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# Heterocyclization of Functionalized Heterocumulenes with C,N- and C,O-Binucleophiles: VI.* Synthesis of Carbofused 2,3-Dihydro-1,3-oxazin-4-ones and 3,4-Dihydro-1,3-oxazin-2-ones

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**Abstract**—Condensations of 1-phenyl-2,2,2-trifluoro-1-chloroethyl isocyanate and 1-chlorobenzyl isocyanate with cyclic 1,3-diketones yield respectively carbofused 2,3-dihydro-1,3-oxazin-4-ones and 3,4-dihydro-1,3-oxazin-2-ones.

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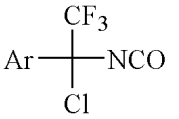
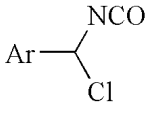
1-Aryl-2,2,2-trifluoro-1-chloroethyl isocyanates **I** that we have investigated systematically for the last 25 years exhibit pronounced bielectrophilic properties and are capable to undergo cyclocondensation with various binucleophilic reagents forming partially hydrogenated heterocyclic systems. The high regioselectivity of these processes combined with the possibility to monitor their course using $^{19}F$ NMR spectra show that compounds **I** can be convenient synthetic equivalents of the 1,3-heterodiene synthon $[–C=N–C=O]^{2+}$ [2]. At the same time much less attention was paid to simpler in structure and more available 1-chlorobenzylisocyanates **II** [3] apparently due to their high reactivity and consequently to low selectivity in condensations with binucleophiles.




**I**



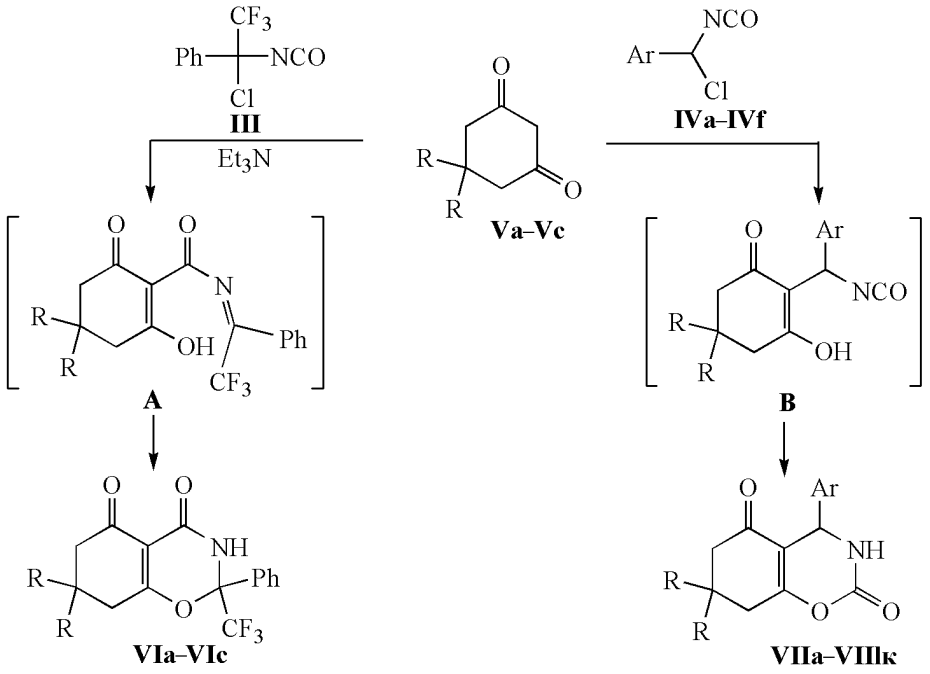

**II**

We formerly developed a new approach to the synthesis of fused 1,3-oxazine systems based on applying $[–C=N–C=O]^{2+}$ + $[–C=C–O]^{2–}$ synthon model of building up the oxazine ring. It was shown by an example of reaction between compounds **I** and 3-alkoxyphenols [4, 5] and 3-dialkylaminophenols [6] that the structure of compounds obtained depended essentially on the nature of the nucleophilic component. In particular, in the former case an isomerization was observed of *N*-alkylidenecarbamates into 1-aryloxyalkyl isocyanates that underwent cyclization into 2,3-dihydrobenz[1,3]oxazin-4-ones. In event of more electron-donor dialkylamino group no thermal rearrangement occurred with the corresponding *N*-alkylidenecarbamates, and isomeric 3,4-dihydrobenz[1,3]oxazin-2-ones were obtained. We established also that dimedone (5,5-dimethylcyclohexane-1,3-dione) cleanly reacted both with isocyanates **I** [7] and their analogs, *N*-(1-aryl-2,2,2-trifluoro-1-chloro)-ethyl-*N*'-arylcarbodiimides [8] in the presence of triethylamine giving respectively carbofused 2,3-dihydro-1,3-oxazin-4-ones and their 4-arylimino derivatives. Therewith the target products form along essentially different pathways, indicating the importance of the nature of the 1,3-bielectrophilic reagent.

Aiming at synthesis of new derivatives of 1,3-oxazines we investigated in more detail cyclocondensation of two types of 1-chloroalkyl isocyanates, 1-phenyl-2,2,2-trifluoro-1-chloroethyl isocyanate (**III**), and 1-chlorobenzyl isocyanates **IVa–IVf** with cyclic 1,3-diketones **Va–Vc**. The published approaches to preparation of 3,4-dihydro-1,3-oxazin-2-ones include reactions of vinyl isocyanate with dimedone [9], of chlorosulfonyl isocyanate with α,β-unsaturated ketones [10], and also of N-alkoxycarbonyliminium salts with propargyltrimethylsilane [11]. The examples of the synthesis of the regioisomeric heterocyclic system, 2,3-dihydro-1,3-oxazin-4-one, are lim-

* For communication V see [1].

**Scheme 1.**



**IV**, Ar = Ph (**a**), 2-$FC_6H_4$ (**b**), 3-$BrC_6H_4$ (**c**), 4-$ClC_6H_4$ (**d**), 4-$BrC_6H_4$ (**e**), 4-$NO_2C_6H_4$ (**f**); **V, VI**, R = H (**a**), Me (**b**), R,R = $(CH_2)_5$ (**c**); **VII**, R = H, Ar = Ph (**a**), 3-$BrC_6H_4$ (**b**); R = Me, Ar = Ph (**c**), 2-$FC_6H_4$ (**d**), 3-$BrC_6H_4$ (**e**), 4-$ClC_6H_4$ (**f**), 4-$BrC_6H_4$ (g), 4-$NO_2C_6H_4$ (**h**); R,R = $(CH_2)_5$, Ar = 2-$FC_6H_4$ (**i**), 4-$ClC_6H_4$ (**j**).

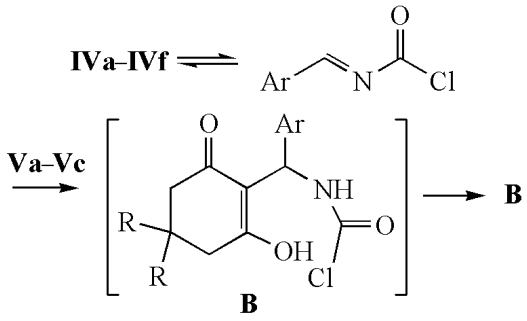
ited to reactions of Schiff bases with 2-diazo-1,3-cyclopentane-dione [12] and Meldrum's acid derivatives [13].

It was established that isocyanate **I** reacted with cyclohexanediones **Va–Vc** in toluene only in the presence of an organic base giving in high yields 2,3-dihydro-1,3-oxazin-4-ones **VIa–VIc**. On the contrary, 1-chlorobenzyl isocyanates **IVa–IVf** reacted with diketones **Va–Vc** in toluene at room temperature without organic base and in 73–84% yield formed regioisomeric 3,4-dihydro-1,3-oxazin-2-ones **VIIa–VIIj** (Scheme 1). This reaction is among the first successful examples of applying compounds **IV** in heterocyclization.

Obviously the different behavior of 1-chloroalkyl isocyanates (**III**) and compounds **IVa–IVf** demonstrates the crucial distinctions in the electrophilic character of these reagents. The reaction of isocyanate **III** with 1,3-diketones **Va–Vc** started exclusively in the presence in the reaction mixture of an organic base (triethylamine) assisting in formation of anion of the 1,3-dicarbonyl compound, whose carbon atom suffered later the isocyanate group attack. N-akylidene intermediate **A** formed underwent fast cyclization inti compound **VIa–VIc**. More electrophilic 1-chlorobenzyl isocyanates **IVa–IVf** possessing pronounced alkylating properties give intermediate compounds of **B** type where further carbamoylation of the hydroxy group of enol resulted in oxazines **VIIa–VIIj**. Taking into consideration the data of previous studies in the field of the chemistry of 1-func-tionalized isocyanates [2] it is presumable that isocyanates **IVa–IVf** most likely reacted with nonionized enols of diketones **Va–Vc** in the tautomeric *N*-benzylidenecarba-moyl chloride form leading to carbamoyl chlorides of **C** type. The latter are able to easily eliminate nydrogen chloride converting into intermediates of **B** type (Scheme 2).

The structure of regioisomeric 1,3-oxazin-4-ones **VIa–VIc** and 1,3-oxazin-2-ones **VIIa–VIIj** was exactly proved by a complex physicochemical investigation. The IR spectra of the synthesizes dihydrooxazinones turned out to be

**Scheme 2.**



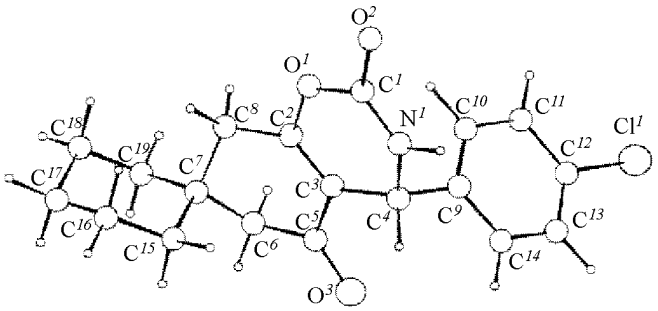



**Fig. 1.** General view of molecule of 4-(4-chlorophenyl)-4,8-dihydrospiro(1,3-benzoxazine-7,1'-cyclohexane)-2,5(3*H*,6*H*)-dione (**VIIj**).

sufficiently characteristic for their unambiguous attribution to a definite structural type. In the spectra of compounds **VIa–VIc** amide fragment gave rise to absorption bands at 1720–1730 cm$^{-1}$ whereas the absorption band of the carbamate carbonyl in the spectra of compounds **VIIa–VIIj** appeared at 1765–1780 cm$^{-1}$ [6]. In the $^1$H NMR spectra of 3,4-dihydrooxazin-2-ones **VIIa–VIIj** singlets from protons belonging to groups CH and NH were observed in the regions 5.08–5.26 and 8.57–8.78 ppm respectively. In the $^{19}$F NMR spectra of oxazines **VIa–VIc** the fluorine atoms of the trifluoromethyl group appeared in the region from –80.7 to –80.8 ppm indicating the presence in the structure of the molecule of an oxyaminal fragment [O–C($CF_3$)Ph–NH] [5]. In the $^{13}$C NMR spectra the signals of C$^4$ atoms in the spectra of compounds **VIIa–VIIj** were located in the region 49–52 ppm, and the signals belonging to C$^2$ atoms of compounds

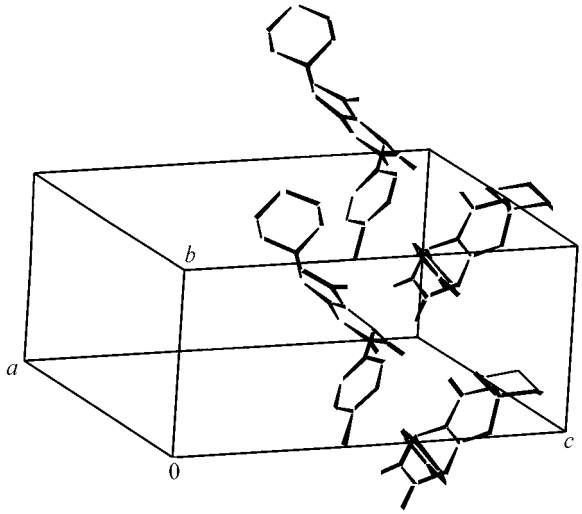



**Fig. 2.** Crystal packing of 4-(4-chlorophenyl)-4,8-dihydrospiro(1,3-benzoxazine-7,1'-cyclohexane)-2,5(3*H*,6*H*)-dione (**VIIj**). The intermolecular hydrogen bond N$^1$–H$^1$···O$^3$ is shown by a dotted line.

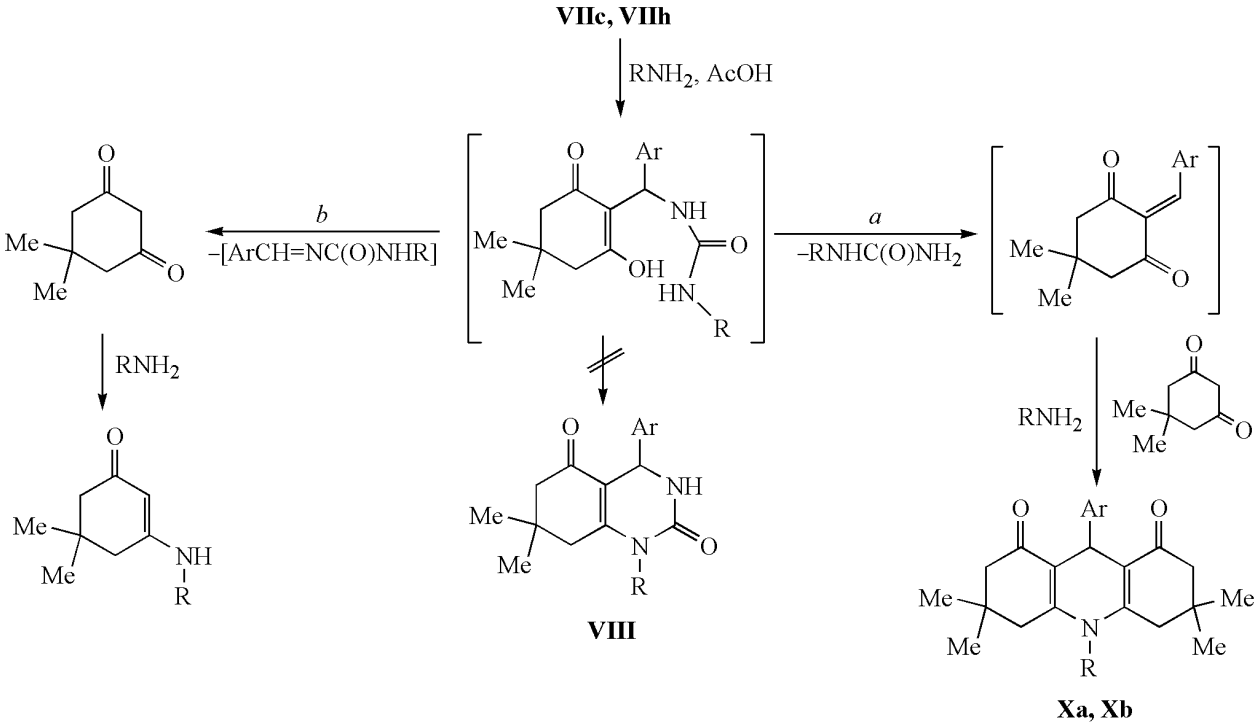
**VIa–VIc** appeared at 89–90 ppm as a quartet with a constant $^2J_{C-F}$ 32–33 Hz. The unambiguous proof of compounds **VII** structure was obtained by X-ray crystallography by an example of chlorophenyl derivative **VIIj**. The general view of molecule **VIIj** is presented on Fig.1.*

The main bond lengths (Å) and bond angles (deg) are as follows: O$^1$–C$^1$ 1.395 (2), O$^1$–C$^2$ 1.372 (2), O$^2$–C$^1$ 1.198 (2), O$^3$–C$^5$ 1.229 (2), N$^1$–C$^1$ 1.335 (2), N$^1$–C$^4$ 1.462 (2), N$^1$–H$^1$ 0.88 (2), C$^2$–C$^3$ 1.337 (2), C$^2$–C$^8$ 1.492 (3), C$^3$–C$^4$ 1.505 (2), C$^3$–C$^5$ 1.459 (3), C$^4$–C$^9$ 1.521 (2), C$^4$–H$^2$ 0.965 (18), C$^5$–C$^6$ 1.504 (3), C$^6$–C$^7$ 1.540 (3), C$^7$–C$^8$ 1.538 (3); C$^1$O$^1$C$^2$121.12 (14), C$^1$N$^1$C$^4$128.45 (16), C$^1$N$^1$H$^1$114.0 (14), C$^4$N$^1$H$^1$116.5 (13), O$^1$C$^1$O$^2$117.37 (17), O$^1$C$^1$N$^1$116.03 (16), O$^2$C$^1$N$^1$126.59 (18), O$^1$C$^2$C$^3$122.48 (16), O$^1$C$^2$C$^8$111.93 (14), C$^3$C$^2$C$^8$125.58 (17), C$^2$C$^3$C$^4$121.64 (16), C$^2$C$^3$C$^5$119.68 (16), C$^4$C$^3$C$^5$118.68 (15), N$^1$C$^4$C$^3$108.60 (14), N$^1$C$^4$C$^9$110.66 (15), C$^3$C$^4$C$^9$112.75 (14), N$^1$C$^4$H$^2$107.6 (10), C$^3$C$^4$H$^2$108.6 (10), C$^9$C$^4$H$^2$108.4 (10), O$^3$C$^5$C$^3$ 121.15 (16), O$^3$C$^5$C$^6$122.08 (17), C$^3$C$^5$C$^6$116.75 (16), C$^5$C$^6$C$^7$113.80 (15), C$^6$C$^7$C$^8$107.94 (16), C$^2$C$^8$C$^7$113.36 (15). The central bicyclic system O$^1$N$^1$C$^{1–8}$ is essentially nonplanar: the deviations of atoms from the least-mean-squares plane reach 0.406 Å. Therewith the heterocycle O$^1$N$^1$C$^{1–4}$ is planar within 0.074 Å, whereas the cyclic system C$^{2,3,5–8}$ exists in a conformation of a notably flattened *semiboat* (modified Cremer–Pople parameters [14] are *S* 0.19, ψ 29.7, θ 66.3 deg). Due to steric factors the benzene ring C$^{9–14}$ is virtually normal to the central bicyclic system (the corresponding dihedral angle amounts to 82.9 deg). The cyclohexane substituent has a common *chair* conformation. The N$^1$ atom has a trigonal plane configuration of its bonds (the sum of the bond angles at this atom is 359.0 deg). The conjugation between the unshared electron pair of this atom and the π-system of C$^1$=O$^1$ bond caused significant shortening of the formally ordinary N$^1$–C$^1$ bond [1.335(2) Å] compared to the values 1.43–1.45 Å, characteristic of a pure ordinary bond N($sp^2$)-C($sp^2$) [15, 16]. In the crystal the molecules of compound **VIIj** are joined into an infinite chain by intermolecular hydrogen bonds N$^1$–H$^1$···O$^3$ [N$^1$–H$^1$ 0.88(2), N$^1$···O$^3$ 3.030(2), H$^1$···O$^3$ 2.20(2) Å, N$^1$H$^1$O$^3$156(1) deg] (Fig. 2).

Oxazin-2-ones **VII** contain a vinilog O-acylcarbamine fragment possessing two electrophilic sites: C$^2$ and C$^{8a}$ atoms. At the attack on the C$^2$ atom by nucleophiles like ammonia or primary amines the opening of the oxazine

* The numbering of atoms is different from that used in the name of the compound.

**Scheme 2.**




**IX**, R = 4-$ClC_6H_4$ (**a**), 4-$MeOC_6H_4$ (**b**); X, R = H, Ar = Ph (**a**), 4-$ClC_6H_4$ (**b**).

ring is expected to occur giving intermediates of **D** type that are also intermediates in the synthesis of dihydropyrimidinones **VIII** by Biginelli reaction [17]. We found, that in no case after heating oxazines **VII** in ethanol with free bases like ammonia, benzylamine or anisidine the corresponding dihydropyrimidones of **VIII** type were isolated. At the use of ammonium acetate or an aromatic amine in the presence of 1 equiv of acetic acid we detected by GC-MS procedure the formation of 3-arylamino-5,5-di-methylcyclohex-2-en-1-ones **IXa** and **IXb**, and hexa-hydroacridine-1,8-diones **Xa** and **Xb** that were also isolated from the reaction mixture and identified in an individual state. The scheme of these compounds formation contains at least two alternatives of transformations. Presumably first the amino group attacks $C^2$ atom, but under the conditions of the process the arising intermediate **D** does not undergo cyclization into compounds of **VIII** type and decomposes with elimination either of urea (path a) or *N*-benzylideneurea (path b) giving as a result compounds **IXa** and **IXb**, **Xa** and **Xb** (Scheme 3).

## EXPERIMENTAL

X-ray crystallographic investigation of a single crystal of compound **VIIj** having spherical form, diameter 0.43 mm, was carried out at room temperature on an automatic four-circle diffractometer Enraf-Nonius CAD-4 (Cu$K_\alpha$-radiation, λ 1.54178 Å, the ratio of scanning rates 2θ/ω 1.2, $\theta_{max.}$ 60 deg, spherical segment $0 \le h \le 14$, $0 \le k \le 8$, $-19 \le l \le 18$). 2851 reflections were collected. Crystals of compound **VIIj** monoclinic, *a* 12.722(4), *b* 7.932(4), *c* 16.925(6) Å, β 97.75(3) deg, *V* 1692.3 $Å^3$, *M* 271.3, *Z* 4, $d_{calc}$ 1.36 g/$cm^3$, μ 21.4 $cm^{-1}$, *F*(000) 570.6, space group $P2_1/C$ (N 14). The structure was solved by the direct method and refined by the least-mean-squares method in full-matrix anisotropic approximation using software CRYSTALS [18]. Refining was performed with the use of 2153 reflections with $I > 3\sigma(I)$ (297 refined parameters, 7.2 reflection per parameter). All hydrogen atoms were revealed from the difference synthesis and refined isotropically. The refining was performed applying the weight Chebyshev scheme [19] containing 5 parameters: 4.16, –2.29, 1.98, –0.74, and –0.87. The final values of divergence factors are *R* 0.040 and $R_W$ 0.041, GOF 0.991. The residual electron density from the difference Fourier series was 0.18 and –0.26 ε/$Å^3$. The extinction in the crystal was estimated by azimuthal scanning [20]. The complete set of X-ray crystallographic data for compound **VIIj** are deposited in the Cambridge Structural Database (CCDC 277102).

IR spectra were recorded on a spectrophotometer UR-20 from KBr pellets. $^1$H, $^{13}$C, and $^{19}$F NMR spectra in DMSO-$d_6$ were registered on a spectrometer Varian-Gemini (299.95, 75.4, 282.2 MHz respectively), internal references TMS ($^1$H, $^{13}$C) and $CCl_3F$ ($^{19}$F). 1-Phenyl-2,2,2-trifluoro-1-chloroethyl isocyanate (**III**) and 1-chlorobenzyl isocyanates **IVa–IVf** were prepared by procedures [21] and [3] respectively.

**2-Aryl-2-trifluoromethyl-7,8-dihydrobenz-2*H*-1,3-oxazine-4,5(3*H*,6*H*)-diones VIa–VIc**. To a solution of 1.17 g (5 mmol) of isocyanate **III** in 20 ml of anhydrous toluene was added 5 mmol of diketone **Va–Vc**, and then at stirring was added within 1 h 0.7 ml (5 mmol) of triethylamine in 10 ml of anhydrous toluene. The reaction mixture was stirred for 4 h, the separated precipitate was filtered off, washed with water, dried, and recrystallized from ethanol.

**2-Trifluoromethyl-2-phenyl-7,8-dihydro-2*H*-1,3-benzoxazine-4,5(3*H*,6*H*)-dione (VIa)**. Yield 71%, mp 160–162°C. IR spectrum, cm$^{-1}$: 3200, 3100 (NH), 1730 (C=O). $^1$H NMR spectrum, δ, ppm: 1.91 m (2H$_{aliph}$), 2.17 m (1H$_{aliph}$), 2.26 m (1H$_{aliph}$), 2.71 m (2H$_{aliph}$), 7.49 m (3H$_{arom}$), 7.62 m (2H$_{arom}$), 9.85 C (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 19.46, 28.59, 37.94 (3CH$_2$), 89.78 q (C$^2$, *J* 32.5 Hz), 109.83 (C$^{4a}$), 121.93 q (CF$_3$, *J* 285 Hz), 127.15, 129.33, 131.26, 133.97 (C$_{arom}$), 158.23, 179.18, 192.27 (C$^{8a}$, C$^4$, C$^5$). $^{19}$F NMR spectrum, δ, ppm: –80.73. Found, %: C 57.61; H 3.80; N 4.62. $C_{15}H_{12}F_3NO_3$. Calculated, %: C 57.88; H 3.89; N 4.50.

**7,7-Dimethyl-2-trifluoromethyl-2-phenyl-7,8-dihydro-2*H*-1,3-benzoxazine-4,5(3*H*,6*H*)-dione (VIb)**. Yield 82%, mp 158–160°C [7]. IR spectrum, cm$^{-1}$: 3210, 3100 (NH), 1730 (C=O). $^1$H NMR spectrum, δ, ppm: $^{13}$C NMR spectrum, δ, ppm: 27.17, 27.37 (2CH$_3$), 31.55 (C$^7$), 41.06 (CH$_2$), 51.32 (CH$_2$), 88.99 q (C$^2$, *J* 32 Hz), 108.50 (C$^{4a}$), 122.05 q (CF$_3$, *J* 284 Hz), 126.76, 128.79, 130.79, 133.60 (C$_{arom}$), 157.76, 177.34, 191.80 (C$^{8a}$, C$^4$, C$^5$). $^{19}$F NMR spectrum, δ, ppm: –80.78. Found, %: C 60.37; H 4.83; N 4.02. $C_{17}H_{16}F_3NO_3$. Calculated, %: C 60.18; H 4.75; N 4.13.

**2-Trifluoromethyl-2-phenyl-7,8-dihydrospiro-(1,3-benzoxazine-7,1'-cyclohexane)-4,5(3*H*,6*H*)-dione (VIc)**. Yield 77%, mp 195–197°C. IR spectrum, cm$^{-1}$: 3210 (NH), 1725 (C=O). $^1$H NMR spectrum, δ, ppm: 1.20–1.44 m (10H$_{aliph}$), 2.12 d (1H, C$\underline{H}^A$H$^B$, *J* 16.2 Hz), 2.30 d (1H, CH$^A\underline{H}^B$, *J* 16.2 Hz), 2.74 m (2H, CH$_2$), 7.49 m (3H$_{arom}$), 7.61 m (2H$_{arom}$), 9.90 C (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 21.32, 25.95, 34.94, 35.45, 36.25, 50.05 (C$_{aliph}$), 88.95 q (C$^2$, *J* 33 Hz), 109.23 (C$^{4a}$), 124.55 q (CF$_3$, *J* 285 Hz), 127.27, 129.21, 131.27, 134.13 (C$_{arom}$), 158.18, 177.55, 192.05 (C$^{8a}$, C$^4$, C$^5$). $^{19}$F NMR spectrum, δ, ppm: –80.81. Found, %: C 63.05; H 5.25; N 3.60. $C_{20}H_{20}F_3NO_3$. Calculated, %: C 63.32; H 5.31; N 3.69.

**4-Aryl-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-diones VIIa–VIIj**. To a solution of 5 mmol of isocyanate **IVa–IVf** in 20 ml of anhydrous toluene was added 5 mmol of diketone **Va–Vc**, and the mixture was stirred for 24 h at room temperature. The separated precipitate was filtered off and recrystallized from a mixture ethyl acetate–hexane, 2:1.

**4-Phenyl-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIa)**. Yield 73%, mp 150–152°C. IR spectrum, cm$^{-1}$: 3320 (NH), 1770, 1720, 1680 (C=O). $^1$H NMR spectrum, δ, ppm: 2.01 m (2H, CH$_2$), 2.30 m (2H, CH$_2$), 2.60 m (2H, CH$_2$), 5.09 s (1H, CH), 7.27 m (5H$_{arom}$), 8.62 s (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 20.41, 26.78, 36.59 (3CH$_2$), 52.32 (CH), 112.86 (C$^{4a}$), 127.17, 128.26, 129.05, 142.79 (C$_{arom}$), 147.97, 166.92, 195.47 (C$^{8a}$, C$^2$, C$^4$). Found, %: C 68.99; H 5.33; N 5.71. $C_{14}H_{13}NO_3$. Calculated, %: C 69.12; H 5.39; N 5.76.

**4-(3-Bromophenyl)-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIb)**. Yield 75%, mp 151–153°C. IR spectrum, cm$^{-1}$: 3330 (NH), 1770, 1730, 1680 (C=O). $^1$H NMR spectrum, δ, ppm: 2.01 m (2H, CH$_2$), 2.32 m (2H, CH$_2$), 2.61 m (2H, CH$_2$), 5.11 s (1H, CH), 7.28 m (2H$_{arom}$), 7.43 m (2H$_{arom}$), 8.66 s (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 20.35, 26.82, 36.55 (3CH$_2$), 51.96 (CH), 112.12 (C$^{4a}$), 122.12, 126.21, 130.20, 131.17, 131.36, 145.36 (C$_{arom}$), 147.66, 167.33, 195.52 (C$^{8a}$, C$^2$, C$^4$). Found, %: C 52.32; H 3.81; N 4.28. $C_{14}H_{12}BrNO_3$. Calculated, %: C 52.20; H 3.75; N 4.35.

**7,7-Dimethyl-4-phenyl-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIc)**. Yield 82%, mp 209–211°C. IR spectrum, cm$^{-1}$: 3330 (NH), 1765, 1730, 1680 (C=O). $^1$H NMR spectrum, δ, ppm: 0.98 s (3H, CH$_3$), 1.08 s (3H, CH$_3$), 2.20 m (2H, CH$_2$), 2.49 m (2H, CH$_2$), 5.08 s (1H, CH), 7.25 m (3H$_{arom}$), 7.30 m (2H$_{arom}$), 8.64 s (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 27.50, 28.72 (2CH$_3$), 32.62, 40.04 (2CH$_2$), 50.32 (C$^7$), 52.43 (CH), 111.85 (C$^{4a}$), 127.17, 128.29, 129.05, 142.77 (C$_{arom}$), 147.96, 164.95, 195.23 (C$^{8a}$, C$^2$, C$^4$). Found, %: C 71.20; H 6.44; N 5.03. $C_{16}H_{17}NO_3$. Calculated, %: C 70.83; H 6.32; N 5.16.

**7,7-Dimethyl-4-(2-fluorophenyl)-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIId)**. Yield 77%, mp 198–200°C. IR spectrum, cm$^{-1}$: 3320 (NH), 1770, 1735, 1670 (C=O). $^1$H NMR spectrum, δ,

ppm: 0.98 s (3H, $CH_3$), 1.08 s (3H, $CH_3$), 2.11 d (1H, $C\underline{H}^AH^B$, *J* 16.0 Hz), 2.21 d (1H, $CH^A\underline{H}^B$, *J* 16.0 Hz), 2.49 m (2H, $CH_2$), 5.25 s (1H, CH), 7.14 m ($2H_{arom}$), 7.29 m ($2H_{arom}$), 8.60 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 27.21, 28.82 ($2CH_3$), 32.60, 40.02 ($2CH_2$), 48.47 ($C^7$), 50.25 (CH), 109.98 ($C^{4a}$), 116.15, 124.94, 129.19, 130.47, 130.55, 147.64 ($C_{arom}$), 159.74, 165.11, 195.12 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 66.21; H 5.52; N 4.92. $C_{16}H_{16}FNO_3$. Calculated, %: C 66.43; H 5.57; N 4.84.

**4-(3-Bromophenyl)-7,7-dimethyl-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIe)**. Yield 81%, mp 163–165°C. IR spectrum, $cm^{-1}$: 3330 (NH), 1770, 1720, 1680 (C=O). $^1H$ NMR spectrum, δ, ppm: 0.99 s (3H, $CH_3$), 1.08 s (3H, $CH_3$), 2.17 d (1H, $C\underline{H}^AH^B$, *J* 16.4 Hz), 2.21 d (1H, $CH^A\underline{H}^B$, *J* 16.4 Hz), 2.48 m (2H, $CH_2$), 5.08 s (1H, CH), 7.28 m ($2H_{arom}$), 7.40 m ($2H_{arom}$), 8.66 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 27.56, 28.62 ($2CH_3$), 32.66, 40.02 ($2CH_2$), 50.26 ($C^7$), 52.08 (CH), 111.09 ($C^{4a}$), 122.09, 126.23, 130.24, 131.21, 131.41, 145.32 ($C_{arom}$), 147.64, 165.85, 195.32 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 55.20; H 4.69; N 4.03. $C_{16}H_{16}BrNO_3$. Calculated, %: C 54.87; H 4.61; N 4.00.

**7,7-Dimethyl-4-(4-chlorophenyl)-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIf)**. Yield 84%, mp 191–193°C. IR spectrum, $cm^{-1}$: 3330 (NH), 1770, 1720, 1680 (C=O). $^1H$ NMR spectrum, δ, ppm: 0.98 s (3H, $CH_3$), 1.08 s (3H, $CH_3$), 2.15 d (1H, $C\underline{H}^AH^B$, *J* 16.2 Hz), 2.21 d (1H, $CH^A\underline{H}^B$, *J* 16.2 Hz), 2.49 m (2H, $CH_2$), 5.10 s (1H, CH), 7.27 d (2H, $H_{arom}$, *J* 8.7 Hz), 7.33 d (2H, $H_{arom}$, *J* 8.7 Hz), 8.67 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 27.04, 28.14 ($2CH_3$), 32.09, 39.50 ($2CH_2$), 49.76 ($C^7$), 51.47 (CH), 110.87 ($C^{4a}$), 128.52, 128.67, 132.34, 141.22 ($C_{arom}$), 147.22, 164.56, 194.75 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 62.94; H 5.33; N 4.48. $C_{16}H_{16}ClNO_3$. Calculated, %: C 62.85; H 5.27; N 4.58.

**4-(4-Bromophenyl)-7,7-dimethyl-4,6,7,8-tetrahydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIg)**. Yield 80%, mp 195–196°C. IR spectrum, $cm^{-1}$: 3320 (NH), 1765, 1720, 1680 (C=O). $^1H$ NMR spectrum, δ, ppm: 0.98 s (3H, $CH_3$), 1.08 s (3H, $CH_3$), 2.15 d (1H, $C\underline{H}^AH^B$, *J* 16.4 Hz), 2.21 d (1H, $CH^A\underline{H}^B$, *J* 16.4 Hz), 2.49 m (2H, $CH_2$), 5.09 s (1H, CH), 7.22 d (2H, $H_{arom}$, *J* 8.8 Hz), 7.50 d (2H, $H_{arom}$, *J* 8.8 Hz), 8.66 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 27.58, 28.65 ($2CH_3$), 32.60, 40.06 ($2CH_2$), 50.30 ($C^7$), 52.05 (CH), 111.36 ($C^{4a}$), 121.38, 129.37, 131.95, 142.15 ($C_{arom}$), 147.72, 165.08, 195.23 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 54.68; H 4.65; N 3.87. $C_{16}H_{16}BrNO_3$. Calculated, %: C 54.87; H 4.61; N 4.00.

**7,7-Dimethyl-4-(4-nitrophenyl)-4,6,7,8-tetra-hydro-2*H*-1,3-benzoxazine-2,5(3*H*)-dione (VIIh)**. Yield 79%, mp 120–122°C. IR spectrum, $cm^{-1}$: 3330 (NH), 1770, 1680 (C=O). $^1H$ NMR spectrum, δ, ppm: 0.98 s (3H, $CH_3$), 1.09 s (3H, $CH_3$), 2.15 d (1H, $C\underline{H}^AH^B$, *J* 16.4 Hz), 2.23 d (1H, $CH^A\underline{H}^B$, *J* 16.4 Hz), 2.49 m (2H, $CH_2$), 5.26 s (1H, CH), 7.55 d (2H, $H_{arom}$, *J* 8.6 Hz), 8.19 d (2H, $H_{arom}$, *J* 8.6 Hz), 8.78 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 27.58, 28.61 ($2CH_3$), 32.62, 40.01 ($2CH_2$), 50.22 ($C^7$), 52.21 (CH), 110.85 ($C^{4a}$), 124.29, 128.83, 147.51 ($C_{arom}$), 147.72, 165.08, 195.23 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 60.54; H 4.97; N 8.83. $C_{16}H_{16}N_2O_5$. Calculated, %: C 60.76; H 5.10; N 8.86.

**4-(2-Fluorophenyl)-4,8-dihydrospiro(1,3-benzoxazine-7,1'-cyclohexane)-2,5(3*H*,6*H*)-dione (VIIi)**. Yield 79%, mp 120–122°C. IR spectrum, $cm^{-1}$: 3340 (NH), 1775, 1740, 1670 (C=O). $^1H$ NMR spectrum, δ, ppm: 1.28–1.40 m ($10H_{aliph}$), 2.24 m (2H, $CH_2$), 2.49 m (2H, $CH_2$), 5.24 s (1H, CH), 7.14 m ($2H_{arom}$), 7.28 m ($2H_{arom}$), 8.57 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 21.45, 26.10, 35.20, 36.87, 37.74, 48.21 ($C_{aliph}$), 48.43 (CH), 109.99 ($C^{4a}$), 116.16, 124.95, 129.10, 130.40, 130.47, 147.67 ($C_{arom}$), 159.73, 164.71, 194.89 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 69.51; H 6.15; N 4.20. $C_{19}H_{20}FNO_3$. Calculated, %: C 69.29; H 6.12; N 4.25.

**4-(4-Chlorophenyl)-4,8-dihydrospiro(1,3-benzoxazine-7,1'-cyclohexane)-2,5(3*H*,6*H*)-dione (VIIj)**. Yield 79%, mp 158–160°C. IR spectrum, $cm^{-1}$: 3330 (NH), 1770, 1720, 1680 (C=O). $^1H$ NMR spectrum, δ, ppm: 1.29–1.50 m ($10H_{aliph}$), 2.54 m (4H, $2CH_2$), 5.10 s (1H, CH), 7.28 d (2H, $H_{arom}$, *J* 8.8 Hz), 7.35 d (2H, $H_{arom}$, *J* 8.8 Hz), 8.65 s (1H, NH). $^{13}C$ NMR spectrum, δ, ppm: 21.47, 21.52, 35.31, 35.59, 36.67, 37.75, 48.26 ($C_{aliph}$), 51.98 (CH), 111.40 ($C^{4a}$), 128.66, 129.18, 132.85, 141.71 ($C_{arom}$), 147.76, 164.69, 195.01 ($C^{8a}$, $C^2$, $C^4$). Found, %: C 66.33; H 5.86; N 3.92. $C_{19}H_{20}ClNO_3$. Calculated, %: C 65.99; H 5.83; N 4.05.

**3-Arylamino-5,5-dimethyl-2-cyclohexen-1-ones IXa and IXb**. To a solution of 1.35 g (5 mmol) of compound **VIIc** in 30 ml of ethanol was added 10 mmol of an appropriate substituted aniline, 0.6 ml (10 mmol) of acetic acid, and the mixture was boiled for 10 h. The reaction mixture was diluted with 60 ml of water, the separated precipitate was filtered off, dried, and recrystallized from a mixture ethyl acetate–hexane, 1:1.

**5,5-Dimethyl-3-(4-chlorophenylamino)-2-cyclohexen-1-one (IXa)**. Yield 34%, mp 205–207°C [22].

**5,5-Dimethyl-3-(4-methoxyphenylamino)-2-cyclohexen-1-one (IXb)**. Yield 30%, mp 186–188°C [22].

**9-Aryl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8(2*H*,5*H*)-acridinediones Xa and Xb**. To a solution of 5 mmol of compound **VIIc** or **VIIf** in 30 ml of ethanol was added 1.54 g (20 mmol) of ammonium acetate, and the mixture was boiled for 10 h. The reaction mixture was diluted with 60 ml of water, the separated precipitate was filtered off, dried, and recrystallized from a mixture ethanol–water, 2:1.

**3,3,6,6-Tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydro-1,8(2*H*,5*H*)-acridinedione (Xa)**. Yield 38%, mp 290–292°C [23].

**3,3,6,6-Tetramethyl-9-(4-chlorophenyl)-3,4,6,7,9,10-γεqCahydro-1,8(2*H*,5*H*)-acridinedione (Xb)**. Yield 40%, mp 298–300°C [23].

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