colorless crystals after recrystallization from benzene. Yield of compound **4a** was 51%; mp 120-127°C, R_f 0.4. IR spectrum, ν, cm^{-1}: 3443 (O–H), 1700 br (C=O). ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.21-7.45 (7H, m, H-6,8,9, H-3′,4′,5′,6′); 5.02 (1H, d, J = 9.34, OH); 4.47 (1H, d, J = 9.33, H-3); 3.52 (3H, s, CH$_3$). Mass spectrum, *m/z* (I_{rel}, %): 378 (10) [M]$^+$, 349 (100) [M-CHO]$^+$, 334 (7) [M-CO_2]$^+$. Found, %: C 50.56; H 3.24; N 7.25. $C_{16}H_{12}BrClN_2O_2$. Calculated, %: C 50.62; H 3.19; N 7.38.

7-Bromo-5-(2-chlorophenyl)-1-dodecyl-1,2,4,5-tetrahydro-3H-1,4-benzodiazepine-2,3-dione (3c) from 7-Bromo-5-(2-chlorophenyl)-1-dodecyl-3-hydroxy-1,2-dihydro-3H-1,4-benzodiazepin-2-one (4c). A mixture of compound **4c** (0.1 g, 0.18 mmol), ethanol (6 ml), and 30% KOH solution (4 ml) was stirred at room temperature for 2.5 h. Chloroform (10 ml) was added to the reaction mixture, which was then washed with water (3×10 ml). The chloroform was evaporated on a rotary evaporator at reduced pressure. The residue was recrystallized from chloroform and colorless crystals of compound **3c** were obtained. Yield 0.095 g (95%); mp 97-100°C, R_f 0.54.

Compound 3d was obtained analogously to compound **3c** from compound **4d** (0.1 g, 0.18 mmol) as colorless crystals. Yield 0.095 g (95%); mp 87-89°C, R_f 0.63.

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