

## SYNTHESIS OF 3,1-BENZOXAZINES FROM N-SUBSTITUTED *ortho*-(CYCLOALK-1-ENYL OR ALK-2-EN-2-YL)ANILINES\*

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*New derivatives of 3,1-benzoxazine have been synthesized by the cyclization of RCO-substituted at the nitrogen atom (R = OEt, Me, NH<sub>2</sub>) ortho-(cycloalk-1-enyl or alken-1-yl)anilines under mild conditions.*

**Keywords:** *ortho*-alkenylanilines, arylureas, arylurethanes, 3,1-benzoxazines, cyclization.

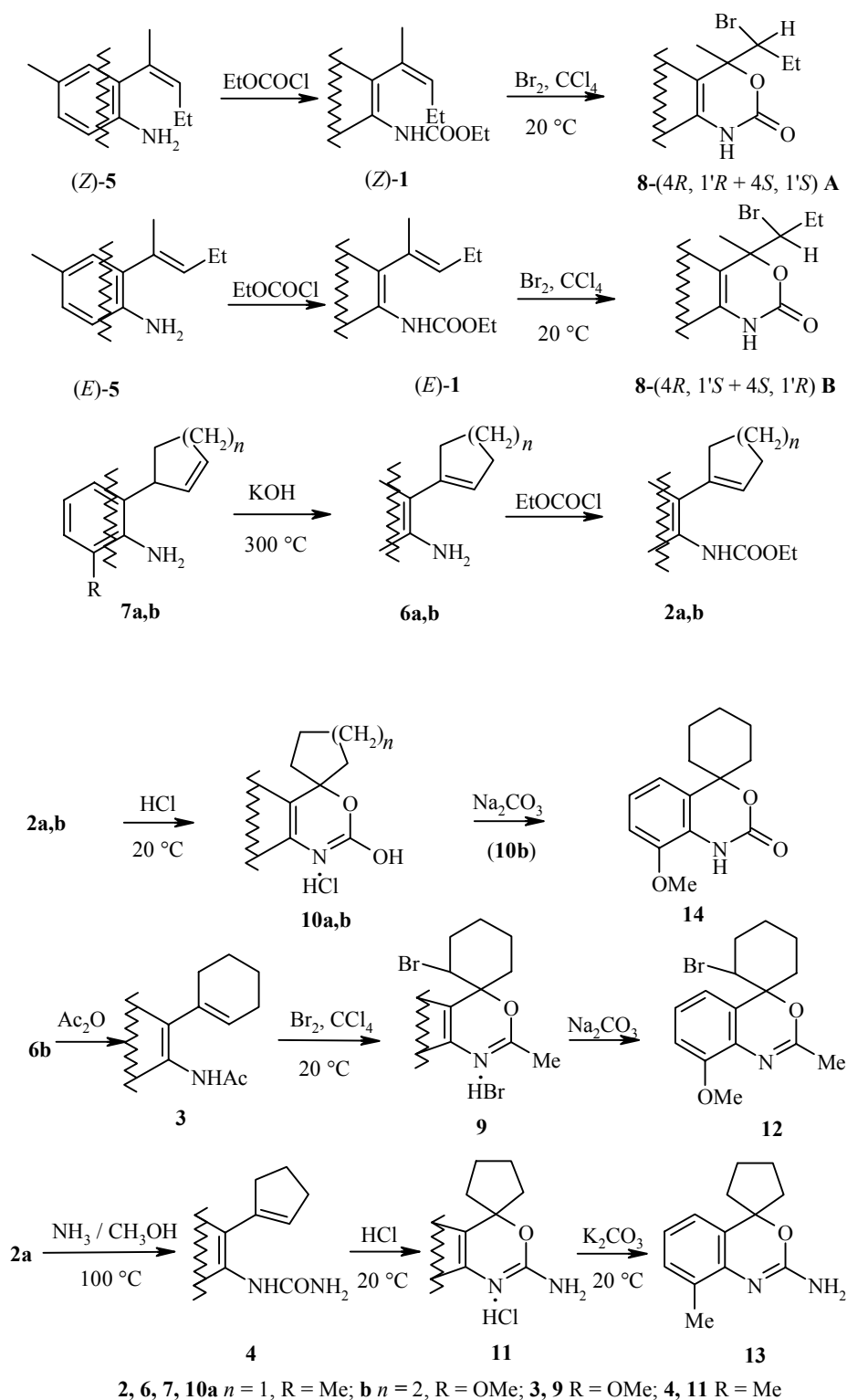
The high biological activity of certain compounds of the benzoxazine series stimulates investigation in this area. The synthesis of highly effective cardiostimulants [1] or oxytocin antagonists from anthranilic acid [2] has been described. 2-Aminoalkyl-3,1-benzoxazines, which potentially are active inhibitors of chymase, have been obtained from phthalimide [3]. An inhibitor of reverse transcriptase HIV-1 belonging to this series has been synthesized [4].

On continuation of our investigations on the heterocyclization of 2-(alkenyl)-N-acylanilines under mild conditions [5-7] new examples of this reaction are given, carried out with such substrates as N-ethoxycarbonylanilines **1** and **2a,b**, acetanilide **3**, and N-carbamoylaniline **4**.

Urethanes (*Z*)-**1**, (*E*)-**1** and **2a,b** were synthesized by the ethoxycarbonylation of the (*Z*)- and (*E*)-isomers of 4-methyl-2-(pent-2-en-2-yl)aniline (**5**) and also of the 2-R-6-(cycloalk-1-enyl)anilines **6a** [5] and **6b** obtained from cycloalk-2-enyl-substituted isomers **7a** and **7b** respectively. Anilide **3** was obtained by the acetylation of aniline **6b**, and arylurea **4** was obtained by the ammonolysis of urethane **2a** [8].

Compounds **1-4** were subjected to heterocyclization under various conditions. The action of Br<sub>2</sub> in CCl<sub>4</sub> on the (*Z*)- and (*E*)-isomers of 4-methyl-2-(pent-2-en-2-yl)urethane (**1**) gave diastereomers (**A** and **B**) of 4,4-dimethyl-4-(1-bromopropyl)-(4H)-3,1-benzoxazin-2-one (**8**). Isomer **A** is (4*R*,1'*R*+4*S*,1'*S*) and **B** – (4*R*,1'*S*+4*S*,1'*R*). The formation of enantiomer **A** from isomer (*Z*)-**1** is more probable since on cyclization of similar olefins by the action of halogens it is generally accepted that the reaction proceeds through the stage of an onium complex [9]. Under the conditions indicated anilide **3** was converted into 2'-bromo-2-methyl-8-methoxyspiro[4H-3,1-benzoxazine-4,1'-cyclohexane] hydrobromide (**9**). Treatment of urethanes **2a,b** and urea **4** with HCl in EtOH or C<sub>2</sub>H<sub>4</sub>Cl<sub>2</sub> led to the hydrochlorides **10a,b** and **11** respectively. The desired derivatives of 2-substituted 3,1-benzoxazine **12** and **13** were obtained from hydrohalides **9** and **11** respectively by the action of aqueous Na<sub>2</sub>CO<sub>3</sub> or K<sub>2</sub>CO<sub>3</sub> solution, and 3,1-benzoxazine derivative **14** was obtained similarly from hydrochloride **10a,b**.

\* Dedicated to Academician of the Russian Academy of Sciences M. G. Voronkov on his 80<sup>th</sup> Birthday.



The composition and structures of the compounds synthesized were confirmed by the results of elemental analysis, and by data of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra and of IR spectra (see Experimental).

## EXPERIMENTAL

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were taken on a Bruker AM 300 instrument with an operating frequency of 300.13 and 75.47 MHz for solutions in  $\text{CDCl}_3$ , internal standard was  $\text{Me}_4\text{Si}$ . The IR spectra were obtained on a UR 20 instrument. A check on the purity of products was effected on a Chrom 4 chromatograph and on Silufol UV 254 plates.

**6-(Cyclohex-1-enyl)-2-methoxyaniline (6b).** A mixture of amine **7b** (10 g) and KOH (10 g) was kept for 1 h at  $300^\circ\text{C}$ . After cooling, benzene (50 ml) was added to the reaction mixture, stirred, and decanted. After evaporation of benzene the residue was distilled in vacuum. Product **6b** (8.7 g) was obtained; bp  $125\text{--}128^\circ\text{C}$  (3 mm Hg), mp  $41\text{--}43^\circ\text{C}$  (pentane). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3260, 3320 ( $\text{NH}_2$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.52–1.63 (4H, m,  $2\text{CH}_2$ ); 2.18 (2H, m,  $\text{CH}_2$ ); 2.21 (2H, m,  $\text{CH}_2$ ); 3.64 (3H, s,  $\text{OCH}_3$ ); 4.58 (2H, br s,  $\text{NH}_2$ ); 5.77 (1H, m,  $=\text{CH}$ ); 6.50–6.67 (3H, m,  $\text{H}_{\text{Ar}}$ ).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 20.1 ( $\text{C}_{(4)}$ ); 24.4 ( $\text{C}_{(5)}$ ); 25.1 ( $\text{C}_{(3)}$ ); 28.2 ( $\text{C}_{(6)}$ ); 55.0 ( $\text{CH}_3\text{O}$ ); 108.3 ( $\text{C}_{(4)}$ ); 110.4 ( $\text{C}_{(3)}$ ); 120.5 ( $\text{C}_{(5)}$ ); 126.3 ( $\text{C}_{(2)}$ ); 126.4 ( $\text{C}_{(6)}$ ); 133.5 ( $\text{C}_{(1)}$ ); 136.5 ( $\text{C}_{(1)}$ ); 145.7 ( $\text{C}_{(2)}$ ). Found, %: C 76.18; H 8.03; N 6.55.  $\text{C}_{13}\text{H}_{17}\text{NO}$ . Calculated, %: C 76.81; H 8.43; N 6.89.

**Ethoxycarbonylation of Compounds (Z)-5, (E)-5, and 6a,b (General Method).** Potassium carbonate (10 g) was introduced into solution of compound (Z)-5, (E)-5, or **6a,b** (10 mmol) in  $\text{CH}_2\text{Cl}_2$  (20 ml). Solution of ethyl chloroformate (15 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 ml) was added dropwise with stirring at  $20^\circ\text{C}$ . The reaction mixture was stirred for 2 h and kept for 16 h at the same temperature. The inorganic solid was filtered off, washed with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 10$  ml), and the filtrate was washed with 10% aqueous  $\text{NaHCO}_3$  solution until cessation of  $\text{CO}_2$  evolution, then with water, and dried over  $\text{MgSO}_4$ . The solvent was distilled off, and the product purified by distillation in vacuum.

**6-(Cyclohex-1'-enyl)-N-(ethoxycarbonyl)-2-methoxyaniline (2b).** Yield 83%; bp  $180\text{--}183^\circ\text{C}$  (3 mm Hg); mp  $58\text{--}61^\circ\text{C}$  ( $\text{CCl}_4$ ). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3270 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm,  $J$  (Hz): 1.07 (3H, t,  $J = 7.0$ ,  $\text{CH}_3\text{CH}_2$ ); 1.47–1.61 (4H, m,  $2\text{CH}_2$ ); 2.04 (2H, m,  $\text{CH}_2$ ); 2.19 (2H, m,  $\text{CH}_2$ ); 3.60 (3H, s,  $\text{OCH}_3$ ); 4.04 (2H, q,  $J = 7.0$ ,  $\text{CH}_2\text{CH}_3$ ); 6.53 (1H, br. s, NH); 5.82 (1H, m,  $=\text{CH}$ ); 6.60–6.72 (3H, m,  $\text{H}_{\text{Ar}}$ ).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 14.4 ( $\text{CH}_3$ ); 20.2 ( $\text{C}_{(4)}$ ); 24.9 ( $\text{C}_{(5)}$ ); 25.2 ( $\text{C}_{(3)}$ ); 28.3 ( $\text{C}_{(6)}$ ); 55.0 ( $\text{CH}_3\text{O}$ ); 60.3 ( $\text{CH}_2\text{O}$ ); 108.8 ( $\text{C}_{(4)}$ ); 114.4 ( $\text{C}_{(3)}$ ); 120.3 ( $\text{C}_{(5)}$ ); 122.3 ( $\text{C}_{(1)}$ ); 126.3 ( $\text{C}_{(2)}$ ); 126.4 ( $\text{C}_{(6)}$ ); 136.1 ( $\text{C}_{(1)}$ ); 142.5 ( $\text{C}_{(2)}$ ); 154.1 ( $\text{C}_{(1)}$ ). Found, %: C 67.42; H 7.29; N 4.82.  $\text{C}_{16}\text{H}_{21}\text{NO}_3$ . Calculated, %: C 69.79; H 7.69; N 5.09.

**N-(Ethoxycarbonyl)-4-methyl-2-[(Z)-pent-2'-en-1'-yl]aniline [(Z)-1].** Yield 95%, oil; bp  $146\text{--}148^\circ\text{C}$  (3 mm Hg). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3270 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm,  $J$  (Hz): 0.92 (3H, t,  $J = 7.5$ ,  $\text{CH}_3$ ); 1.34 (3H, t,  $J = 7.0$ ,  $\text{CH}_3$ ); 1.78 (2H, q,  $J = 7.0$ ,  $\text{CH}_2$ ); 2.05 (3H, s,  $\text{CH}_3$ ); 2.30 (3H, s,  $\text{CH}_3$ ); 4.16 (2H, q,  $J = 7.5$ ,  $\text{CH}_2$ ); 5.71 (1H, dt,  $J = 1.0$ ,  $J = 7.0$ ,  $=\text{CH}$ ); 6.65 (1H, d,  $J = 8.4$ , 6-H); 6.79 (1H, s, 3-H); 7.14 (1H, d,  $J = 8.4$ , 5-H); 8.02 (1H, s, NH).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 13.8, 14.4, 20.6, 22.4 ( $4\text{CH}_3$ ); 24.9 ( $\text{C}_{(3)}$ ); 60.9 ( $\text{CH}_2\text{O}$ ); 118.4 ( $\text{C}_{(6)}$ ); 128.1 ( $\text{C}_{(2)}$ ); 128.5 ( $\text{C}_{(5)}$ ); 130.7 ( $\text{C}_{(1)}$ ); 131.7 ( $\text{C}_{(2)}$ ); 131.8 ( $\text{C}_{(4)}$ ); 132.1 ( $\text{C}_{(1)}$ ); 132.4 ( $\text{C}_{(3)}$ ); 153.6 ( $\text{O}=\text{C}=\text{O}$ ). Found, %: C 72.42; H 8.29; N 5.21.  $\text{C}_{15}\text{H}_{21}\text{NO}_2$ . Calculated, %: C 72.83; H 8.57; N 5.66.

**N-(Ethoxycarbonyl)-4-methyl-2-[(E)-1'-methylbut-1'-enyl]aniline [(E)-1].** Yield 95%, oil; bp  $140\text{--}142^\circ\text{C}$  (3 mm Hg). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3290 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm,  $J$  (Hz): 1.04 (3H, t,  $J = 7.3$ ,  $\text{CH}_3$ ); 1.31 (3H, t,  $J = 7.1$ ,  $\text{CH}_3$ ); 1.94 (3H, s,  $\text{CH}_3$ ); 2.22 (2H, m,  $\text{CH}_2$ ); 2.33 (3H, s,  $\text{CH}_3$ ); 4.18 (2H, m,  $\text{CH}_2$ ); 5.43 (1H, t,  $J = 6.9$ ,  $=\text{CH}$ ); 6.74 (1H, d,  $J = 8.4$ , 6-H); 6.82 (1H, s, 3-H); 6.95 (1H, d,  $J = 8.4$ , 5-H); 7.76 (1H, s, NH).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 13.8, 14.4, 17.5, 20.5 ( $4\text{CH}_3$ ); 21.5 ( $\text{C}_{(3)}$ ); 60.8 ( $\text{CH}_2\text{O}$ ); 119.3 ( $\text{C}_{(6)}$ ); 127.5 ( $\text{C}_{(2)}$ ); 128.6 ( $\text{C}_{(5)}$ ); 131.6 ( $\text{C}_{(1)}$ ); 132.0 ( $\text{C}_{(2)}$ ); 132.1 ( $\text{C}_{(4)}$ ); 133.4 ( $\text{C}_{(3)}$ ); 140.1 ( $\text{C}_{(1)}$ ); 153.5 ( $\text{O}=\text{C}=\text{O}$ ). Found, %: C 72.42; H 8.29; N 5.21.  $\text{C}_{15}\text{H}_{21}\text{NO}_2$ . Calculated, %: C 72.83; H 8.57; N 5.66.

**N-Acetyl-6-(cyclohex-1-enyl)-2-methoxyaniline (3).** Acetic anhydride (1.5 ml, 15 mmol) was added to solution of aniline **6b** (2.3 g, 10 mmol) in  $\text{CH}_2\text{Cl}_2$  (20 ml) and the mixture was kept for 2 h at room temperature. The reaction mixture was treated with 10%  $\text{Na}_2\text{CO}_3$ , the organic portion was separated, dried over  $\text{MgSO}_4$ , and the solvent evaporated. Anilide **3** (2.25 g, 91%) was obtained; mp  $99\text{--}101^\circ\text{C}$  ( $\text{CCl}_4$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.51–1.68 (4H, m,  $2\text{CH}_2$ ); 2.14 (2H, m,  $\text{CH}_2$ ); 2.23 (3H, s,  $\text{CH}_3\text{--CO}$ ); 2.24 (2H, m,  $\text{CH}_2$ ); 3.72 (3H, s,  $\text{CH}_3\text{--O}$ );

6.77 (1H, m, =CH); 6.88-7.47 (3H, m, H<sub>Ar</sub>); 8.25 (1H, s, NH). <sup>13</sup>C NMR spectrum, δ, ppm: 20.3 (C<sub>(4)</sub>); 23.5 (CH<sub>3</sub>); 24.8 (C<sub>(5)</sub>); 25.5 (C<sub>(3)</sub>); 28.4 (C<sub>(6)</sub>); 55.1 (C–O); 109.0 (C<sub>(3)</sub>); 114.7 (C<sub>(4)</sub>); 122.0 (C<sub>(5)</sub>); 124.3 (C<sub>(1)</sub>); 126.4 (C<sub>(2)</sub>); 127.5 (C<sub>(6)</sub>); 136.0 (C<sub>(1)</sub>); 148.3 (C<sub>(2)</sub>); 168.3 (C=O). Found, %: C 72.70; H 7.30; N 5.04. C<sub>15</sub>H<sub>19</sub>NO<sub>2</sub>. Calculated, %: C 73.44; H 7.81; N 5.71.

**Cyclization of Compounds 3, (Z)-1, and (E)-1 under the Action of Br<sub>2</sub>.** Solution of Br<sub>2</sub> (0.1 ml, 1.9 mmol) in CCl<sub>4</sub> (5 ml) was added dropwise to solution of compound 3, (Z)-1, or (E)-1 (1.86 mmol) in dry CCl<sub>4</sub> (20 ml). The solid hydrobromide 9 was filtered off and washed with CCl<sub>4</sub> (10 ml). (R,S) and (R,R) benzoxazinones 8 were isolated by evaporating the solvent.

**2'-Bromo-8-methoxy-2-methylspiro[4H-3,1-benzoxazine-4,1'-cyclohexane] Hydrobromide (9).** Yield 86%; mp 132-134°C (CHCl<sub>3</sub>). <sup>1</sup>H NMR spectrum, δ, ppm, *J* (Hz): 1.61-2.82 (8H, m, 4CH<sub>2</sub>); 3.11 (3H, s, CH<sub>3</sub>); 4.05 (3H, s, OCH<sub>3</sub>); 4.51 (1H, m, CHBr); 6.92 (1H, d, *J* = 7.9, 5-H); 7.02 (1H, d, *J* = 8.4, 7-H); 7.41 (1H, dd, *J* = 7.9, *J* = 8.4, 6-H); 14.90 (1H, br. s, HBr). <sup>13</sup>C NMR spectrum, δ, ppm: 19.6 (CH<sub>3</sub>); 20.0 (C<sub>(5)</sub>); 20.3 (C<sub>(4)</sub>); 30.5 (C<sub>(6)</sub>); 31.4 (C<sub>(3)</sub>); 52.5 (C<sub>(2)</sub>); 56.3 (OCH<sub>3</sub>); 88.6 (C<sub>(4)</sub>); 112.9 (C<sub>(7)</sub>); 116.9 (C<sub>(4a)</sub>); 118.2 (C<sub>(5)</sub>); 124.3 (C<sub>(8a)</sub>); 130.1 (C<sub>(6)</sub>); 149.3 (C<sub>(8)</sub>); 171.5 (C<sub>(2)</sub>). Found, %: C 44.03; H 4.03; Br 39.17; N 3.01. C<sub>15</sub>H<sub>18</sub>BrNO<sub>2</sub>·HBr. Calculated, %: C 44.47; H 4.73; Br 39.45; N 3.46.

**(4R\*), (1'R\*)-4-(1-Bromopropyl)-4,6-dimethyl-4H-3,1-benzoxazin-2-one (8A).** Yield 88%; mp 149-151°C (CCl<sub>4</sub>). <sup>1</sup>H NMR spectrum, δ, ppm, *J* (Hz): 1.14 (3H, t, *J* = 7.2, CH<sub>3</sub>); 1.83 (3H, s, CH<sub>3</sub>); 2.14 (2H, m, CH<sub>2</sub>); 2.26 (3H, s, CH<sub>3</sub>); 4.11 (1H, d, *J* = 2.0, *J* = 11.4, CHBr); 6.78 (1H, d, *J* = 8.0, 8-H); 6.91 (1H, s, 5-H); 7.13 (1H, d, *J* = 8.0, 7-H); 9.85 (1H, s, NH). <sup>13</sup>C NMR spectrum, δ, ppm: 13.1, 20.9, 25.0 (3CH<sub>3</sub>); 26.0 (C<sub>(3)</sub>); 64.0 (C<sub>(2)</sub>); 86.3 (C<sub>(4)</sub>); 114.7 (C<sub>(5)</sub>); 122.0 (C<sub>(6)</sub>); 126.0 (C<sub>(7)</sub>); 130.1 (C<sub>(8)</sub>); 131.7 (C<sub>(4a)</sub>); 132.7 (C<sub>(8a)</sub>); 152.3 (C<sub>(2)</sub>). Found, %: C 51.83; H 5.22; Br 26.06; N 4.14. C<sub>13</sub>H<sub>16</sub>BrNO<sub>2</sub>. Calculated, %: C 52.37; H 5.41; Br 26.80; N 4.70.

**(4R\*), (1'S\*)-4-(1-Bromopropyl)-4,6-dimethyl-4H-3,1-benzoxazin-2-one (8B).** Yield 85%; mp 134-136°C (CCl<sub>4</sub>). <sup>1</sup>H NMR spectrum, δ, ppm, *J* (Hz): 1.12 (3H, t, *J* = 7.0, CH<sub>3</sub>); 1.74 (2H, m, CH<sub>2</sub>); 1.85 (3H, s, CH<sub>3</sub>); 2.32 (3H, s, CH<sub>3</sub>); 4.28 (1H, dd, *J* = 2.4, *J* = 11.2, CHBr); 6.81 (1H, d, *J* = 8.0, 8-H); 6.98 (1H, s, 5-H); 7.08 (1H, dd, *J* = 1.1, *J* = 8.0, 7-H); 9.55 (1H, s, NH). <sup>13</sup>C NMR spectrum, δ, ppm: 13.5, 20.3, 24.8 (3CH<sub>3</sub>); 22.0 (C<sub>(3)</sub>); 64.3 (C<sub>(2)</sub>); 85.4 (C<sub>(4)</sub>); 117.4 (C<sub>(5)</sub>); 121.4 (C<sub>(6)</sub>); 125.0 (C<sub>(7)</sub>); 128.9 (C<sub>(8)</sub>); 131.3 (C<sub>(4a)</sub>); 131.9 (C<sub>(8a)</sub>); 151.8 (C<sub>(2)</sub>). Found, %: C 51.94; H 5.17; Br 26.30; N 4.45. C<sub>13</sub>H<sub>16</sub>BrNO<sub>2</sub>. Calculated, %: C 52.37; H 5.41; Br 26.80; N 4.70.

**Cyclization of Urethanes 2a,b and Urea 4 under the Action of HCl.** Hydrogen chloride was passed for 5 min into solution of urethane 2a,b or urea 4 (1 mmol) in ethyl alcohol or dichloroethane (20 ml). The reaction mixture was then left for 1 h at room temperature. The solvent was evaporated in vacuum. Hydrochlorides 10a,b and 11 were obtained. Benzoxazine hydrochloride 10b was treated with Na<sub>2</sub>CO<sub>3</sub> solution without isolation.

**2-Hydroxy-8-methylspiro[4H-3,1-benzoxazine-4,1'-cyclopentane] Hydrochloride (10a).** Yield 98%; mp 128-131°C. *R<sub>f</sub>* 0.37 (CH<sub>2</sub>Cl<sub>2</sub>-MeOH, 9:1). <sup>1</sup>H NMR spectrum, δ, ppm: 1.11-2.58 (8H, m, 4CH<sub>2</sub>); 2.40 (3H, s, CH<sub>3</sub>); 6.78-7.23 (3H, m, H<sub>Ar</sub>); 9.36 (1H, s, NH); 10.22 (1H, s, HCl). <sup>13</sup>C NMR spectrum, δ, ppm: 16.7 (CH<sub>3</sub>); 23.2 (C<sub>(3)</sub>, C<sub>(4)</sub>); 38.8 (C<sub>(2)</sub>, C<sub>(5)</sub>); 92.0 (C<sub>(4)</sub>); 120.0 (C<sub>(7)</sub>); 122.4 (C<sub>(8)</sub>); 122.8 (C<sub>(5)</sub>); 124.2 (C<sub>(6)</sub>); 129.8 (C<sub>(8a)</sub>); 132.7 (C<sub>(4a)</sub>); 152.8 (C<sub>(2)</sub>). Found, %: C 61.12; H 6.37; Cl 14.03; N 5.07. C<sub>13</sub>H<sub>15</sub>NO<sub>2</sub>·HCl. Calculated, %: C 61.54; H 6.31; Cl 14.00; N 5.52.

**2-Amino-8-methylspiro[4H-3,1-benzoxazine-4,1'-cyclopentane] Hydrochloride (11).** Yield 95%; mp 122-124°C. <sup>1</sup>H NMR spectrum, δ, ppm: 1.67-2.58 (8H, m, 4CH<sub>2</sub>); 2.44 (3H, s, CH<sub>3</sub>); 6.89 (1H, m, 6-H); 7.05 (2H, m, 7-H, 5-H); 8.77 (1H, s, =NH); 9.21 (1H, s, NH); 11.45 (1H, s, HCl). <sup>13</sup>C NMR spectrum, δ, ppm: 18.6 (CH<sub>3</sub>); 23.5 (C<sub>(3)</sub>, C<sub>(4)</sub>); 39.2 (C<sub>(2)</sub>, C<sub>(5)</sub>); 96.5 (C<sub>(4)</sub>); 120.2 (C<sub>(4a)</sub>); 124.0 (C<sub>(5)</sub>); 125.3 (C<sub>(6)</sub>); 126.5 (C<sub>(8)</sub>); 128.8 (C<sub>(7)</sub>); 131.2 (C<sub>(8a)</sub>); 157.7 (C<sub>(2)</sub>). Found, %: C 61.47; H 6.72; Cl 14.15; N 10.77. C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O·HCl. Calculated, %: C 61.78; H 6.73; Cl 14.06; N 11.09.

**Preparation of 3,1-Benzoxazines 12 and 14 as Bases.** Hydrohalides **9** or **10b** (5 mmol) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (50 ml) and treated with 10% Na<sub>2</sub>CO<sub>3</sub> solution (10 ml). The organic phase was washed with water (10 ml), dried over MgSO<sub>4</sub>, evaporated at reduced pressure, and bases **12** and **14** respectively were obtained.

**8-Methoxyspiro[3,1-benzoxazine-4,1'-cyclohexan]-2-one (14).** Yield 87%; mp 158-160°C (CCl<sub>4</sub>), *R<sub>f</sub>* 0.47 (benzene–AcOEt, 6:1). <sup>1</sup>H NMR spectrum, δ, ppm, *J* (Hz): 1.46-1.75 (10H, m, 5CH<sub>2</sub>); 3.74 (3H, s, OCH<sub>3</sub>); 6.45 (1H, d, *J* = 7.0, 7-H); 7.02 (1H, d, *J* = 7.0, 5-H); 7.63 (1H, t, *J* = 7.0, 6-H). <sup>13</sup>C NMR spectrum, δ, ppm: 22.6 (C<sub>(3'</sub>), C<sub>(5')</sub>); 24.4 (C<sub>(4')</sub>); 34.9 (C<sub>(2')</sub>, C<sub>(6')</sub>); 55.1 (OCH<sub>3</sub>); 82.6 (C<sub>(4)</sub>); 109.7 (C<sub>(7)</sub>); 122.5 (C<sub>(5)</sub>); 122.8 (C<sub>(8a)</sub>); 125.4 (C<sub>(6)</sub>); 128.3 (C<sub>(4a)</sub>); 144.7 (C<sub>(8)</sub>); 154.5 (C<sub>(2)</sub>). Found, %: C 67.33; H 6.09; N 5.07. C<sub>15</sub>H<sub>17</sub>NO<sub>2</sub>. Calculated, %: C 68.00; H 6.93; N 5.66.

**2'-Bromo-8-methoxy-2-methylspiro[3,1-benzoxazine-4,1'-cyclohexane] (12).** Yield 90%; mp 82-85°C (CCl<sub>4</sub>). *R<sub>f</sub>* 0.75 (benzene–AcOEt, 9:1). <sup>1</sup>H NMR spectrum, δ, ppm, *J* (Hz): 1.47-2.68 (8H, m, 4CH<sub>2</sub>); 2.22 (3H, s, CH<sub>3</sub>); 3.87 (3H, s, OCH<sub>3</sub>); 4.40 (1H, m, CHBr); 6.77 (1H, d, *J* = 9.0, 7-H); 6.85 (1H, d, *J* = 9.0, 5-H); 7.06 (1H, t, *J* = 9.0, 6-H). <sup>13</sup>C NMR spectrum, δ, ppm: 19.1 (CH<sub>3</sub>); 19.5 (C<sub>(5')</sub>); 20.2 (C<sub>(4')</sub>); 29.4 (C<sub>(6')</sub>); 29.9 (C<sub>(3')</sub>); 53.5 (C<sub>(2')</sub>); 55.8 (OCH<sub>3</sub>); 78.6 (C<sub>(4)</sub>); 110.9 (C<sub>(7)</sub>); 118.3 (C<sub>(5)</sub>); 125.8 (C<sub>(6)</sub>); 127.0 (C<sub>(8a)</sub>); 127.9 (C<sub>(4a)</sub>); 151.8 (C<sub>(8)</sub>); 158.8 (C<sub>(2)</sub>). Found, %: C 55.33; H 5.43; Br 24.07; N 4.07. C<sub>15</sub>H<sub>18</sub>BrNO<sub>2</sub>. Calculated, %: C 55.57; H 5.60; Br 24.65; N 4.32.

**2-Amino-8-methylspiro[3,1-benzoxazine-4,1'-cyclopentane] (13).** Solution of hydrochloride **11** (50 mg, 0.2 mmol) in CHCl<sub>3</sub> (20 ml) was stirred with K<sub>2</sub>CO<sub>3</sub> (0.5 g) at 20°C for 2 h. The precipitate was filtered off, the filtrate was evaporated in vacuum, and base **13** (42 mg, 97.6%) was obtained as an amorphous powder. <sup>1</sup>H NMR spectrum, δ, ppm, *J* (Hz): 1.57-2.31 (8H, m, 4CH<sub>2</sub>); 2.32 (3H, s, CH<sub>3</sub>); 5.30 (2H, br. s, NH<sub>2</sub>); 6.67 (1H, t, *J* = 7.4, 6-H); 6.44 (1H, d, *J* = 7.4, 7-H); 7.08 (1H, d, *J* = 7.4, 5-H). <sup>13</sup>C NMR spectrum, δ, ppm: 17.4 (CH<sub>3</sub>); 23.3 (C<sub>(2')</sub>, C<sub>(5')</sub>); 38.8 (C<sub>(3')</sub>, C<sub>(4')</sub>); 89.8 (C<sub>(4)</sub>); 119.1 (C<sub>(5)</sub>); 121.5 (C<sub>(6)</sub>); 129.3 (C<sub>(7)</sub>); 126.8 (C<sub>(4a)</sub>); 130.0 (C<sub>(8)</sub>); 140.0 (C<sub>(8a)</sub>); 154.1 (C<sub>(2)</sub>). Found, %: C 71.85; H 7.07; N 12.52. C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O. Calculated, %: C 72.19; H 7.46; N 12.95.

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