Photochemistry of heterocycles XVI.* Preparation and photochemistry of derivatives of 3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazole

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Preparation and photochemistry of isoxazolines fused pyrrolidine derivatives is described. The title compounds were prepared by 1,3-dipolar cycloaddition of the substituted benzenenitrile oxides on *N*-phenyl-3-pyrroline, *N*-benzyl-3-pyrroline, and *N*-phenyl-2,5-dioxo-3-pyrroline. Whereas structures with the pyrrolidine ring were photolabile, those having maleinimide moiety underwent methanolysis when irradiated in methanol, followed by the photolysis of the primary products to enamino aldehydes. The methanolysis was studied, its outcome was found to depend on reaction conditions. Reduction of the maleinimide derivative with $NaBH_4$ proceeded selectively.

Описано получение и фотохимические превращения пирролидиновых производных, конденсированных с изоксазолинами. Заглавные соединения были синтезированы посредством 1,3-диполярного циклоприсоединения замещенных окисей бензонитрила к *N*-фенил-3-пирролину, *N*-бензил-3-пирролину и *N*-фенил-2,5-диоксо-3-пирролину. В то время, как соединения, включающие пирролидиновое кольцо, были фотолабильны, соединения, содержащие малеинимидную часть, подвергались метанолизу при облучении в растворе метанола, а затем первичные продукты фотолитически превращались в енаминоальдегиды. При изучении метанолиза было обнаружено, что его выход зависит от условий реакции. Восстановление малеинимидного производного с $NaBH_4$ проходило селективно.

There has been a surge of interest in photochemistry of isoxazolines recently [1—9]. After the N · · O biradical has been formed in the primary photochemi-

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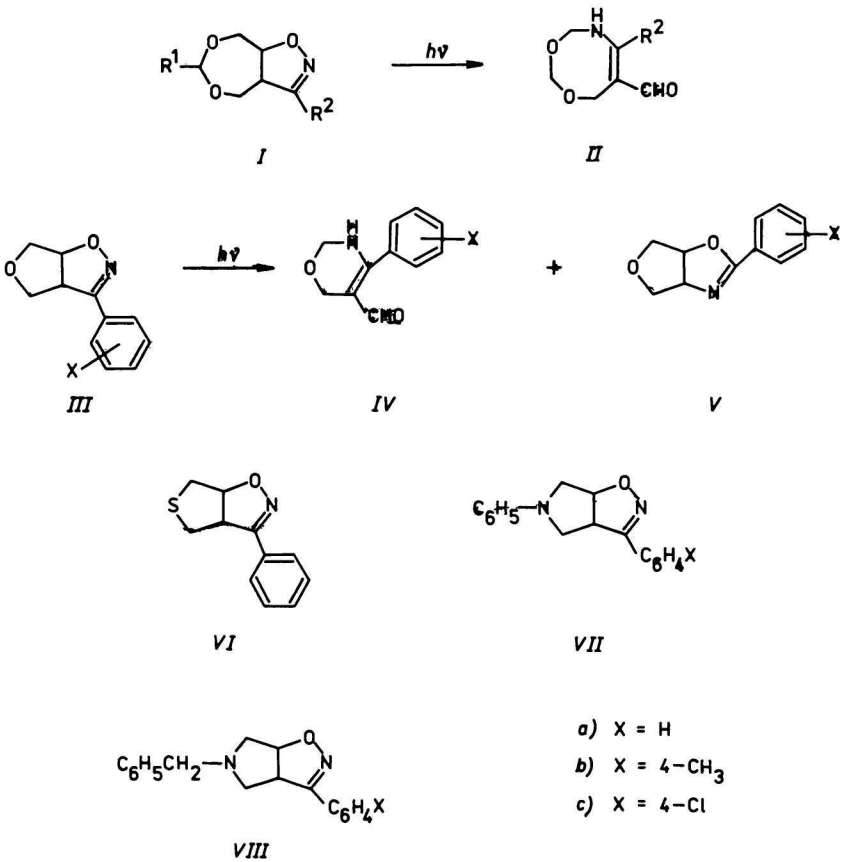
cal step, its fate varies widely, depending on the structural features. The outcome of the irradiation is thus usually a nonselective formation of a mixture of products, *e.g.* oxazolines [1—6, 8], β-aminochalcones [1—3, 6, 8], 1,3-oxàzepines [6], cyclic enamino aldehydes [6, 7], [2 + 2] cycloadducts on the C=N bond [8, 9], as well as products resulting from hydrogen abstraction [9]. We have discovered [10—20] the stabilizing effect of the heteroatom, particularly of oxygen in β-position with respect to the oxygen of isoxazoline ring, on the primary biradical, enabling it to rearrange selectively to cyclic enamino aldehydes, $I \xrightarrow{h\nu} II$ [10—12] and $III \xrightarrow{h\nu} IV$ [13—16], as well as to noncyclic enamino aldehydes [17, 18]. Experiments with other potential stabilizers, such as sulfur atoms [19], or oxygens in α-position [19], or a carbonyl group in the abutting skeleton [20] led to photolabile products. This paper examines the role of nitrogen atom in the photochemistry of fused isoxazolines.



Scheme 1

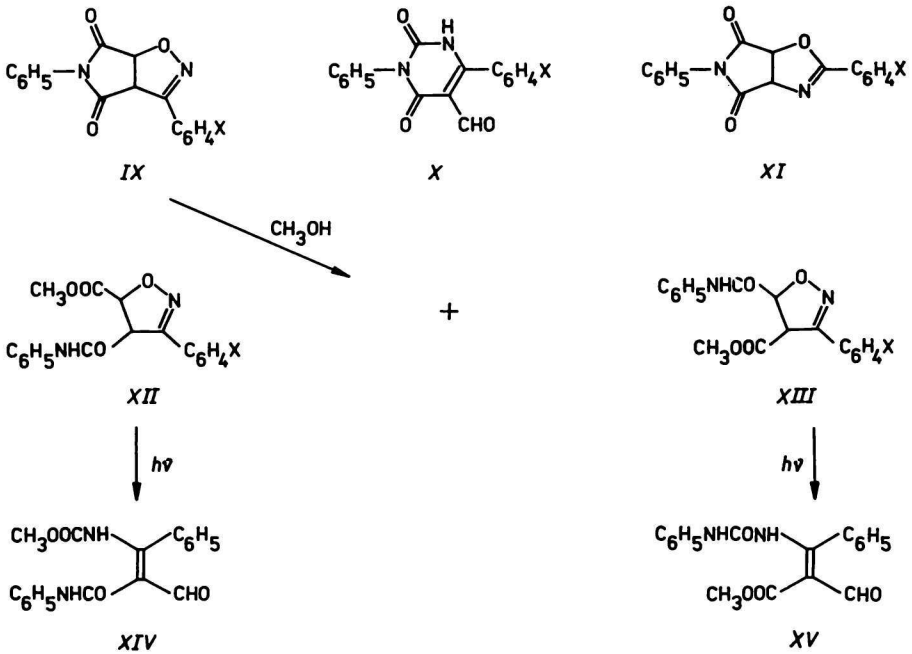
Isoxazolines fused with tetrahydropyrrole ring were prepared *via* 1,3-dipolar cycloaddition of substituted benzenenitrile oxides on *N*-phenyl-3-pyrroline (derivatives *VII*), *N*-benzyl-3-pyrroline (derivatives *VIII*), and *N*-phenyl-2,5-dioxo--3-pyrroline (derivatives *IX*). The requisite nitrile oxides had to be prepared by classical route from hydroximoyl chlorides and triethylamine [21], since the newer method starting from benzaldoximes directly [22] could not be used, although in case of 2,5-dihydrofuran derivatives it worked well [15—20]. Instead of the expected cycloaddition the hypochlorite attacked the 3-pyrroline at the double bond, just as it did with the 2,3-dihydrofuran [19]. Both heterocycles possess higher Π-electron density at the double bond than 2,5-dihydrofuran, and instead of cycloaddition add chlorine. Structures of the tentative 3a,4,6,6a--tetrahydropyrrolo[3,4-*d*]isoxazoles were confirmed by spectral data. Thus ^{1}H NMR spectrum of 3,5-diphenyl-3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazole (*VIIIa*) displayed typical signal of the bridge protons (doublet of doublets) at $\delta = 5.42$ ppm (H-6a) with coupling constant $J(3a,6a) = 9.0$ Hz, characteristic of the *cis* arrangement in addition to the multiplet at $\delta = 4.24$—4.50 ppm of the H-3a proton. ^{13}C NMR spectrum showed doublets of C-6a and C-3a carbons at $\delta = 84.92$ ppm and 51.58 ppm, respectively, different triplets of C-6 ($\delta = 56.65$ ppm) and C-4 ($\delta = 52.36$ ppm) due to the influence of the adjacent oxygen, asserting itself in the bent structure of the bicyclic *VII*. Analogical spectra possessed the 4-methylphenyl- (*VIIb*) and 4-chlorophenyl-substituted derivative (*VIIc*). Compared with 2,5-dihydrofuran *N*-phenyl-3-pyrroline gave much lower yields; 38 % of *VIIa*, 28 % of *VIIb*, and 40 % of *VIIc*. Main products were the dimers of nitrile oxides. In the same pattern reacted also 9-anthracenenitrile oxide, giving yields much lower than with other heterocycles [23]. An interesting feature of the 3-(9-anthryl)-3a,4,6,6a-tetrahydropyrrolo[3,4--*d*]isoxazole (*VIId*) was the identical chemical shift of C-4 and C-6 triplets, indicating a geometry changed on account of the bulky 9-anthryl substituent. Similar reasoning applies for the *N*-benzyl derivatives *VIIIa*, *VIIIb*, where the $\Delta\delta$ for C-4 and C-6 carbon was only 1.5 ppm. In contrast to derivatives with the tetrahydrofuran skeleton (*III*), those with the tetrahydropyrrole ring (*VII*, *VIII*) showed in their NMR spectra upfield shifted both signals of the methylene hydrogens and C-6, C-8 carbons. Surprisingly, this trend was observed even for the bridge carbons C-6a ($\Delta\delta \approx 1.5$ ppm) and C-3a ($\Delta\delta \approx 2$ ppm). Yields of cycloadditions grew progressively higher from *N*-phenyl- to *N*-benzyl--substituted pyrrolines, the highest were those of *N*-phenylmaleinimide (*IXa* — 80 %, *IXb* — 68 %).

Since the typical UV absorption maximum of the prepared isoxazolines appeared at $\lambda \approx 263$ nm, they were irradiated with the light of the low-pressure mercury lamp. As a model derivative for the comparison with the oxygen--containing systems *I* and *III* as well as with other isoxazolines *N*-phenyl-

-substituted 3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazole was chosen. Its UV maximum was blue-shifted by about 10 nm (*VIIa* $\lambda_{max} = 253$ nm, *VIIb* $\lambda_{max} = 256$ nm, *VIIc* $\lambda_{max} = 252$ nm). Beside the isoxazoline chromophore Ar—C= =N—O there is a distinct contribution from the *N*-phenyl chromophore, absent in spectra of *N*-benzyl derivatives *VIII*. For *VIII* UV maxima were the typical isoxazoline chromophore absorption maxima (*VIIIa* $\lambda_{max} = 266$ nm, *VIIIb* $\lambda_{max} = 267$ nm). Monitoring of the photochemical reaction of *N*-phenyl derivatives *VIIa*—*VIIc* by LC method revealed the formation of short-lived photolabile intermediates. This finding was corroborated by UV spectral monitoring as well, the photochemistry was in this case done at concentrations 5×10^{-5} mol dm^{-3} The depletion of the starting material was clearly visible, although there was no UV maximum at $\lambda \approx 310$ nm, indicative of the presence of enamino aldehydes, analogical to those found during the irradiation of the derivatives *I* and *III*. Despite wide variation of irradiation conditions (acetonitrile, benzene, methanol) with or without the presence of oxygen only intractable tarry material was formed. The clue to this behaviour may lie in the fact that the *N*-phenyl chromophore absorbs the excitation energy, leading in effect to the destructive photochemistry of an aniline derivative. The decomposition pattern was more complicated though, for *N*-benzyl derivatives produced tars as well. Monitoring of the irradiation of *VIIIb* at the concentration 5×10^{-4} mol dm^{-3} by UV spectra revealed the formation of two new maxima at 235 nm and 340 nm, belonging to the presumable unstable intermediate, never isolated in preparative experiments. Quantum yields (Φ) were determined from the decreasing concentration of the starting material, being 0.011 for *VIIa*, 0.012 for *VIIc*. In *N*-benzyl series *VIIIa* had $\Phi = 0.099$, *VIIIb* $\Phi = 0.046$. These values are comparable to those of the oxygen analogues ($\Phi = 0.08$ for *IIIa*) and higher than those of *N*-phenyl derivatives.

Next the photochemistry of 4,6-dioxo-3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazole system *IX* was studied. The skeleton was chosen as a potential precursor of uracil or tetrahydropyrrolooxazole derivatives, both not readily accessible. Irradiation of *IXa* in methanol produced two regioisomeric pairs, containing an additional methoxycarbonyl group, excluding structures *X*, *XI*. They were assigned the structure of 3-phenyl-4-phenylcarbamoyl-5-methoxycarbonylisoxazoline *XIIa* and the regioisomeric 3-phenyl-4-methoxycarbonyl-5-phenylcarbamoylisoxazoline *XIIIa*. Structure assignment was done from spectral data (see Experimental). Compound with the higher value of chemical shift of H-5 proton was assigned structure *XII*. Both isoxazolines arised without the action of light, as proved by independent methanolysis of *IXa*. At room temperature *XIIa* and *XIIIa* were formed in 5 : 3 mass ratio, which changed to 1 : 8 at 65 °C and to 4 : 3 in acid-catalyzed methanolysis. Methanolysis of *IXb* at room temperature produced only *XIIb*, at 65 °C the mass ratio of *XIIb* to *XIIIb*

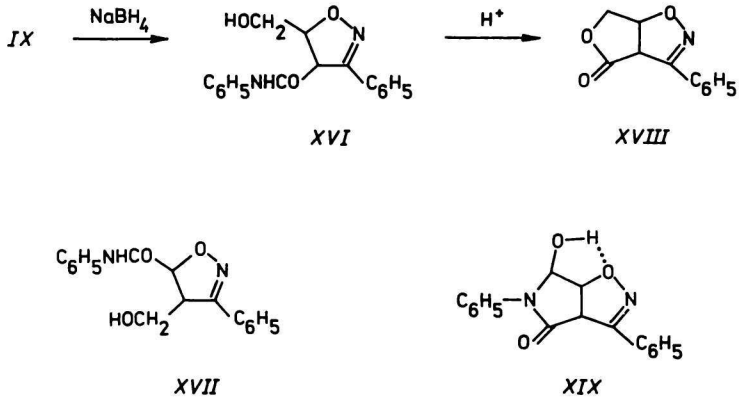
was 1:6. Another two products *XIV* and *XV* formed during the irradiation displayed very simple ^{1}H NMR spectrum, consisting of an aldehydic singlet and singlets of methoxycarbonyl groups at $\delta = 8.61$ ppm and 3.57 ppm, m.p. = = 175—177 °C (*XIV*) and at $\delta = 8.47$ ppm and 3.68 ppm, m.p. = 215—218 °C (*XV*). Independent experiment showed that they were the products of photorearrangement of *XII* and *XIII* respectively, proceeding with different quantum yields (0.018 for *XIIb* and 0.006 for *XIIIb*), measured from the waning concentration of the starting material in methanol. Irradiation of *IXa*, *IXb* performed in solvents other than benzene and acetonitrile led to tars.



Scheme 2

As can be seen from the experimental data, the reaction of *IX* with methanol is nonselective, being dependent on temperature and catalysis. When reducing *IX* with $NaBH_4$ two isomers, *XVI* and *XVII*, could have been formed, though in fact only one, 3-phenyl-4-phenylcarbamoyl-5-hydroxymethylisoxazoline (*XVI*) was isolated. Its structure was supported by both spectral data and hydrolysis, furnishing 3-phenyl-4-oxo-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazole, identical with the one, prepared already by 1,3-dipolar cycloaddition of benzenenitrile oxide to 5*H*-furan-2-one [20]. Selectivity of reduction can be accounted for by the formation of the hydrogen bond-stabilized hydroxy derivative *XIX*

in the first reaction step. Regioselective reduction of 3-acetoxy-1-(4-trimethylsilyl-3-butyl)-2,5-dioxopyrrole with $NaBH_4$ was recently observed [24].



Scheme 3

Experimental

^1H NMR spectra of the synthesized derivatives were recorded with a Tesla 80 MHz spectrometer, type BS 487 C, ^{13}C NMR spectra with the Jeol JX-60 in deuteriochloroform using tetramethylsilane as internal standard, unless otherwise stated. UV spectra were measured with Perkin—Elmer 323, ε values expressed in $m^2\,mol^{-1}$ Mass spectra were recorded on the MS 902 S spectrometer equipped with the direct inlet system, ionizing energy 70 eV. Melting points are corrected.

Preparative photochemical experiments were performed in a forced circulation 300 cm^3 reactor with quartz sleeve, housing low-pressure Hg lamp Toshiba GL-15, at 25 °C, monitored by TLC or UV spectra recorded on an Optica Milano spectrometer.

Quantum yields were measured according to [25], using monochromatic light $\lambda = 253.7$ nm, at concentrations 5×10^{-5} mol dm^{-3} in methanol up to 20 % conversion of the starting material.

The requisite hydroximoyl chlorides were prepared by the chlorination of the corresponding oximes according to [21], with modified chlorine introduction, using liquid chlorine. *N*-Phenyl-3-pyrroline and *N*-benzyl-3-pyrroline were snythesized by the reaction of aniline or benzylamine with *cis* 1,4-dichloro-2-butene, as described in [26]. Dichlorobutene was obtained from *cis* 2-butene-1,4-diol by the action of thionylchloride. All derivatives were crystallized from dichloromethane — hexane mixture.

3,5-Diphenyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]isoxazole (VIIa)

To a mixture of *N*-phenyl-3-pyrroline (1.45 g; 10 mmol) and benzhydroximoyl chloride (1.55 g; 10 mmol) in 20 cm^3 of dry ether was during an hour added triethylami-

ne (1.3 g; 13 mmol) in 20 cm^3 of dry ether at 0 °C. During the addition triethylammonium chloride and the product started to precipitate. Stirring was continued overnight, crystals separated, washed thoroughly with water, to produce 1 g (38 %) of product, m.p. = 136—138 °C. For $C_{17}H_{16}N_2O$ (M_r = 264.31) w_i(calc.): 77.25 % C, 6.10 % H, 10.60 % N; w_i(found): 77.28 % C, 6.04 % H, 10.40 % N. UV spectrum, λ_{max}/nm (log {ε}): 253 (2.96). ^{1}H NMR spectrum, δ/ppm: 6.57—7.70 (m, 10H, H_{arom}), 5.42 (d, d, J(3a,6a) = 9.0 Hz, 1H, H-6a), 4.24—4.50 (m, 1H, H-3a), 3.30—4.0 (m, 4H, H_2-4, H_2-6). ^{13}C NMR spectrum, δ/ppm: 157.75 (s, C=N), 147.62, 130.14, 129.16, 128.90, 128.58, 126.95, 118.25, 114.09 (C_{arom}), 84.92 (d, C-6a), 56.65 (t, C-6), 52.36 (t, C-4), 51.58 (d, C-3a).

The procedure described above was utilized for the preparation of derivatives *VII—IX*.

3-(4-Methylphenyl)-5-phenyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (VIIb)

Compound prepared in 28 % yield, m.p. = 140—141 °C. For $C_{18}H_{18}N_2O$ (M_r = 278.34) w_i(calc.): 77.67 % C, 6.52 % H, 10.07 % N; w_i(found): 77.70 % C, 6.33 % H, 9.70 % N. UV spectrum, λ_{max}/nm (log {ε}): 256 (3.23). ^{1}H NMR spectrum, δ/ppm: 6.56—7.62 (m, 9H, H_{arom}), 5.40 (m, 1H, H-6a), 4.41 (m, 1H, H-3a), 3.28—3.98 (m, 4H, H_2-4, H_2-6), 2.38 (s, 3H, CH_3). ^{13}C NMR spectrum, δ/ppm: 157.68 (s, C=N), 129.62, 129.10, 126.89, 118.18, 114.02, (C_{arom}), 84.72 (d, C-6a), 56.65 (t, C-6), 52.36 (t, C-4), 51.71 (d, C-3a), 21.44 (q, CH_3).

3-(4-Chlorophenyl)-5-phenyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (VIIc)

Compound prepared in 40 % yield, m.p. = 184—185 °C. For $C_{17}H_{15}N_2OCl$ (M_r = 298.45) w_i(calc.): 68.35 % C, 5.02 % H, 9.38 % N; w_i(found): 68.39 % C, 5.31 % H, 9.50 % N. UV spectrum, λ_{max}/nm (log {ε}): 252 (3.07). ^{1}H NMR spectrum, δ/ppm: 6.60—7.68 (m, 9H, H_{arom}), 5.45 (m, 1H, H-6a), 4.32 (m, 1H, H-3a), 3.30—4.02 (m, 4H, H_2-4, H_2-6). ^{13}C NMR spectrum, δ/ppm: 156.78 (s, C=N), 147.55, 136.11, 129.23, 128.19, 118.44, 114.15 (C_{arom}), 85.17 (d, C-6a), 56.72 (t, C-6), 52.23 (t, C-4), 51.39 (d, C-3a).

3-(9-Anthryl)-5-phenyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (VIId)

The title compound prepared by heating 9-anthracenenitrile oxide and *N*-phenyl-3-pyrroline in benzene for 6 h under reflux. Yield = 30 %, m.p. = 234—236 °C. For $C_{25}H_{20}N_2O$ (M_r = 364.43) w_i(calc.): 82.39 % C, 5.53 % H, 7.69 % N; w_i(found): 82.18 % C, 6.04 % H, 7.66 % N. UV spectrum, λ_{max}/nm (log {ε}): 256 (3.28), 317 (2.36),

333 (2.59), 349 (2.83), 361 (2.96), 371 (2.93). ^{1}H NMR spectrum, δ/ppm: 8.52 (s, 1H, H_{arom}), 6.55—6.90 and 7.12—7.56 (m, 13H, H_{arom}), 5.61 (d, d, J(3a,6a) = 9.0 Hz, 1H, H-6a), 2.71—4.57 (m, H-3a, H_2-4, H_2-6). ^{13}C NMR spectrum, δ/ppm: 156.38 (s, C=N), 147.81 (s, C_{arom}), 131.18, 130.70, 129.10, 128.90, 128.58, 126.89, 125.52, 124.88, 122.17, 118.64, 114.67 (C_{arom}), 83.49 (d, C-6a), 57.56 (t, C-4, C-6), 51.26 (d, C-3a).

3-Phenyl-5-benzyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (VIIIa)

Compound prepared in 33 % yield, m.p. = 68—69 °C. For $C_{18}H_{18}N_2O$ (M_r = 278.34) w_i(calc.): 77.67 % C, 6.52 % H, 10.07 % N; w_i(found): 77.88 % C, 6.61 % H, 10.04 % N. UV spectrum, λ_{max}/nm (log {ε}): 266 (3.03). ^{1}H NMR spectrum, δ/ppm: 7.23—7.70 (m, 10H, H_{arom}), 5.15 (m, 1H, H-6a), 4.11 (m, 1H, H-3a), 3.60 (s, 2H, CH_2), 2.46—3.25 (m, 4H, H_2-4, H_2-6). ^{13}C NMR spectrum, δ/ppm: 157.42 (s, C=N), 138.13, 129.81, 129.29, 128.77, 128.32, 127.15, 126.95, 108.56 (C_{arom}), 85.24 (d, C-6a), 61.85 (t, CH_2), 58.80 (t, C-6), 57.30 (t, C-4), 52.43 (d, C-3a).

3-(4-Methylphenyl)-5-benzyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (VIIIb)

Compound prepared in 71 % yield, m.p. = 79—81 °C. For $C_{19}H_{20}N_2O$ (M_r = 292.37) w_i(calc.): 78.05 % C, 6.90 % H, 9.58 % N; w_i(found): 78.12 % C, 7.04 % H, 9.52 % N. UV spectrum, λ_{max}/nm (log {ε}): 267 (3.16). ^{1}H NMR spectrum, δ/ppm: 7.12—7.73 (m, 9H, H_{arom}), 5.16 (m, 1H, H-6a), 4.13 (m, 1H, H-3a), 3.62 (s, 2H, CH_2), 2.50—3.25 (m, 4H, H_2-4, H_2-6), 2.37 (s, 3H, CH_3). ^{13}C NMR spectrum, δ/ppm: 157.36 (s, C=N), 139.95, 137.87, 129.10, 128.25, 126.17, 108.43 (C_{arom}), 84.85 (d, C-6a), 61.72 (t, CH_2), 58.67 (t, C-6), 57.17 (t, C-4), 52.30 (d, C-3a), 21.37 (q, CH_3).

3-(9-Anthryl)-5-benzyl-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (VIIId)

Compound prepared by procedure described for *VIId*, yield = 70 %, m.p. = 174—176 °C. For $C_{26}H_{22}N_2O$ (M_r = 378.45) w_i(calc.): 82.51 % C, 5.86 % H, 7.40 % N; w_i(found): 82.63 % C, 5.91 % H, 7.54 % N. UV spectrum, λ_{max}/nm (log {ε}): 254 (3.28), 314 (2.32), 331 (2.58), 349 (2.82), 361 (2.97), 370 (2.93). ^{1}H NMR spectrum, δ/ppm: 8.41 (s, 1H, H_{arom}), 6.91—7.46 and 7.86—8.21 (m, 13H, H_{arom}), 5.32 (d, d, d, J(3a,6a) = 10.0 Hz, 1H, H-6a), 4.18 (m, 1H, H-3a), 3.50 (s, 2H, CH_2), 1.93—3.68 (m, 4H, H_2-4, H_2-6). ^{13}C NMR spectrum, δ/ppm: 156.30 (s, C=N), 138.19 (C_{arom}), 131.16, 130.79, 128.77, 128.38, 127.48, 127.10, 126.50, 125.46, 123.26, 116.30 (C_{arom}), 84.14 (d, C-6a), 62.50 (t, CH_2), 58.99 (t, C-6), 57.84 (t, C-4), 56.39 (d, C-3a).

3,5-Diphenyl-4,6-dioxo-3a,4,6,6a-tetrahydropyrrolo[3,4-d]-isoxazole (IXa)

Compound prepared in 80 % yield, m.p. = 172—173 °C. For $C_{17}H_{12}N_2O_3$ (M_r = 292.28) w_i(calc.): 69.85 % C, 4.14 % H, 9.59 % N; w_i(found): 70.03 % C, 4.18 % H, 9.51 % N. UV spectrum, λ_{max}/nm (log {ε}): 261 (3.14). ^{1}H NMR spectrum, δ/ppm: 7.12—7.75 and 7.83—7.95 (m, 10H, H_{arom}), 5.69 (d, J(3a,6a) = 10.0 Hz, 1H, H-6a), 5.31 (d, 1H, H-3a). ^{13}C NMR spectrum, δ/ppm: 171.93 (s, C=O), 170.87 (s, C=O), 153.33 (s, C=N), 131.50, 130.72, 128.90, 128.64, 127.86, 126.82 (C_{arom}), 81.21 (d, C-6a), 55.22 (d, C-5).

3-(4-Methylphenyl)-5-phenyl-4,6-dioxo-3a,4,6,6a-tetrahydropyrrolo-[3,4-d]isoxazole (IXb)

Compound prepared in 68 % yield, m.p. = 177—178 °C. For $C_{18}H_{14}N_2O_3$ (M_r = 306.31) w_i(calc.): 70.58 % C, 4.61 % H, 9.15 % N; w_i(found): 70.43 % C, 4.90 % H, 9.31 % N. ^{1}H NMR spectrum, δ/ppm: 5.90—7.83 (m, 9H, H_{arom}), 5.68 (d, J(3a,6a) = 10.0 Hz, 1H, H-6a), 5.29 (d, 1H, H-3a), 2.30 (s, 3H, CH_3). ^{13}C NMR spectrum, δ/ppm: 171.28 (s, C=O), 168.43 (s, C=O), 154.01 (s, C=N), 138.95, 129.21, 128.56, 126.45, 120.36 (C_{arom}), 86.61 (d, C-6a), 59.08 (d, C-3a), 20.77 (q, CH_3).

3-Phenyl-4-phenylcarbamoyl-5-hydroxymethylisoxazoline (XVI)

To the solution of the adduct *IXa* (1.35 g; 5 mmol) in a mixture of 2-propanol—water (volume ratio = 7.7 : 1.3, 150 cm^3), stirred by magnetic stirrer, $NaBH_4$ (0.85 g; 25 mmol) was added and the reaction mixture was allowed to stand for 24 h at laboratory temperature. Liquid portion of the mixture was then concentrated *in vacuo* and separated on a silica gel column, eluted with hexane—ethyl acetate mixture (volume ratio = 1 : 4). The chromatography yielded 0.5 g (37 %) of *XVI*, m.p. = 177—179 °C. For $C_{17}H_{16}N_2O_3$ (M_r = 296.31) w_i(calc.): 68.90 % C, 5.44 % H, 9.45 % N; w_i(found): 69.09 % C, 5.71 % H, 9.55 % N. ^{1}H NMR spectrum, δ/ppm (deuterated dimethyl sulfoxide): 10.60 and 5.19 (broad singlet, 1H, 1H, OH and NH), 7.23—7.64 (m, 10H, H_{arom}), 4.70 (m, 2H, H-4, H-5), 3.67 (m, 2H, CH_2).

3-Phenyl-4-oxo-3a,4,6,6a-tetrahydrofuro[3,4-d]isoxazole (XVIII)

The title compound was prepared by heating *XVI* (0.1 mmol) in 10 cm^3 of dioxan in the presence of catalytic amount of H_2SO_4 (3 drops) in a glass autoclave at 116 °C for 24 h. Concentrated and chromatographed (silica gel column, hexane—ethyl acetate (volume ratio = 1 : 4)), it gave 85 % of *XVIII*, melting point and spectral data were identical with the compound *XVIII* obtained by 1,3-dipolar cycloaddition of benzenenitrile oxide and 5*H*-furan-2-one [20].

Methanolysis of IXa

Reaction mixture consisting of 1 g of *IXa* in 50 cm^3 of methanol was left to stand overnight. After the workup two compounds could be isolated:

a) 0.5 g (50 %) of 3-phenyl-4-phenylcarbamoyl-5-methoxycarbonylisoxazoline (*XIIa*), m.p. = 163—165 °C. For $C_{18}H_{16}N_2O_4$ (M_r = 324.32) w_i(calc.): 66.66 % C, 4.97 % H, 8.64 % N; w_i(found): 66.51 % C, 5.06 % H, 8.47 % N. ^{1}H NMR spectrum, δ/ppm: 10.71 (s, 1H, NH), 6.92—8.0 (m, 10H, H_{arom}), 5.63 (d, J(3a,6a) = 12.0 Hz, 1H, H-6a), 5.11 (d, 1H, H-3a), 3.52 (s, 3H, CH_3). ^{13}C NMR spectrum, δ/ppm: 167.07 (s, C=O), 165.03 (s, C=O), 155.02 (s, C=N), 138.0, 130.07, 128.64, 127.86, 126.95, 126.30, 123.84, 119.42 (C_{arom}), 81.08 (d, C-6a), 57.43 (d, C-3a), 51.71 (q, CH_3).

b) 0.3 g (30 %) of 3-phenyl-4-methoxycarbonyl-5-phenylcarbamoylisoxazoline (*XIIIa*), m.p. = 115—117 °C. For $C_{18}H_{16}N_2O_4$ (M_r = 324.32) w_i(calc.): 66.66 % C, 4.97 % H, 8.64 % N; w_i(found): 66.93 % C, 4.95 % H, 8.59 % N. ^{1}H NMR spectrum, δ/ppm: 10.37 (s, 1H, NH), 7.02—7.80 (m, 10H, H_{arom}), 5.57 (d, J(3a,6a) = 4.0 Hz, 1H, H-6a), 5.14 (d, 1H, H-3a), 3.63 (s, 3H, CH_3). ^{13}C NMR spectrum, δ/ppm: 168.80 (s, C=O), 166.20 (s, C=O), 154.50 (s, C=N), 138.0, 130.46, 128.77, 128.51, 127.47, 126.95, 123.95, 120.46, 119.04 (C_{arom}), 83.42 (d, C-6a), 55.74 (d, C-3a), 52.75 (q, CH_3).

Methanolysis performed in boiling methanol (10 h) gave *XIIa* and *XIIIa* in the mass ratio of 1 : 8. If under the same conditions sulfuric acid was added as catalyst, the mass ratio changed to 4 : 3.

Methanolysis of IXb

The above-described procedure gave 30 % of 3-(4-methylphenyl)-4-phenylcarbamoyl-5-methoxycarbonylisoxazoline (*XIIb*), m.p. = 185—187 °C. For $C_{19}H_{18}N_2O_4$ (M_r = 338.35) w_i(calc.): 67.44 % C, 5.36 % H, 8.28 % N; w_i(found): 67.66 % C, 5.33 % H, 8.19 % N. ^{1}H NMR spectrum, δ/ppm: 10.66 (s, 1H, NH), 7.0—7.62 (m, 9H, H_{arom}), 5.60 (d, J(3a,6a) = 12.0 Hz, 1H, H-6a), 5.07 (d, 1H, H-3a), 3.53 (s, 3H, OCH_3), 2.25 (s, 3H, CH_3). ^{13}C NMR spectrum, δ/ppm: 168.02 (s, C=O), 165.29 (s, C=O), 155.02 (s, C=N), 140.21, 138.13, 129.29, 128.64, 127.73, 126.30, 125.13, 123.97, 119.55 (C_{arom}), 81.08 (d, C-6a), 57.69 (d, C-3a), 51.84 (q, OCH_3), 20.66 (q, CH_3).

Refluxing of *IXb* in methanol for 10 h gave beside *XIIb* 3-(4-methylphenyl)-4-methoxycarbonylphenyl-5-phenylcarbamoylisoxazoline (*XIIIb*), m.p. = 115—118 °C. For $C_{19}H_{18}N_2O_4$ (M_r = 338.35) w_i(calc.): 67.44 % C, 5.36 % H, 8.28 % N; w_i(found): 67.51 % C, 5.44 % H, 8.28 % N. ^{1}H NMR spectrum, δ/ppm: 10.32 (s, 1H, NH), 7.0—7.66 (m, 9H, H_{arom}), 5.51 (d, J(3a,6a) = 4 Hz, 1H, H-6a), 5.06 (d, 1H, H-3a), 3.60 (s, 3H, OCH_3), 2.26 (s, 3H, CH_3).

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