1,3-Dipolar cycloadditions of heterocycles XIX.* Cycloaddition of furonitrile oxides to oxygen-containing heterocycles

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1,3-Dipolar cycloadditions of 5-X-2-furonitrile oxides (X = H, NO_2, 4- and 3-nitrophenyl) with 5,6-bis(methoxycarbonyl)-7-oxabicyclo[2,2,1]hept-2-ene, 1,4-epoxy-1,4-dihydronaphthalene, 2,3- and 2,5-dihydrofuran, 2,3-dihydropyran, and 2-R-substituted 1,3-dioxep-5-enes (R = H, CH_3, phenyl), respectively, are described. Regioselectivity as well as *endo-exo* stereoselectivity is discussed.

Описано 1,3-диполярное циклоприсоединение 5-X-2-фуронитрилоксидов (X = H, NO_2, 4- или 3-нитрофенил) с 5,6-бис(метоксикарбонил)-7-оксабицикло[2,2,1]-2-гептеном, 1,4-эпокси-1,4-дигидронафталином, 2,3- и 2,5-дигидрофураном, 2,3-дигидропираном и 2-R-замещенными 1,3-диоксеп-5-енами (R = H, метил или фенил). Обсуждается региоселективность и *эндо-экзо*-стереоселективность циклоприсоединений.

1,3-Dipolar cycloaddition reactions represent one of the best approaches to five-membered heterocycles [1]. Simple procedure, high stereoselectivity, predictable regioselectivity combined with the possibility to apply the products as synthons contributed to the popularity 1,3-cycloadditions are currently enjoying in the synthesis [2]. Recently isoxazolines proved to be an important group of cycloaddition products [3]. We have discovered [4—8] that an introduction of oxygen in the β-position with respect to the oxygen of isoxazoline enabled its facile highly selective photorearrangement to cyclic enamino aldehydes. Now we have undertaken the investigation of the role of furan in such photorearrangements, having in mind also possible biological activity of the furan-substituted isoxazolines. Although many furan derivatives exhibit significant biological activity [9], those possessing an isoxazoline ring are but few [10—12]. So far only some cycloadditions of 2-furonitrile oxide (*Ia*) and 5-nitro-2-furonitrile oxide (*Ib*) with selected alkenes and alkynes were described

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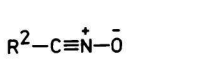
[10—12]. Furyl-substituted condensed isoxazolines were not yet described in the literature.

We now describe reactions of 2-furonitrile oxides (*Ia—Id*), generated from the corresponding carbohydroximoyl chlorides, with heterocycles, containing oxygen. Further we discuss the regio- and stereoselectivity of such reactions.

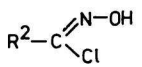
Cycloaddition of substituted furonitrile oxides with suitable dipolarophiles, such as 5,6-bis(methoxycarbonyl)-7-oxabicyclo[2,2,1]hept-2-ene, 1,4-epoxy--1,4-dihydronaphthalene, 2,3- and 2,5-dihydrofuran, 2,3-dihydropyran, and 2-R-2*H*,4*H*,7*H*-1,3-dioxepine (*III*) (R = H, phenyl, methyl) furnished in case of *Ia* isoxazolines *IVa—XIIIa* in 45—88 % yields, in case of *Ib* isoxazolines *IVb—XIb* in 47—89 % yield; 5-(4-nitrophenyl)-2-furonitrile oxide (*Ic*) gave isoxazolines *IVc—XIc* in 67—92 % yield, 5-(3-nitrophenyl)-2-furonitrile oxide (*Id*) gave isoxazolines *IVd*, *Vd*, and *IXd* in 86—93 % yields (Scheme 1). Cycloadditions of furonitrile oxides *Ia* and *Ib* proceeded with yields comparable to those of benzonitrile oxide [4—6], yields of *Ib* being somewhat higher than those of *Ia*. In contrast to benzonitrile oxide, which needed high temperature for the reactions with 2,3-dihydropyran [13], furonitrile oxides *Ia—Id* reacted at temperatures as low as 0—5 °C, giving high yields. Surprisingly arylated furonitrile oxides *Ic* and *Id* gave very high yields, so that an explanation seemed necessary. Two factors can be responsible — conjugation of the furan ring with benzene in *Ic* and *Id* lowers their LUMO energy and makes the dominant frontier MO interactions LUMO(nitrile oxide)—HOMO(heterocycle) all the more favourable [13—15]. Another contribution comes from the suppression of side reactions, mainly the dimerization of furonitrile oxide *Ic* and *Id*, due to steric hindrance by bulky substituents. Experimental support for the latter factor comes from the finding that in contrast to cycloadditions of *Ia* and *Ib*, where furonitrile oxide dimers were found, there were none in cycloadditions of *Ic* and *Id*.

Structure of the 30 prepared isoxazolines *IV—XIII* has been determined mainly by correlation of the corresponding chemical shifts in ^{1}H and ^{13}C NMR spectra with those found for analogous phenyl [4—7], 9-anthryl [15], and biphenyl [13] derivatives. Thus based on zero coupling constants $J_{1,2}$ and $J_{5,6}$ *exo* structure has been assigned to *IVa-exo* with respect to oxygen bridge. Both bridge protons H-2 and H-5 were in ^{1}H NMR spectra equivalent, giving a singlet at $\delta = 4.97$ ppm. In case of an *endo* arrangement of rings coupling constants on the order of 5 Hz would have been expected. Protons H-1 and H-6 produced doublets at $\delta = 5.00$ ppm and 4.13 ppm, respectively, with the coupling constant $J_{1,6} = 10.0$ Hz. Such value of interaction constant, found also in spectra of *IV—XIII* testifies to *cis* stereospecificity of the concerted 1,3-dipolar cycloaddition of furonitrile oxides *Ia—Id*. The presence of another four doublets (C-2, C-5, C-1, C-6) in ^{13}C NMR spectra at δ/ppm: 86.60, 85.30, 81.15, and 47.17,

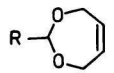
respectively, confirms the structure suggested for *IVa*. Cycloaddition of *Ia* with 1,4-epoxy-1,4-dihydronaphthalene also gave exclusively an *exo* adduct *Va*. Again coupling constants $J_{3a,4}$ and $J_{9,9a}$ were zero. The singlet of bridge protons H-4, H-9 was, compared with that in *IVa*, downfield shifted to $\delta = 5.56$ ppm, due probably to the anisotropy of the benzene ring in *V*.



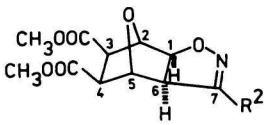
Ia–Id



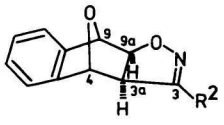
IIa–IId



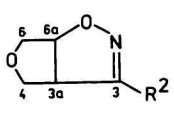
III



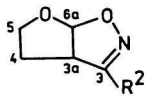
IV



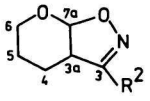
V



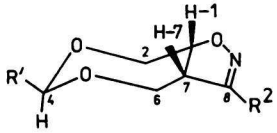
VI



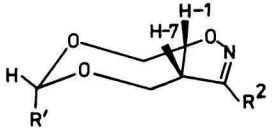
VII



VIII



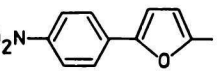
IX, X, XII

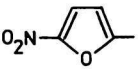


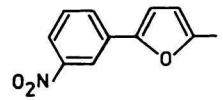
IX, XI, XIII

IX: R′ = H; *X*, *XI*: R′ = C_6H_5; *XII*, *XIII*: R′ = CH_3

a: R^2 = 

c: R^2 = 

b: R^2 = 

d: R^2 = 

Scheme 1

Cycloaddition reactions at 5-membered heterocyclic rings, represented by 2,3- and 2,5-dihydrofuran were analyzed utilizing the fact that 2,5-dihydrofuran gave only one product *VIa*. This was then used as a model compound for elucidation of regioisomerism, encountered in reactions of 2,3-dihydrofuran. ^{1}H NMR spectrum of 3-(2-furyl)-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazole (*VIa*), prepared in 45 % yield showed a doublet at $\delta = 5.35$ ppm with $J_{3a,6a} = 9.0$ Hz and $J_{6,6a} = 5.0$ Hz, assigned to H-6a. Signals of other protons (H_2-6, H_2-4, H-3a) constituted a multiplet at $\delta = 3.58$—4.45 ppm.

3-(2-Furyl)-3a,4,5,6a-tetrahydrofuro[3,2-*d*]isoxazole (*VIIa*) has been isolated from the reaction of *Ia* with 2,3-dihydrofuran. In this case two regioisomers are possible, namely a head-to-head and head-to-tail isomer. Considering chemical shifts of the relevant signals in both ^{1}H and ^{13}C NMR spectra, *VIIa* has been assigned a head-to-head structure. The doublet of H-6a at $\delta = 6.22$ ppm (for *VIa* $\delta = 5.35$ ppm) and doublet of C-6a at $\delta = 108.85$ ppm (for *VIb* $\delta = 88.62$ ppm) are both at higher δ values, caused by deshielding by two neighbouring oxygen atoms in *VIIa*. Similarly cycloaddition of *Ia* with 2,3-dihydropyran gave exclusively the head-to-head regioisomer *VIIIa*. The structure of 3-(2-furyl)-3a,4,5,7a-tetrahydro-6*H*-pyrano[3,2-*d*]isoxazole (*VIIIa*) has been confirmed by the presence of a doublet of H-7 proton, found at $\delta = 5.87$ ppm with $J_{3a,7a} = 8.0$ Hz, as well as by C-7a doublet at $\delta = 101.39$ ppm. Furonitrile oxides *Ib*—*Id* also gave in cycloadditions with 2,3-dihydrofuran and 2,3-dihydropyran only head-to-head regioisomers, in accord with our previous results, concerning cycloadditions of benzonitrile oxide [13], biphenylnitrile oxide [13], and 9-anthracenenitrile oxide [15]. An explanation of the phenomenon can also be found there.

Methylenic protons doublets of 8-(2-furyl)-3,5,10-trioxa-9-azabicyclo[5,3,0]-decane (*IXa*), prepared in 51 % yield from *Ia* and 2*H*,4*H*,7*H*-1,3-dioxepine (*III*), were found at different δ values due to the bent arrangement of the bicyclic system (for H_A-4 $\delta = 4.75$ ppm, for H_B-4 $\delta = 4.30$ ppm). A bridge proton H-1 multiplet can be found at $\delta = 4.68$ ppm. Triplet at $\delta = 99.41$ ppm was assigned to C-4, triplets at $\delta = 70.75$ ppm and $\delta = 68.41$ ppm to C-2 and C-6, respectively. Higher δ values of C-2, compared with those of C-6 as well as those of C-1 ($\delta = 84.33$ ppm) compared with C-7 ($\delta = 53.47$ ppm) can be accounted for by deshielding caused by oxygen atom [5, 6].

Cycloaddition of *Ia* with 2-phenyl- and 2-methyl-2*H*,4*H*,7*H*-1,3-dioxepine, respectively, gave a mixture of an *exo* adduct (*Xa*, *XIIa*) and an *endo* adduct (*XIa*, *XIIIa*). In all cases, as with the reactions of *Ib* and *Ic*, both stereoisomers could be isolated by column chromatography. Structure assignment [5, 6] has been performed based on different chemical shifts of C-2, C-6 triplets — a manifestation of the bent structure of *IX*. *Exo* isomers (*X*, *XII*) and *endo* isomers (*XI*, *XIII*) were formed in 1 : 3 ratio in favour of *exo* isomer. Analogous

results have been observed in cycloadditions of benzonitrile oxide [5, 6], cyanonitrile oxide [16], and methoxycarbonylnitrile oxide [17]. The corresponding *endo* derivatives of *XI*, *XIII* displayed shifted C-2, C-6 signals, the shift being caused by 1,3-diaxial interactions of the substituent R′ (a phenyl or methyl) with C-2 and C-6 (for γ-effect see Experimental). Accordingly for 4-phenyl *exo* derivative (*Xa*) $\delta = 69.63$ ppm (C-2) and $\delta = 66.53$ ppm (C-6), whereas for *endo* derivative (*XIa*) $\delta = 65.60$ ppm (C-2) and $\delta = 63.79$ ppm (C-6).

NMR spectra of furonitrile oxides cycloadducts *Ib*—*Id* were practically identical with those measured for *Ia* cycloadducts. Significant differences were observed only in chemical shift of isoxazoline C-3, since its δ value depended strongly on the substituted furyl substituent. Thus 2-furyl-substituted derivatives displayed the corresponding C-3 singlet at $\delta \approx 150$ ppm, whereas 5-nitro-2--furyl-substituted derivatives and their arylated analogues showed it at $\delta \approx$ ≈ 152—154 ppm. In both cases chemical shifts were smaller than those found for the corresponding phenyl-substituted derivatives ($\delta = 155$—157 ppm).

Experimental

Melting points were determined on a Kofler hot-stage apparatus, NMR spectra were taken with an 80 MHz Tesla model BS 487 C (proton) and Jeol FX-100 (carbon) in hexadeuteriodimethyl sulfoxide (unless otherwise stated) using tetramethylsilane as internal standard. Electronic spectra were measured with a Perkin—Elmer model 323 in methanolic solutions, absorption coefficients are given in $m^2 mol^{-1}$.

Reactions were monitored by TLC and UV spectra measurements. Preparation of starting dipolarophiles has been described earlier [4—6]. Chlorides derived from 2-furohydroximic acid (*IIa*), 5-nitro-2-furohydroximic acid (*IIb*), 5-(4-nitrophenyl)-2--furohydroximic acid (*IIc*), and 5-(3-nitrophenyl)-2-furohydroximic acid (*IId*) were prepared by chlorination of the corresponding oximes with nitrosyl chloride in ether at −20 °C according to [18, 19]. Chloride *IIa* was generated *in situ* and used as ethereal solution.

Isoxazolines IV—XIII

To the ethereal solution of *IIb*—*IId* (0.01 mol) (diethyl ether used for *Ia*, *IIa*, *IIb*, tetrahydrofuran for *IIc* and *IId* (100 cm^3)) and the requisite dipolarophile (0.01—0.05 mol), stirred at −5 to −10 °C triethylamine (0.013 mol) in 50 cm^3 of ether was added during 4 h. The stirred mixture was left to stand overnight, the precipitated triethylammonium chloride removed and the solid residue crystallized from methanol or purified by column chromatography on a silica gel column using chloroform or hexane—ethyl acetate as eluant.

3,4-Dimethoxycarbonyl-7-(2-furyl)-8-aza-9,10-dioxatricyclo[4,3,0,$1^{2,5}$]decane (IVa), yield = 68 %, m.p. = 163—164 °C. For $C_{15}H_{15}NO_7$ (M_r = 321.28) w_i(calc.): 56.07 % C, 4.71 % H, 4.36 % N; w_i(found): 56.23 % C, 4.64 % H, 4.48 % N. UV spectrum, λ_{max}/nm (log{ε}): 276 (3.34). ^{1}H NMR spectrum (d_6-acetone), δ/ppm: 7.66 (d, J = 1.8 Hz, 1H, H-5′), 6.99 (d, J = 3.5 Hz, 1H, H-3′), 6.56 (d, d, 1H, H-4′), 5.00 (d, J = 8.0 Hz, 1H, H-1), 4.97 (s, 2H, H-2, H-5), 4.13 (d, 1H, H-6), 3.57 (s, 6H, 2 × $COOCH_3$), 3.41 (d, J = 9.5 Hz, 1H, H-3), 3.22 (d, 1H, H-4). ^{13}C NMR spectrum, δ/ppm: 206.28 (s, C=O), 171.39, 147.94, 145.67 and 112.72 (furan carbons), 86.60 (d, C-2), 85.30 (d, C-5), 81.15 (d, C-1), 59.12 (q, OCH_3), 52.23 (d, C-3), 50.67 (d, C-4), 47.17 (d, C-6).

3-(2-Furyl)-3a,4,9,9a-tetrahydro-4,9-epoxynaphthaleno[3,2-d]isoxazole (Va), yield = = 88 %, m.p. = 160—161 °C. For $C_{15}H_{11}NO_3$ (M_r = 253.25) w_i(calc.): 71.14 % C, 4.37 % H, 5.53 % N; w_i(found): 71.09 % C, 4.51 % H, 5.28 % N. ^{1}H NMR spectrum, δ/ppm: 7.83 (d, J = 1.8 Hz, 1H, H-5′), 7.12—7.51 (m, 5H, aromatic protons, H-3′), 6.62 (d, d, J = 3.5 Hz, 1H, H-4′), 5.56 (s, 2H, H-4, H-9), 4.95 (d, $J_{3a,9a}$ = 7.0 Hz, 1H, H-9a), 3.97 (d, 1H, H-3a).

3-(2-Furyl)-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (VIa), yield = 45 %, m.p. = = 99—101 °C. For $C_9H_9NO_3$ (M_r = 179.17) w_i(calc.): 60.33 % C, 5.06 % H, 7.82 % N; w_i(found): 60.17 % C, 5.31 % H, 7.79 % N. ^{1}H NMR spectrum (d_6-acetone), δ/ppm: 7.70 (d, J = 1.8 Hz, 1H, H-5′), 6.85 (d, J = 3.5 Hz, 1H, H-3′), 6.60 (d, d, 1H, H-4′), 5.35 (d, d, $J_{3a,6a}$ = 9.0 Hz, $J_{6,6a}$ = 5.0 Hz, 1H, H-6a), 3.58—4.45 (m, 5H, H-3a, H_2-4, H_2-6).

3-(2-Furyl)-3a,4,5,6a-tetrahydrofuro[3,2-d]isoxazole (VIIa), yield = 74 %, m.p. = = 71—73 °C. For $C_9H_9NO_3$ (M_r = 179.17) w_i(calc.): 60.33 % C, 5.06 % H, 7.82 % N; w_i(found): 60.47 % C, 4.98 % H, 7.91 % N. UV spectrum, λ_{max}/nm (log {ε}): 271 (3.38). ^{1}H NMR spectrum (deuteriochloroform), δ/ppm: 7.52 (d, J = 1.8 Hz, 1H, H-5′), 6.80 (d, J = 3.4 Hz, 1H, H-3′), 6.52 (d, d, 1H, H-4′), 6.22 (d, $J_{3a,6a}$ = 6.0 Hz, 1H, H-6a), 3.91 —4.26 (m, 2H, H_2-5), 3.55 (d, d, $J_{3a,4}$ = 16 Hz, 1H, H-3a), 2.12—2.38 (m, 2H, H_2-4). ^{13}C NMR spectrum (deuteriochloroform), δ/ppm: 150.05 (s, C-3), 144.38, 144.56, 112.14, 111.79 (furan carbons), 108.85 (d, C-6a), 66.51 (t, C-5), 52.06 (d, C-3a), 30.53 (t, C-4).

3-(2-Furyl)-3a,4,5,7a-tetrahydro-6H-pyrano[3,2-d]isoxazole (VIIIa), yield = 54 %, m.p. = 61—62 °C. For $C_{10}H_{11}NO_3$ (M_r = 193.2) w_i(calc.): 62.16 % C, 5.74 % H, 7.25 % N; w_i(found): 62.41 % C, 5.88 % H, 7.14 % N. UV spectrum, λ_{max}/nm (log {ε}): 272 (3.23). ^{1}H NMR spectrum (deuteriochloroform), δ/ppm: 7.50 (d, J = 1.8 Hz, 1H, H-5′), 6.80 (d, J = 3.5 Hz, 1H, H-3′), 6.51 (d, d, 1H, H-4′), 5.87 (d, $J_{3a,7a}$ = 8.0 Hz, 1H, H-7a), 3.40—3.80 (m, 2H, H_2-6), 1.25—2.16 (m, 4H, H_2-4, H_2-5). ^{13}C NMR spectrum, δ/ppm: 152.11 (s, C-3), 145.27, 143.98, 112.68, 111.92 (furan carbons), 101.39 (d, C-7a), 58.80 (d, C-3a), 42.95 (t, C-6), 19.25 (t, C-5), 18.61 (t, C-4).

8-(2-Furyl)-3,5,10-trioxa-9-azabicyclo[5,3,0]decane (IXa), yield = 51 %, m.p. = = 100—101 °C. For $C_{10}H_{11}NO_4$ (M_r = 209.20) w_i(calc.): 57.41 % C, 5.30 % H, 6.70 % N; w_i(found): 57.49 % C, 5.05 % H, 6.89 % N. UV spectrum, λ_{max}/nm (log{ε}): 274 (3.22). ^{1}H NMR spectrum, δ/ppm: 7.70 (d, J = 1.8 Hz, 1H, H-5′), 6.85 (d, J = 3.5 Hz, 1H, H-3′), 6.50 (d, d, 1H, H-4′), 4.75 (d, J = 8.0 Hz, 1H, H_A-4), 4.68 (m, 1H, H-1), 4.30 (d, 1H, H_B-4), 3.66—4.28 (m, 5H, H_2-2, H_2-6, H-7). ^{13}C NMR spectrum (d_6-acetone), δ/ppm: 149.89 (s, C-8), 146.32, 145.02, 112.53, 111.68 (furan carbons), 99.41 (t, C-4), 84.33 (d, C-1), 70.75 (t, C-2), 68.41 (t, C-6), 53.47 (d, C-7).

exo-4-Phenyl-8-(2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (Xa), yield =

= 48 %, obtained by chromatography on a column (silica gel, eluant hexane—ethyl acetate, volume ratio 4 : 1), m.p. = 179—181 °C. For $C_{16}H_{15}NO_4$ (M_r = 285.29) w_i(calc.): 67.36 % C, 5.30 % H, 4.91 % N; w_i(found): 67.52 % C, 5.18 % H, 5.04 % N. UV spectrum, λ_{max}/nm (log{ε}): 270 (3.31). ^{1}H NMR spectrum, δ/ppm: 7.72 (d, J = 1.6 Hz, 1H, H-5′), 7.22 (s, 5H, aromatic protons), 6.91 (d, J = 3.4 Hz, 1H, H-3′), 6.53 (d, d, 1H, H-4′), 5.44 (s, 1H, H-4), 4.87 (d, $J_{1,7}$ = 11.0 Hz, 1H, H-1), 3.87—4.56 (m, 5H, H_2-2, H_2-6, H-7). ^{13}C NMR spectrum, δ/ppm: 144.93, 129.02, 128.61, 127.03, 112.40, 110.45 (aromatic and furan carbons), 107.02 (d, C-4), 84.09 (d, C-1), 69.63 (t, C-2), 66.53 (t, C-6), 52.96 (d, C-7).

endo-4-Phenyl-8-(2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (XIa), yield = = 16 %, isolated as compound *Xa*, m.p. = 121—123 °C. For $C_{16}H_{15}NO_4$ (M_r = 285.29) w_i(calc.): 67.36 % C, 5.30 % H, 4.91 % N; w_i(found): 67.44 % C, 5.22 % H, 5.09 % N. UV spectrum, λ_{max}/nm (log{ε}): 274 (3.31). ^{1}H NMR spectrum, δ/ppm: 7.71 (d, J = 1.8 Hz, 1H, H-5′), 7.28—7.50 (m, 5H, aromatic protons), 5.70 (d, J = 3.5 Hz, 1H, H-3′), 6.56 (d, d, 1H, H-4′), 5.73 (s, 1H, H-4), 4.87 (m, 1H, H-1), 4.00—4.37 (m, 5H, H_2-2, H_2-6, H-7). ^{13}C NMR spectrum, δ/ppm: 145.58, 139.49, 129.19, 128.84, 127.09, 112.87, 112.64 (aromatic and furan carbons), 104.80 (d, C-4), 84.26 (d, C-1), 65.60 (t, C-2), 63.79 (t, C-6), 52.55 (d, C-7).

exo-4-Methyl-8-(2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (XIIa), yield = = 41 %, obtained by column chromatography (silica gel, eluant hexane—ethyl acetate, volume ratio 4 : 1), m.p. = 109—111 °C. For $C_{11}H_{13}NO_4$ (M_r = 223.22) w_i(calc.): 59.18 % C, 5.87 % H, 6.28 % N; w_i(found): 59.31 % C, 5.71 % H, 6.16 % N. UV spectrum, λ_{max}/nm (log{ε}): 274 (3.37). ^{1}H NMR spectrum (deuteriochloroform), δ/ppm: 7.51 (d, J = 1.0 Hz, 1H, H-5′), 6.78 (d, J = 3.5 Hz, 1H, H-3′), 6.48 (d, d, 1H, H-4′), 5.32 (q, 1H, H-4), 4.82 (d, $J_{1,7}$ = 11.0 Hz, 1H, H-1), 3.30—4.63 (m, 5H, H_2-2, H_2-6, H-7), 1.22 (d, J = 4.0 Hz, 3H, CH_3).

endo-4-Methyl-8-(2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (XIIIa), yield = = 13 %, isolated as compound *XIIa*, m.p. = 92—94 °C. For $C_{11}H_{13}NO_4$ (M_r = 223.22) w_i(calc.): 59.18 % C, 5.87 % H, 6.28 % N; w_i(found): 59.33 % C, 6.03 % H, 6.14 % N. UV spectrum, λ_{max}/nm (log{ε}): 275 (3.29). ^{1}H NMR spectrum (deuteriochloroform), δ/ppm: 7.52 (d, J = 1.6 Hz, 1H, H-5′), 6.75 (d, J = 3.5 Hz, 1H, H-3′), 6.48 (d, d, 1H, H-4′), 5.33 (q, 1H, H-4), 4.87 (d, d, $J_{1,7}$ = 10.0 Hz, $J_{1,2}$ = 6.0 Hz, 1H, H-1), 3.62—4.35 (m, 5H, H_2-2, H_2-6, H-7), 1.33 (d, J = 5.0 Hz, 3H, CH_3).

3,4-Dimethoxycarbonyl-7-(5-nitro-2-furyl)-8-aza-9,10-dioxatricyclo[4.3,0,1^{2,5}]decane (IVb), yield = 81 %, m.p. = 191—192 °C. For $C_{15}H_{14}N_2O_9$ (M_r = 366.28) w_i(calc.): 49.18 % C, 3.85 % H, 7.65 % N; w_i(found): 49.41 % C, 4.07 % H, 7.39 % N. UV spectrum, λ_{max}/nm (log{ε}): 251 (2.97), 342 (3.22). ^{1}H NMR spectrum, δ/ppm: 7.76 (d, J = 3.5 Hz, 1H, H-4′), 7.45 (d, 1H, H-3′), 5.07 (d, $J_{1,6}$ = 8.0 Hz, 1H, H-1), 4.88 (s, 1H, H-2), 4.83 (s, 1H, H-5), 4.07 (d, 1H, H-6), 3.50 (s, 6H, 2 × $COOCH_3$), 3.30 (m, 2H, H-3, H-4). ^{13}C NMR spectrum, δ/ppm: 170.54 (s, C=O), 170.42 (s, C=O), 152.17 (s, C-7), 146.67, 145.74, 115.78, 114.14 (furan carbons), 86.71 (d, C-1), 83.66 (d, C-2), 79.57 (d, C-5), 56.58 (d, C-6), 51.72 (q, CH_3), 49.09 (d, C-3), 45.64 (d, C-4).

3-(5-Nitro-2-furyl)-3a,4,9,9a-tetrahydro-4,9-epoxynaphthaleno[3,2-d]isoxazole (Vb), yield = 89 %, m.p. = 212—213 °C. For $C_{15}H_{10}N_2O_5$ (M_r = 298.25) w_i(calc.): 60.40 % C, 3.38 % H, 9.39 % N; w_i(found): 60.28 % C, 3.51 % H, 9.12 % N. UV spectrum, λ_{max}/nm

(log{ε}): 345 (3.16). ^{1}H NMR spectrum, δ/ppm: 7.81 (d, J = 3.5 Hz, 1H, H-4′), 7.54 (d, 1H, H-3′), 7.13—7.46 (m, 4H, aromatic protons), 5.64 (s, 2H, H-4, H-9), 5.12 (d, $J_{3a,9a}$ = 8.0 Hz, 1H, H-9a), 4.07 (d, 1H, H-3a).

3-(5-Nitro-2-furyl)-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (VIb), yield = 65 %, m.p. = 173—174 °C. For $C_9H_8N_2O_5$ (M_r = 224.17) w_i(calc.): 48.22 % C, 3.60 % H, 12.50 % N; w_i(found): 48.44 % C, 3.71 % H, 12.33 % N. UV spectrum, λ_{max}/nm (log{ε}): 248 (2.92), 342 (3.14). ^{1}H NMR spectrum, δ/ppm: 7.73 (d, J = 3.5 Hz, 1H, H-4′), 7.25 (d, 1H, H-3′), 5.40 (d, d, $J_{3a,6a}$ = 8.0 Hz, $J_{6,6a}$ = 6.0 Hz, 1H, H-6a), 3.47—4.45 (m, 5H, H_2-6, H_2-4, H-3a). ^{13}C NMR spectrum, δ/ppm: 153.46 (s, C-3), 149.57, 147.88, 114.6, 114.09 (furan carbons), 88.62 (d, C-6a), 76.41 (t, C-6), 72.25 (t, C-4), 54.05 (d, C-3a).

3-(5-Nitro-2-furyl)-3a,4,5,6a-tetrahydrofuro[3,2-d]isoxazole (VIIb), yield = 71 %, m.p. = 166—167 °C. For $C_9H_8N_2O_5$ (M_r = 224.17) w_i(calc.): 48.22 % C, 3.60 % H, 12.50 % N; w_i(found): 48.09 % C, 3.87 % H, 12.39 % N. UV spectrum, λ_{max}/nm (log{ε}): 236 (3.02), 337 (3.20). ^{1}H NMR spectrum, δ/ppm: 7.80 (d, J = 3.5 Hz, 1H, H-4′), 7.35 (d, 1H, H-3′), 6.35 (d, $J_{3a,6a}$ = 7.5 Hz, 1H, H-6a), 3.35—4.45 (m, 3H, H_2-5, H-3a), 2.03—2.30 (m, 2H, H_2-4). ^{13}C NMR spectrum, δ/ppm: 152.00 (s, C-3), 149.66, 146.09, 115.37, 114.09 (furan carbons), 109.82 (d, C-6a), 66.35 (t, C-5), 50.67 (d, C-3a), 29.96 (t, C-4).

3-(5-Nitro-2-furyl)-3a,4,5,7a-tetrahydro-6H-pyrano[3,2-d]isoxazole (VIIIb), yield = 47 %, m.p. = 117—118 °C. For $C_{10}H_{10}N_2O_5$ (M_r = 238.20) w_i(calc.): 50.42 % C, 4.23 % H, 11.76 % N; w_i(found): 50.49 % C, 4.11 % H, 11.99 % N. UV spectrum, λ_{max}/nm (log{ε}): 235 (3.02), 337 (3.23). ^{1}H NMR spectrum, δ/ppm: 7.75 (d, J = 3.5 Hz, 1H, H-3′), 7.32 (d, 1H, H-4′), 5.98 (d, $J_{3a,7a}$ = 8.0 Hz, 1H, H-7a), 3.50—3.75 (m, 2H, H_2-6), 1.15—2.07 (m, 4H, H_2-4, H_2-5).

8-(5-Nitro-2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (IXb), yield = 73 %, m.p. = 168—169 °C. For $C_{10}H_{10}N_2O_6$ (M_r = 254.20) w_i(calc.): 47.25 % C, 3.97 % H, 11.02 % N; w_i(found): 47.42 % C, 4.15 % H, 10.91 % N. UV spectrum, λ_{max}/nm (log{ε}): 257 (2.95), 345 (3.23). ^{1}H NMR spectrum (d_6-acetone), δ/ppm: 7.60 (d, J = 3.5 Hz, 1H, H-4′), 7.20 (d, 1H, H-3′), 5.06 (d, $J_{1,7}$ = 11.0 Hz, 1H, H-1), 4.90 (d, J = 6.0 Hz, 1H, H_A-4), 3.87—4.69 (m, 6H, H_2-2, H-4, H_2-6, H-7). ^{13}C NMR spectrum, δ/ppm: 152.72 (s, C-8), 148.80, 148.10, 113.8, 113.51 (furan carbons), 99.23 (t, C-4), 85.43 (d, C-1), 71.21 (t, C-2), 67.82 (t, C-6), 52.31 (d, C-7).

exo-4-Phenyl-8-(5-nitro-2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (Xb), yield = 45 %, obtained by column chromatography (silica gel, eluant chloroform), m.p. = 173—175 °C. For $C_{16}H_{14}N_2O_6$ (M_r = 330.29) w_i(calc.): 58.18 % C, 4.27 % H, 8.48 % N; w_i(found): 58.33 % C, 4.17 % H, 8.21 % N. UV spectrum, λ_{max}/nm (log{ε}): 339 (2.86). ^{1}H NMR spectrum, δ/ppm: 7.76 (d, J = 3.5 Hz, 1H, H-4′), 7.33 (d, 1H, H-3′), 7.25 (s, 5H, aromatic protons), 5.46 (s, 1H, H-4), 5.05 (d, $J_{1,7}$ = 11.0 Hz, 1H, H-1), 4.01—4.62 (m, 5H, H_2-2, H_2-6, H-7).

endo-4-Phenyl-8-(5-nitro-2-furyl)-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (XIb), yield = 15 %, isolated as derivative *Xb*, m.p. = 233—234 °C. For $C_{16}H_{14}N_2O_6$ (M_r = 330.29) w_i(calc.): 58.18 % C, 4.27 % H, 8.48 % N; w_i(found): 58.09 % C, 4.11 % H, 8.66 % N. UV spectrum, λ_{max}/nm (log{ε}): 341 (2.86). ^{1}H NMR spectrum, δ/ppm: 7.65 (d, J = 3.5 Hz, 1H, H-4′), 7.32 (d, 1H, H-3′), 7.25—7.92 (m, 5H, aromatic protons), 5.72 (s, 1H, H-4), 4.95 (d, d, 1H, H-1), 3.92—4.30 (m, 5H, H_2-2, H_2-6, H-7).

3,4-Dimethoxycarbonyl-7-[5-(4-nitrophenyl)-2-furyl]-8-aza-9,10-dioxatricyclo[4,3,0,

$I^{2,5}$]decane (IVc), yield = 89 %, m.p. = 208—210 °C. For $C_{21}H_{18}N_2O_9$ (M_r = 442.37) w_i(calc.): 57.01 % C, 4.10 % H, 6.33 % N; w_i(found): 57.19 % C, 4.01 % H, 6.57 % N. UV spectrum, λ_{max}/nm (log{ε}): 365 (3.45). ^{1}H NMR spectrum, δ/ppm: 7.87—8.32 (d, d, 4H, aromatic protons), 7.43 and 7.27 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 5.00 (d, $J_{1,6}$ = 8.0 Hz, 1H, H-1), 4.86 (s, 2H, H-2, H-5), 4.08 (d, 1H, H-6), 3.53 (s, 6H, 2 × $COOCH_3$), 3.35 (m, 2H, H-3, H-4).

3-[5-(4-Nitrophenyl)-2-furyl]-3a,4,9,9a-tetrahydro-4,9-epoxynaphthaleno[3,2-d]isoxazole (Vc), yield = 92 %, m.p. = 224—226 °C. For $C_{21}H_{14}N_2O_5$ (M_r = 374.34) w_i(calc.): 67.37 % C, 3.77 % H, 7.48 % N; w_i(found): 67.41 % C, 3.98 % H, 7.24 % N. UV spectrum, λ_{max}/nm (log{ε}): 272 (3.07), 366 (3.36). ^{1}H NMR spectrum, δ/ppm: 7.90—8.29 (m, 4H, aromatic protons), 7.12—7.57 (m, 4H, aromatic protons), 5.61 (s, 1H, H-9), 5.57 (s, 1H, H-4), 4.97 (d, $J_{3a,9a}$ = 7.5 Hz, 1H, H-9a), 4.02 (d, 1H, H-3a).

3-[5-(4-Nitrophenyl)-2-furyl]-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (VIc), yield = 79 %, m.p. = 231—232 °C. For $C_{15}H_{12}N_2O_5$ (M_r = 300.26) w_i(calc.): 60.00 % C, 4.03 % H, 9.33 % N; w_i(found): 60.29 % C, 3.97 % H, 9.14 % N. UV spectrum, λ_{max}/nm (log{ε}): 258 (3.47), 360 (3.22). ^{1}H NMR spectrum, δ/ppm: 8.25 (d, 2H, aromatic protons), 7.92 (d, 2H, aromatic protons), 7.37 and 7.07 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 5.37 (d, d, $J_{6,6a}$ = 10.0 Hz, $J_{3a,6a}$ = 5.0 Hz, 1H, H-6a), 3.55—4.47 (m, 5H, H-3a, H_2-4, H_2-6).

3-[5-(4-Nitrophenyl)-2-furyl]-3a,4,5,6a-tetrahydrofuro[3,2-d]isoxazole (VIIc), yield = 85 %, m.p. = 163—166 °C. For $C_{15}H_{12}N_2O_5$ (M_r = 300.26) w_i(calc.): 60.00 % C, 4.03 % H, 9.33 % N; w_i(found): 59.85 % C, 3.84 % H, 9.44 % N. UV spectrum, λ_{max}/nm (log{ε}): 362 (3.41). ^{1}H NMR spectrum, δ/ppm: 8.25 and 7.94 (d, d, 2H, 2H, aromatic protons), 7.43 and 7.15 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 6.31 (d, $J_{3a,6a}$ = 6.0 Hz, 1H, H-6a), 3.87—4.42 (m, 3H, H_2-5, H-3a), 2.12—2.42 (m, 2H, H_2-4). ^{13}C NMR spectrum, δ/ppm: 152.58 (s, C-3), 149.89, 146.50, 115.67, 111.98 (furan carbons), 145.27, 134.91, 124.68, 124.50 (aromatic carbons), 108.88 (d, C-6a), 66.17 (t, C-5), 51.31 (d, C-3a), 30.37 (t, C-4).

3-[5-(4-Nitrophenyl)-2-furyl]-3a,4,5,7a-tetrahydro-6H-pyrano[3,2-d]isoxazole (VIIIc), yield = 67 %, m.p. = 124—125 °C. For $C_{16}H_{14}N_2O_5$ (M_r = 314.29) w_i(calc.): 61.14 % C, 4.49 % H, 8.91 % N; w_i(found): 61.37 % C, 4.28 % H, 9.12 % N. UV spectrum, λ_{max}/nm (log{ε}): 262.81 (2.99), 355 (3.01). ^{1}H NMR spectrum, δ/ppm: 8.25 and 7.93 (d, d, 2H, 2H, aromatic protons), 7.42 and 7.17 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 5.92 (d, $J_{3a,7a}$ = 7.5 Hz, 1H, H-7a), 3.45—3.75 (m, 3H, H_2-6, H-3a), 1.30—2.15 (m, 4H, H_2-4, H_2-5). ^{13}C NMR spectrum, δ/ppm: 152.41 (s, C-3), 146.38, 145.39, 115.08, 111.87 (furan carbons), 151.94, 134.86, 124.56, 124.39 (aromatic carbons), 101.80 (d, C-7a), 58.86 (d, C-3a), 42.65 (t, C-6), 19.19 (t, C-5), 18.61 (t, C-4).

8-[5-(4-Nitrophenyl)-2-furyl]-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (IXc), yield = 74 %, m.p. = 173—175 °C. For $C_{16}H_{14}N_2O_6$ (M_r = 330.29) w_i(calc.): 58.18 % C, 4.27 % H, 8.48 % N; w_i(found): 58.29 % C, 4.17 % H, 8.26 % N. UV spectrum, λ_{max}/nm (log{ε}): 284 (3.05), 366 (3.44). ^{1}H NMR spectrum, δ/ppm: 8.27 and 7.92 (d, d, 2H, 2H, aromatic protons), 7.41 and 7.12 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 4.92 (d, $J_{1,7}$ = 6.5 Hz, 1H, H-1), 4.85 (d, J = 6.5 Hz, 1H, H_A-4), 3.75—4.61 (m, 6H, H_2-2, H_B-4, H_2-6, H-7).

exo-4-Phenyl-8-[5-(4-nitrophenyl)-2-furyl]-9-aza-3,5,10-trioxabicyclo[5,3,0]decane

(Xc), yield = 37 %, m.p. = 240—241 °C. For $C_{22}H_{18}N_2O_6$ (M_r = 406.38) w_i(calc.): 65.02 % C, 4.46 % H, 6.89 % N; w_i(found): 65.18 % C, 4.31 % H, 7.00 % N. UV spectrum, λ_{max}/nm (log{ε}): 267 (3.24), 360 (3.22). ^{1}H NMR spectrum, δ/ppm: 7.87—8.35 (m, 4H, aromatic protons), 7.65 and 7.42 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 7.26 (s, 5H, aromatic protons), 5.49 (s, 1H, H-4), 3.75—5.05 (m, 6H, H-1, H_2-2, H_2-6, H-7).

endo-4-Phenyl-8-[5-(4-nitrophenyl)-2-furyl]-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (XIc), yield = 22 %, obtained from concentrated mother liquor after filtration of *Xc*, m.p. = 195—197 °C. For $C_{22}H_{18}N_2O_6$ (M_r = 406.38) w_i(calc.): 65.02 % C, 4.46 % H, 6.89 % N; w_i(found): 64.88 % C, 4.71 % H, 6.82 % N. UV spectrum, λ_{max}/nm (log{ε}): 3.63 (2.78). ^{1}H NMR spectrum, δ/ppm: 8.32 and 7.98 (d, d, 2H, 2H, aromatic protons), 7.41 and 7.28 (d, d, J = 3.2 Hz, 1H, 1H, H-3′, H-4′), 7.40 (s, 5H, aromatic protons), 5.77 (s, 1H, H-4), 4.05—5.00 (m, 6H, H-1, H_2-2, H_2-6, H-7).

3,4-Dimethoxycarbonyl-7-[5-(3-nitrophenyl)-2-furyl]-8-aza-9,10-dioxatricyclo[4,3,0,$1^{2,5}$]decane (IVd), yield = 91 %, m.p. = 152—154 °C. For $C_{21}H_{18}N_2O_9$ (M_r = 442.37) w_i(calc.): 57.01 % C, 4.10 % H, 6.33 % N; w_i(found): 56.89 % C, 4.17 % H, 6.22 % N. UV spectrum, λ_{max}/nm (log{ε}): 318 (3.50). ^{1}H NMR spectrum, δ/ppm: 7.67—8.41 (m, 4H, aromatic protons), 7.40 and 7.25 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 4.98 (d, $J_{1,6}$ = 8.0 Hz, 1H, H-1), 4.85 (s, 2H, H-2, H-5), 4.07 (d, 1H, H-6), 3.52 (s, 6H, 2 × $COOCH_3$), 3.31 (m, 2H, H-3, H-4). ^{13}C NMR spectrum, δ/ppm: 170.54 (s, C=O), 152.52 (s, C-7), 146.73, 144.22, 115.84, 118.09 (furan carbons), 148.43, 129.94, 122.63, 110.28 (aromatic carbons), 85.42 (d, C-1), 83.84 (d, C-2), 79.86 (d, C-5), 57.34 (d, C-6), 51.72 (q, CH_3), 49.15 (d, C-3), 45.64 (d, C-4).

3-[5-(3-Nitrophenyl)-2-furyl]-3a,4,9,9a-tetrahydro-4,9-epoxynaphthaleno[3,2-d]isoxazole (Vd), yield = 93 %, m.p. = 221—223 °C. For $C_{21}H_{14}N_2O_5$ (M_r = 374.34) w_i(calc.): 67.37 % C, 3.77 % H, 7.48 % N; w_i(found): 67.52 % C, 3.99 % H, 7.31 % N. UV spectrum, λ_{max}/nm (log{ε}): 319 (2.99). ^{1}H NMR spectrum, δ/ppm: 7.27—8.48 (m, 8H, aromatic protons), 5.65 (s, 1H, H-9), 5.61 (s, 1H, H-4), 5.0 (d, $J_{3a,9a}$ = 8.0 Hz, 1H, H-9a), 4.05 (d, 1H, H-3a).

8-[5-(3-Nitrophenyl)-2-furyl]-9-aza-3,5,10-trioxabicyclo[5,3,0]decane (IXd), yield = 86 %, m.p. = 192—194 °C. For $C_{16}H_{14}N_2O_6$ (M_r = 330.29) w_i(calc.): 58.18 % C, 4.27 % H, 8.48 % N; w_i(found): 58.24 % C, 4.12 % H, 8.38 % N. UV spectrum, λ_{max}/nm (log{ε}): 245 (3.12), 317 (3.47). ^{1}H NMR spectrum, δ/ppm: 7.55—8.39 (m, 4H, aromatic protons), 7.27 and 7.02 (d, d, J = 3.5 Hz, 1H, 1H, H-3′, H-4′), 4.90 (m, 2H, H-1, H_A-4), 3.77—4.50 (m, 6H, H_2-2, H_B-4, H_2-6, H-7). ^{13}C NMR spectrum, δ/ppm: 151.70 (s, C-8), 148.49, 144.92, 117.95, 114.03 (furan carbons), 130.76, 129.82, 122.45, 110.22 (aromatic carbons), 98.06 (t, C-4), 83.20 (d, C-1), 70.27 (t, C-2), 67.63 (t, C-6), 51.66 (d, C-7).

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