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# CYCLIZATION OF N-(2-CYCLOPENT-1-EN-1-YLPHENYL)BENZAMIDES IN SOLUTION AND UNDER MASS-SPECTROMETRIC CONDITIONS

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*The cyclization has been studied of N-(2-cyclopent-1-en-1-ylphenyl)benzamides into the corresponding 3,1-benzoxazines by the action of gaseous hydrogen chloride, trifluoroacetic acid, or bromine, and also under conditions of electron impact in the gas phase. A scheme is proposed for the fragmentation of the molecular ions of the products obtained.*

**Keywords**: 3,1-benzoxazines, N-(2-cyclopent-1-en-1-ylphenyl)benzamides, mass spectra of 2-arylspiro-[3,1-benzoxazin-4,1'-cyclopentanes] and N-(2-cyclopentenyl)benzamides, cyclization.

It is known that 3,1-benzoxazines possess marked biological activity so it seemed of interest to synthesize new compounds of this class and study their properties [1]. It should be noted that at the present time there are no general and efficient methods of obtaining heterocycles of this type. According to data of mass spectrometry the formation of 3,1-benzoxazines is possible if there is a fragment in the starting substrate from which a carbenium center of the benzyl type may be generated, and in the position adjoining it there is a triad of NH-C(R)=O with a oxygen atom capable of displaying nucleophilic properties [2]. It was shown in the same study that certain reactions of charged particles, observed under gas phase conditions, are like the reactions in solution. Occasionally it is possible to establish a similarity in behavior of particles under mass-spectrometric conditions and in solution.

For the synthesis of new 3,1-benzoxazines we studied the cyclization under various conditions of the products of interaction of (cyclopent-1-en-1-yl)aniline (**1**) and acid chlorides of carboxylic acids **2a-g**, the amides **3a-g**, satisfying the structural requirements given above.

In searches for an optimum variant of carrying out the indicated reaction we used the following cyclization initiators: gaseous hydrogen chloride, liquid bromine, trifluoroacetic acid, acetic acid, 30% aqueous hydrochloric acid solution, concentrated sulfuric acid, KU-2-8 catalyst, and UV irradiation.

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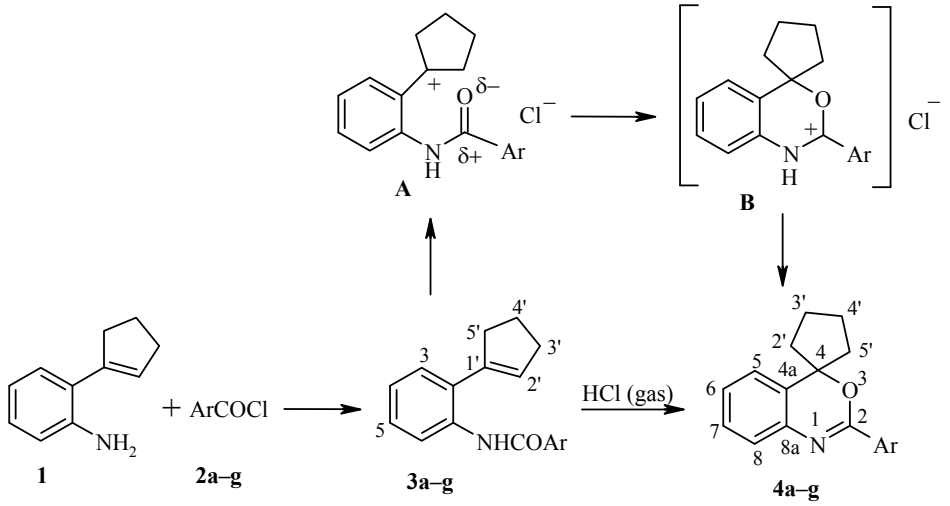
Cyclization was unsuccessful under the action of acetic acid, 30% aqueous hydrochloric acid solution, concentrated sulfuric acid, catalyst KU-2-8, and UV irradiation and the starting amide was resinified.

On catalysis with trifluoroacetic acid the, cyclization of amide **3a** was effected after 18 h, and the yield of product **4a** was 43%. In the case of gaseous HCl, the duration of the same reaction was 5 h, but the yield of compound **4a** was increased to 80%. Consequently compounds **4b-g** were also synthesized under these conditions.



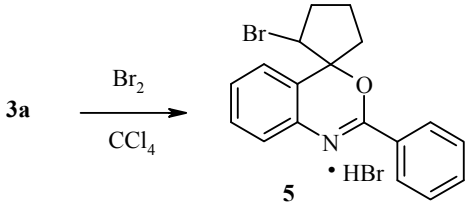

**2–4** Ar = $C_6H_4R$, **a** R = H; **b** R = *m*-Br; **c** R = *p*-Cl; **d** R = *p*-$NO_2$; **e** R = *p*-Me; **f** R = *o*-OMe; **g** R = *m*-OMe

To carry out the cyclization, gaseous hydrogen chloride was bubbled through a solution of amide **3a-g** in methylene chloride. Subsequent treatment of the reaction mixture with 10% aqueous $NaHCO_3$ solution led to the appropriate benzoxazine **4a-g** (52-94% yield).

The reaction is probably initiated by the addition of proton at the double bond of the cyclopentenyl fragment and the generation of a carbenium ion of the benzyl type **A**, subsequent intramolecular stabilization of which by the nucleophilic oxygen atom of the amide fragment led to the heterocyclic ion **B**, the precursor of product **4**. It is known that carbocations of type **A** are also formed under conditions of mass spectrometry [3] (the direction of the conversion of the molecular ions and the structure of the resulting ions for the initial amides **3** and products **4** are considered by us below).

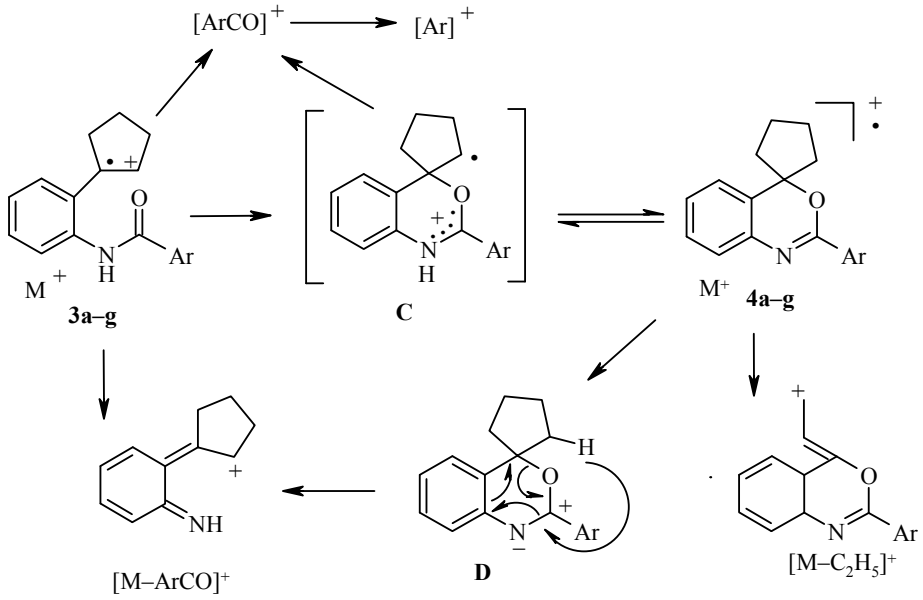
It was established that base **4a** is unstable and on extended storage (more than 3 months from the moment of its preparation without access to oxygen), with one action of high temperatures (above 200°C) or maintaining for 1 h at 250°C in an atmosphere of argon it is quantitatively converted into the starting amide **3a**.

The most effective initiator of cyclization proved to be bromine in $CCl_4$. The reaction proceeded for 20 min and the yield of **5** hydrobromide was 97%.




The composition and structure of amides **3a-g**, synthesized for the first time, were confirmed by results of elemental analysis, and also by data of $^1H$, $^{13}C$ NMR, and mass spectra (see Experimental).

Analysis of the mass spectra of compounds **3a-g** and **4a-g** enabled the characteristic fragment ions to be made apparent, common for amides **3** ($[Ar]^+$, $[ArCO]^+$, $[M\text{-}ArCO]^+$) and specific for benzoxazines **4** ($[M\text{-}C_2H_5]^+$).




The total intensity of the three common ions ($[Ar]^+$, $[ArCO]^+$, and $[M\text{-}ArCO]^+$) was 40-60% of the total ion current for amides **3** and 10-27% for benzoxazines **4** (see Table 1). This suggests that the decomposition of the molecular ions of the indicated compounds proceeds through a common transition state. The high intensity of the $[M\text{-}ArCO]^+$ fragments in the case of the benzoxazines may be explained if it is assumed that this decomposition is brought about through the intermediate 3,1-benzoxazinium ion **D**.

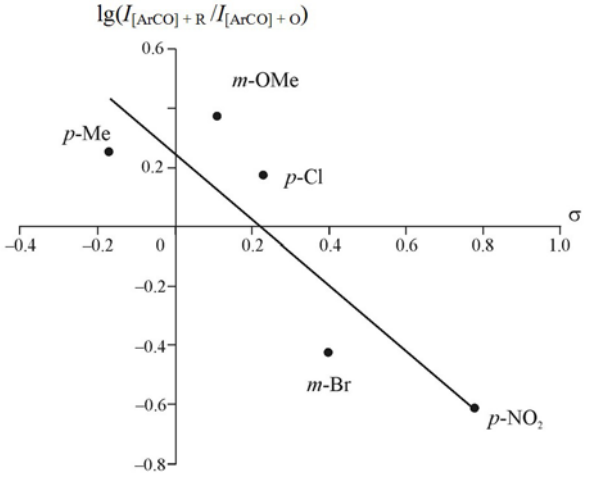



Fig. 1. Dependence of $\log(I_{[ArCO]+R}/I_{[ArCO]+O})$ on the Hammett σ constant of the substituent R for compounds **3b-e**,**g**, $y = 0.25 - 1.1x$ ($r = 0.88$)

It was shown above that in solution the formation of products **4** is also brought about through 3,1-benzoxazinium ions **B**, which is in agreement with the results of special investigations on the transformation of arylamides in solution through stable intermediates [3]. The high intensities of the $[ArCO]^+$ and $[M\text{-}ArCO]^+$

TABLE 1. Contributions (% of Total Ion Current) of Molecular and Characteristic Ion Peaks in the Mass Spectra of Compounds **3a-g** and **4a-g**

| Compound | Intensity, % of total ion current | | | | | |
|---|---|---|---|---|---|---|
| | $M^+$ | $[Ar]^+$ | $[ArCO]^+$ | $[M–ArCO]^+$ | $\sum [Ar]^+$, $[ArCO]^+$, $[M–ArCO]^+$ | $[M–C_2H_5]^+$ |
| **3a** | 10.6 | 9.4 | 17.1 | 20.1 | 46.6 | 0.22 |
| **3b** | 5.0* | 4.2* | 6.3* | 11.4 | 21.9* | 0.14* |
| **3c** | 9.2*[2] | 8.6*[2] | 25.3*[2] | 24.1 | 58.0*[2] | 0.1*[2] |
| **3d** | 10.0 | 0.1 | 4.1 | 24.0 | 28.2 | 0.6 |
| **3e** | 10.7 | 11.0 | 30.4 | 20.2 | 61.6 | 0.21 |
| **3f** | 11.1 | 0.1 | 40.1 | 18.1 | 58.3 | 0.04 |
| **3g** | 10.1 | 0.1 | 40.0 | 16.2 | 56.3 | 0.04 |
| **4a** | 12.7 | 3.6 | 6.4 | 9.8 | 19.8 | 14.1 |
| **4b** | 7.5* | 1.3* | 2.9* | 5.4 | 9.7* | 8.4* |
| **4c** | 10.1*[2] | 2.7*[2] | 7.6*[2] | 9.4 | 19.7*[2] | 11.1*[2] |
| **4d** | 8.8 | 0.2 | 2.1 | 14.2 | 16.5 | 8.4 |
| **4e** | 15.5 | 3.4 | 12.0 | 9.9 | 25.3 | 16.9 |
| **4f** | 6.2 | 0.7 | 17.8 | 7.2 | 25.7 | 6.3 |
| **4g** | 6.1 | 0.3 | 16.3 | 6.9 | 23.5 | 6.2 |

*Includes contribution of fragments with $^{79}Br$ and $^{81}Br$.
*[2]Includes contribution of fragments with $^{35}Cl$ and $^{37}Cl$.

ions in the spectra of compounds **4** are the evidence is, that in the gas phase as also in solution, electrophilic attack occurs just at the oxygen atom. Consequently the mechanism of cyclization of arylamides under mass spectrometry conditions and in solution is identical.

A quantitative assessment of the effect of the nature of substituent R on the formation of fragment $[ArCO]^+$ was carried out with the aid of Hammett constants. In Figure 1 the interdependence of the σ constants and $\log(I_{[ArCO]+R}/I_{[ArCO]+O})$ is represented, where $I$ $[_{ArCO]+R}$ is the intensity of the peaks of $[ArCO]^+$ ions of *para*- and *meta*-substituted compounds **3b-e,g**, and $I_{[ArCO]+O}$ is the intensity of the peaks of the corresponding ions in the spectrum of compound **3a** (R = H). The dependence of the experimentally obtained values of $\log(I_{[ArCO]+R}/I_{[ArCO]+O})$ on the electronic parameters of substituent R is described satisfactorily by the equation $y = 0.25 – 1.1x$, as indicated by the correlation coefficient $r = 0.88$.

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AM 300 spectrometer (at 300 and 75 MHz respectively) in $CDCl_3$, internal standard was TMS. Melting points were measured on a Kofler hot bench with modification S 30A/G (GDR). For analytical TLC Sorbfil plates of type PTSKh-AF-A were used (Sorbpolimer, Krasnodar). Elemental analysis was carried out on a Evro 2000 CHNS(O) analyzer. Preparative separation was carried out by column chromatography on silica gel 40-100 mesh (Lancaster), eluent was petroleum ether–ethyl acetate, 6:1. Mass spectra were recorded on a Thermo Finnigan MAT 95 XP by EI, 70 eV, temperature of ion source 200°C; direct insertion of samples, isotherm 50°C, heating 22°C/min, to temperature 270°C. Precise determination of mass numbers of ions was carried out in the range 1-1000 D at a resolution of 10000 at a height of 10%, for all known ions formed in the source, using procedures for combining peaks. Standard was perfluorokerosene.

**Acid Chlorides of Arenecarboxylic Acids 2a-g (General Method).** Thionyl chloride (15 ml) was added dropwise to a solution of the appropriate arenecarboxylic acid (54 mmol) in absolute toluene (25 ml) and absolute DMF (2 ml). The mixture was maintained at 70°C for 3 h. The excess of thionyl chloride and toluene was then removed at reduced pressure and the residue, acid chloride **2**, was used for the synthesis of amides **3** without purification.

**Arenecarboxylic Acid Amides 3a-g (General Method)**. Amine **1** (7.7 mmol) and $K_2CO_3$ (13 mmol) were added to a solution of acid chloride **2** (10 mmol) in absolute $CH_2Cl_2$ with stirring at room temperature. The reaction mixture was stirred for 24 h (check by TLC). The solid was then filtered off, the filtrate washed with water, with 10% $Na_2CO_3$ solution, dried over $MgSO_4$, and the solvent removed at reduced pressure. Amide **3** was isolated from the residue by column chromatography in an analytically pure state.

**N-(2-Cyclopent-1-en-1-ylphenyl)benzamide (3a).** Yield 70%, white needles, crystallizing as spheres, mp 85-87°C. $^1$H NMR spectrum δ, ppm (*J*, Hz): 2.05 (2H, m, H-4'); 2.61 (2H, m, H-5'); 2.70 (2H, m, H-3'); 5.95 (1H, t, *J* = 2.0, H-2'); 7.15 (1H, t, *J* = 7.1, H-4); 7.28 (2H, m, H-3,5); 7.51 (3H, m, H *m,m'*,*p*-Ar); 7.87 (2H, d, *J* = 7.0, H *o,o'*-Ar); 8.45 (1H, d, *J* = 8.1, H-6); 8.57 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 23.21 (C-4'); 33.66 (C-5'); 36.66 (C-3'); 121.03 (C-2'); 123.87, 126.70, 127.54, 127.58, 127.95, 128.09, 128.62 (C-1'); 130.42, 131.52, 134.56, 134.78, 140.81, 164.80 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 263 $[M]^+$ (52.6), 246 $[M\text{-}OH]^+$ (7.2), 158 $[M\text{-}PhCO]^+$ (100), 130 (22.3), 105 $[PhC{\equiv}O]^+$ (84.9), 77 $[Ph]^+$ (46.5). Found, %: C 82.00; H 5.99; N 5.49. $C_{18}H_{17}NO$. Calculated, %: C 82.10; H 6.51; N 5.32.

**3-Bromo-N-(2-cyclopent-1-en-1-ylphenyl)benzamide (3b).** Yield 79%, yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.0 (2H, m, H-4'); 2.62 (2H, m, H-5'); 2.75 (2H, m, H-3'); 6.0 (1H, t, *J* = 1.9, H-2'); 7.10 (1H, ddd, $J_1$ = 7.6, $J_2$ = 1.1, $J_3$ = 1.1, H-4); 7.20 (1H, dd, $J_1$ = 7.6, $J_2$ = 1.1, H-6); 7.23 (2H, m, H-5,3); 7.33 (1H, t, *J* = 7.6, H *m*-Ar); 7.62 (1H, dt, $J_1$ = 7.6, $J_2$ = 1.1, H *p*-Ar); 7.68 (1H, dt, $J_1$ = 7.6, $J_2$ = 1.1, H *o*-Ar); 7.92 (1H, t, *J* = 1.1, H *o*'-Ar); 8.45 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 23.02 (C-4'); 33.74 (C-5'); 36.14 (C-3'); 115.64 (C-2'); 117.98, 122.91, 125.22, 127.39, 127.70, 127.98 (C-1'); 130.23, 130.65, 134.29, 134.48, 136.86, 140.91, 143.67, 163.23 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 343 $[M+2]^+$ (21.8), 341 $[M]^+$ (22.2), 324 $[M\text{-}OH]^+$ (5.3), 183 $[BrPhCO]^+$ (28.4), 158 $[M\text{-}BrPhCO]^+$ (100), 155 $[M\text{-}PhBr]^+$ (18.9), 130 (23.8), 77 (5.2), 76 (8.1). Found, %: C 63.10; H 4.85; Br 22.95; N 4.15. $C_{18}H_{16}BrNO$. Calculated, %: C 63.17; H 4.71; Br 23.35; N 4.09.

**4-Chloro-N-(2-cyclopent-1-en-1-ylphenyl)benzamide (3c).** Yield 45%, white needles, crytstallizing as spheres, mp 105-107°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.05 (2H, m, H-4'); 2.60 (2H, m, H-5'); 2.70 (2H, m, H-3'); 5.95 (1H, t, *J* = 1.9, H-2'); 7.15 (1H, ddd, $J_1$ = 6.4, $J_2$ = 1.2, $J_3$ = 1.2, H-4); 7.25 (3H, m, H-3,5,6); 7.43 (2H, d, *J* = 8.5, H *m,m*'-Ar); 7.75 (2H, d, *J* = 8.5, H *o,o*'-Ar); 8.47 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 23.34 (C-4'); 33.78 (C-5'); 36.76 (C-3'); 121.26 (C-2'); 124.20, 127.68, 127.73, 128.26, 128.28, 128.88 (C-1'); 128.95, 128.96, 130.52, 133.33, 134.43, 137.88, 140.98, 163.84 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 299 $[M+2]^+$ (12.7), 297 $[M]^+$ (38.1), 280 $[M\text{-}OH]^+$ (8.3), 186 $[M\text{-}PhCl]^+$ (2.3), 158 $[M\text{-}ClPhCO]^+$ (100), 139 $[ClPhCO]^+$ (78.2), 143 (7.2), 130 (24.2), 111 $[PhCl]^+$ (33.3), 75 (8.0). Found, %: C 72.56; H 5.55; Cl 11.85; N 4.42. $C_{18}H_{16}ClNO$. Calculated, %: C 72.60; H 5.42; Cl 11.91; N 4.70.

**N-(2-Cyclopent-1-en-ylphenyl)-4-nitrobenzamide (3d).** Yield 70%, white powder, mp 120-122°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.06 (2H, m, H-4'); 2.62 (2H, m, H-5'); 2.75 (2H, m, H-3'); 6.0 (1H, t, *J* = 1.9, H-2'); 7.08 (1H, ddd, $J_1$ = 7.5, $J_2$ = 7.3, $J_3$ = 0.9, H-4); 7.28 (1H, dd, $J_1$ = 7.5, $J_2$ = 0.9, H-3); 7.32 (1H, ddd, $J_1$ = 7.3, $J_2$ = 7.2, $J_3$ = 0.9, H-5); 8.0 (2H, d, *J* = 8.7, H *o,o*'-Ar); 8.33 (2H, d, *J* = 8.7, H *m,m*'-Ar); 8.42 (1H, dd, $J_1$ = 7.2, $J_2$ = 0.9, H-6); 8.51 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 24.38 (C-4'); 33.52 (C-5'); 37.23 (C-3'); 119.39 (C-2'); 123.13, 124.09, 124.17, 127,47, 128.36, 128.83 (C-1'); 131.85, 132.95, 135.13, 136.68, 137.56, 139.03, 149.14, 161.07 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 308 $[M]^+$ (62.4), 291 $[M\text{-}OH]^+$ (10.4), 279 $[M\text{-}C_2H_5]^+$ (59.4), 278 $[M\text{-}NO]^+$ (25.8), 249 (8.6), 224 $[M\text{-}C_5H_8O]^+$ (3.9), 178 (7.3), 158 $[M\text{-}NO_2PhCO]^+$ (100),

150 $[NO_2PhCO]^+$ (14.6), 143 (13.0), 130 (33.1), 120 $[OPhCO]^+$ (47.2), 104 $[PhCO]^+$ (18.2), 92 $[OPh]^+$ (7.9), 77 (7.3), 76 (14.2). Found, %: C 70.01; H 5.35; N 8.99. $C_{18}H_{16}N_2O_3$. Calculated, %: C 70.12; H 5.23; N 9.09.

**N-(2-Cyclopent-1-en-1-ylphenyl)-4-methylbenzamide (3e).** Yield 40%, yellow needles, crystalli-zing as spheres, mp 75-77°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.09 (2H, m, H-4'); 2.50 (3H, s, $CH_3$); 2.65 (2H, m, H-5'); 2.78 (2H, m, H-3'); 6.0 (1H, t, *J* = 1.9, H-2'); 7.13 (1H, t, *J* = 7.2, H-4); 7.30 (3H, m, H-3,5,6); 7.75 (2H, d, *J* = 8.1, H *m,m*'-Ar); 8.15 (2H, d, *J* = 8.1, H *o,o*'-Ar); 8.50 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 21.24 ($CH_3$); 23.26 (C-4'); 33.68 (C-5'); 36.77 (C-3'); 120.71 (C-2'); 123.60, 126.72, 126.75, 127.54, 127.56, 127.63, 128.34 (C-1'); 129.32, 130.41, 132.12, 134.76, 140.94, 142.04, 164.69 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 277 $[M]^+$ (35.3), 260 $[M\text{-}OH]^+$ (3.0), 158 $[M\text{-}COPhMe]^+$ (66.6), 130 (12.7), 119 $[MePhCO]^+$ (100), 91 $[PhMe]^+$ (36.2). Found %: C 82.10; H 6.85; N 4.95. $C_{19}H_{19}NO$. Calculated, %: C 82.28; H 6.90; N 5.05.

**N-(2-Cyclopent-1-en-1-ylphenyl)-2-methoxybenzamide (3f).** Yield 60%, light-yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.04 (2H, m, H-4'); 2.59 (2H, m, H-5'); 2.71 (2H, m, H-3'); 3.95 (3H, s, $OCH_3$); 5.97 (1H, t, *J* = 1.9, H-2'); 7.01 (1H, d, *J* = 8.3, H *m*-Ar); 7.10 (2H, m, H *m*'-Ar, H-4); 7.20 (1H, dd, $J_1$ = 7.7, $J_2$ = 1.6, H-3); 7.29 (1H, ddd, $J_1$ = 7.6, $J_2$ = 1.6, $J_3$ = 1.6, H-5); 7.48 (1H, td, $J_1$ = 8.3, $J_2$ = 1.8, H *p*-Ar); 8.32 (1H, dd, $J_1$ = 7.8, $J_2$ = 1.8, H *o*-Ar); 8.31 (1H, d, *J* = 7.6, H-6); 10.0 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 23.29 (C-4'); 33.68 (C-5'); 36.30 (C-3'); 55.56 ($OCH_3$); 111.23, 121.22, 121.71, 121.83, 123.58 (C-2'); 127.34, 127.78, 129.19 (C-1'); 130.29, 132.31, 132.98, 135.32, 140.68, 156.89, 163.02 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 293 $[M]^+$ (27.8), 226 $[M\text{-}C_5H_7]^+$ (0.6), 158 $[M\text{-}COPhMe]^+$ (45.2), 135 $[MeOPhCO]^+$ (100), 130 (7.2), 92 (8.2), 77 (15.2). Found, %: C 76.98; H 7.01; N 4.70. $C_{19}H_{19}NO_2$. Calculated, %: C 77.79; H 6.53; N 4.77.

**N-(2-Cyclopent-1-en-1-ylphenyl)-3-methoxybenzamide (3g).** Yield 70%, light-yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.02 (2H, m, H-4'); 2.60 (2H, m, H-5'); 2.73 (2H, m, H-3'); 3.88 (3H, s, $OCH_3$); 5.97 (1H, t, *J* = 2.1, H-2'); 7.10 (2H, m, H *p*-Ar, H-5); 7.40 (6H, m, H *o,o*'-Ar, H *m*-Ar, H 3,4,6); 8.45 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 23.29 (C-4'); 33.77 (C-5'); 36.79 (C-3'); 55.25 ($OCH_3$); 112.22, 117.86, 118.36, 120.81, 123.88, 127.64; 128.53, 129.69 (C-1'); 130.53, 134.63, 136.40, 140.90, 159.89, 164.62 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 293 $[M]^+$ (28.1), 292 $[M\text{-}H]^+$ (2.0), 226 $[M\text{-}C_5H_7]^+$ (2.0), 158 $[M\text{-}COPhOMe]^+$ (40.4), 135 $[MeOPhCO]^+$ (100), 130 (6.4), 92 (8.5), 77 (15.5). Found, %: C 78.00; H 6.47; N 4.83. $C_{19}H_{19}NO_2$. Calculated, %: C 77.79; H 6.53; N 4.77.

**Heterocyclization of Amides 3a-g under the Action of Gaseous Hydrogen Chloride (General Method)**. Gaseous HCl was bubbled through a solution of amide **3** (90 mmol) in $CH_2Cl_2$ (20 ml). After the end of the reaction (check by TLC) the solution of benzoxazine **4** hydrochloride was stirred for 1 h with $NaHCO_3$ powder (2 g), then filtered. The filtrate was evaporated under reduced pressure, and benzoxazine **4** was isolated from the residue by column chromatography.

**2-Phenylspiro[3,1-benzoxazine-4,1'-cyclopentane] (4a).** Yield 80%, yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.90 and 2.35 (4H, two m, both 2H, H-2' and H-5'); 2.00 (4H, m, H-3',4'); 7.17 (1H, m, H-6), 7.30 (3H, m, H-5,7,8); 7.48 (3H, m, H *m,m*',p-Ar); 8.14 (2H, d, *J* = 7.0, H *o,o*'-Ar). $^{13}$C NMR spectrum, δ, ppm: 23.80 (C-3',4'); 40.08 (C-2',5'); 88.90 (C-4); 122.04, 124.63, 126.43, 127.65, 127.78, 128.15, 128.17, 128.21, 128.33, 129.25, 131.16, 139.65, 156.75 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 263 $[M]^+$ (89.9), 262 $[M\text{-}H]^+$ (4.7), 246 $[M\text{-}OH]^+$ (5.2), 234 $[M\text{-}C_2H_5]^+$ (100), 179 $[M\text{-}C_5H_8O]^+$ (23.3), 158 $[M\text{-}PhCO]^+$ (69.7), 130 (11.2), 105 $[PhCO]^+$ (45.5), 77 $[Ph]^+$ (25.6). Found, %: C 81.90; H 6.48; N 4.75. $C_{18}H_{17}NO$. Calculated, %: C 82.10; H 6.51; N 5.32.

**2-(*m*-Bromophenyl)spiro[3,1-benzoxazine-4,1'-cyclopentane] (4b).** Yield 55%, yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.91 and 2.33 (4H, two m, both 2H, H-2' and H-5'); 2.06 (4H, m, H-3',4'); 7.16 (1H, t, *J* = 7.4, H-6); 7.21 (1H, t, *J* = 7.4, H-7); 7.29 (3H, m, H-5,8, H *m*-Ar); 7.62 (1H, d, *J* = 7.9, H *p*-Ar); 8.05 (1H, d, *J* = 7.9, H *o*-Ar); 8.26 (1H, s, H *o*'-Ar). $^{13}$C NMR spectrum, δ, ppm : 23.94 (C-3',4'); 40.32 (C-2',5');

89.34 (C-4); 122.14, 122.40, 125.03, 126.34, 126.87, 128.47, 129.31, 129.71, 130.75, 134.05, 135.34, 139.30, 155.30 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 341 $[M]^+$ (72.7), 324 $[M\text{-}OH]^+$ (8.1), 312 $[M\text{-}C_2H_5]^+$ (73.3), 298 (4.0), 284 (10), 257 $[M\text{-}C_5H_8O]^+$ (5.6), 186 (8.9), 183 $[BrPhCO]^+$ (28.5), 178 (11.5), 151 (10.4), 143 (15.4), 130 (24.0), 77 (13.2), 76 (16.1). Found, %: C 63.25; H 4.52; Br 23.11; N 4.26. $C_{18}H_{16}BrNO$. Calculated, %: C 63.17; H 4.71; Br 23.35; N 4.09.

**2-(*p*-Chlorophenyl)spiro[3,1-benzoxazine-4,1'-cyclopentane] (4c).** Yield 68%, colorless oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.81 and 2.23 (4H, two m, both 2H, H-2' and H-5'); 1.97 (4H, m, H-3',4'); 7.09 (2H, m, H-5,6); 7.21 (2H, m, H-7,8); 7.32 (2H, d, *J* = 8.5, H *o,o*'-Ar); 7.97 (2H, d, *J* = 8.5, H *m,m'*-Ar). $^{13}$C NMR spectrum, δ, ppm : 23.88 (C-3',4'); 40.23 (C-2',5'); 89.22 (C-4); 122.12, 124.91, 126.71, 128.46, 128.51, 128.64, 129.14, 129.20, 129.23, 131.74, 137.37, 139.45, 155.85 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 297 $[M]^+$ (80.7), 280 $[M\text{-}OH]^+$ (7.4), 268 $[M\text{-}C_2H_5]^+$ (87.8), 240 (9.9), 284 (10.0), 213 $[M\text{-}C_5H_8O]^+$ (12.1), 186 $[M\text{-}PhCl]^+$ (3.6), 178 (12.0), 158 $[M\text{-}ClPhCO]^+$ (100), 139 $[ClPhCO]^+$ (61.0), 143 (5.8), 130 (16.1), 111 $[PhCl]^+$ (21.1), 77 (8.0), 76 (10.8). Found, %: C 72.43; H 5.37; N 4.85. $C_{18}H_{16}ClNO$. Calculated, %: C 72.60; H 5.42; Cl 11.91; N 4.70.

**2-(*p*-Nitrophenyl)spiro[3,1-benzoxazine-4,1'-cyclopentane] (4d).** Yield 80%, orange oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.85 and 2.25 (4H, two m, both 2H, H-2' and H-5'); 1.97 (4H, m, H-3',4'); 2.25 (2H, m, H-5'); 7.0 (1H, d, *J* = 7.3, H-5); 7.06-7.21 (3H, H-6,7,8); 8.15 (2H, d, *J* = 7.2, H *o.o*'-Ar); 8.21 (2H, d, *J* = 7.2, H *m,m*'-Ar). $^{13}$C NMR spectrum, δ, ppm: 26.20 (C-3',4'); 38.40 (C-2',5'); 81.21 (C-4), 121.39, 123.25, 123.90, 127.54, 128.93, 129.89, 130.72, 132.12, 136.88, 139.47, 150.57, 150.91, 160.68 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 308 $[M]^+$ (62.4), 291 $[M\text{-}OH]^+$ (10.4), 279 $[M\text{-}C_2H_5]^+$ (59.4), 278 $[M\text{-}NO]^+$ (25.8), 249 (8.6), 224 $[M\text{-}C_5H_8O]^+$ (3.6), 178 (7.3), 158 $[M\text{-}NO_2PhCO]^+$ (100), 150 $[NO_2PhCO]^+$ (14.6), 143 (13.0), 130 (33.1), 120 $[OPhCO]^+$ (47.2), 104 $[PhCO]^+$ (18.2), 92 $[OPh]^+$ (7.9), 77 (7.3), 76 (14.2). Found, %: C 70.20; H 5.13; N 9.16. $C_{18}H_{16}N_2O_3$. Calculated, %: C 70.12; H 5.23; N 9.09.

**2-(*p*-Methylphenyl)spiro[3,1-benzoxazine-4,1'-cyclopentane] (4e).** Yield 69%, light-yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.92 and 2.31 (4H, two m, both 2H, H-2' and H-5'); 2.07 (4H, m, H-3',4'); 2.90 (3H, s, $CH_3$); 7.15-7.35 (6H, m, H-5,6,7,8, H *m,m*'-Ar); 8.02 (2H, d, *J* = 8.2, H *o,o*'-Ar). $^{13}$C NMR spectrum, δ, ppm: 21.43 ($CH_3$); 23.76 (C-3',4'); 39.92 (C-2',5'); 88.67 (C-4); 121.91, 124.68, 126.16, 127.75, 127.82, 128.23, 128.31, 128.64, 129.25, 130.43, 139.82, 141.47, 156.60 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 277 $[M]^+$ (91.9), 246 $[M\text{-}H]^+$ (4.8), 260 $[M\text{-}OH]^+$ (3.4), 248 $[M\text{-}C_2H_5]^+$ (100), 193 $[M\text{-}C_5H_8O]^+$ (17.4), 192 (12.9), 158 $[M\text{-}COPhMe]^+$ (58.8), 130 (8.0), 119 $[MePhCO]^+$ (71.4), 91 $[PhMe]^+$ (20.4). Found, %: C 82.15; H 6.60; N 5.15. $C_{19}H_{19}NO$. Calculated, %: C 82.28; H 6.90; N 5.05.

**2-(*o*-Methoxyphenyl)spiro[3,1-benzoxazine-4,1'-cyclopentane] (4f).** Yield 52%, light-yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.79 and 2.47 (4H, two m, both 2H, H-2' and H-5'); 2.06 (4H, m, H-3',4'); 3.79 (3H, s, $OCH_3$); 6.96 (1H, d, *J* = 8.3, H *m*-Ar); 7.01 (1H, t, *J* = 7.5, H *m'*-Ar); 7.19 (2H, m, H *o,p*-Ar); 7.22-7.43 (3H, m, H-5,6,7); 7.67 (1H, dd, $J_1$ = 7.5, $J_2$ = 1.6, H-8). $^{13}$C NMR spectrum, δ, ppm (*J*, Hz): 23.63 (C-3',4'); 40.09 (C-2',5'); 59.23 ($OCH_3$); 90.03 (C-4); 111.23, 120.03, 120.11, 121.74, 123.16, 124.48, 126.25, 127.96, 129.05, 130.74, 131.53, 131.91, 158.25 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 293 $[M]^+$ (34.9), 292 $[M\text{-}H]^+$ (8.4), 264 $[M\text{-}C_2H_5]^+$ (35.4), 236 (6.1), 209 $[M\text{-}C_5H_8O]^+$ (4.7), 208 (6.8), 180 (12.5), 159 (39.6), 158 $[M\text{-}COPhMe]^+$ (40.5), 135 $[MeOPhCO]^+$ (100), 130 (12.3), 92 (10.0), 77 (22.2). Found, %: C 77.49; H 6.43; N 5.00. $C_{19}H_{19}NO_2$. Calculated, %: C 77.79; H 6.53; N 4.77.

**2-(*m*-Methoxyphenyl)spiro[3,1-benzoxazine-4,1'-cyclopentane] (4g).** Yield 94%, light-yellow oil. $^1$H NMR spectrum, δ, ppm (*J*, Hz); 1.81 and 2.24 (4H, two m, both 2H, H-2' and H-5'): 1.98 (4H, m, H-3',4'); 3.81 (3H, s, $OCH_3$); 6.94-7.30 (7H, m, H-5,6,7, H *o,o',m,p*-Ar); 7.61 (1H, dd, $J_1$ = 8.9, $J_2$ = 1.1, H-8). $^{13}$C NMR spectrum, δ, ppm: 23.65 (C-3'4'); 39.85 (C-2',5'); 55.09 ($OCH_3$); 88.83 (C-4); 112.50, 117.29, 120.17, 121.90, 124.72, 126.40, 128.22, 129.06, 129.13, 134.46, 139.46, 156.47, 159.32 (C-2). Mass spectrum, *m/z* ($I_{rel}$, %): 293 $[M]^+$ (37.6), 292 $[M\text{-}H]^+$ (4.9), 264 $[M\text{-}C_2H_5]^+$ (38.2), 236 (5.9), 209 $[M\text{-}C_5H_8O]^+$ (5.9), 208 (7.6),

180 (13.6), 159 (47.3), 158 $[M\text{-}COPhOMe]^+$ (42.1), 135 $[MeOPhCO]^+$ (100), 130 (12.9), 92 (10.3), 77 (23.0). Found, %: C 76.95; H 6.77; N 4.61. $C_{19}H_{19}NO_2$. Calculated, %: C 77.79; H 6.53; N 4.77.

**2'-Bromo-2-phenylspiro[3,1-benzoxazine-4,1'-cyclopentane] Hydrobromide (5).** A solution of $Br_2$ (0.37 g, 2.3 mmol) in $CCl_4$ (5 ml) was added dropwise with stirring to a solution of amide **3a** (0.6 g, 2.3 mmol) in $CCl_4$ (20 ml). The reaction mixture was stirred for a further 15 min, the precipitated solid was filtered off, washed with $CCl_4$ (10 ml), and dried in vacuum. Product **5** (0.944 g) was obtained, and was recrystallized from $CCl_4$. Yield was 97%, dark-olive-colored powder, mp 160-162°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.32 (2H, m, H-4'); 2.55 (2H, m, H-5'); 2.76 (1H, m, H-3'b); 2.97 (1H, m, H-3'a); 4.51 (1H, m, H-2'); 7.50 (5H, m, H *m,m'*-Ar, H *p*-Ar, H-6,7); 7.70 (2H, m, H *o,o'*-Ar); 8.70 (2H, m, H-5,8). $^{13}$C NMR spectrum, δ, ppm: 20.72 (C-4'); 34.46 (C-5'); 34.97 (C-3'); 55.70 (C-2'); 97.87 (C-1'); 120.10, 121.57, 123.21, 126.53, 128.73, 129.58, 129.78, 130.94, 131.00, 137.56, 164.75 (C-2). Found, %: C 50.89; H 4.28; Br 37.52; N 3.39. $C_{18}H_{17}Br_2NO$. Calculated, %: C 51.09; H 4.05; Br 37.77; N 3.31.

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