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Regioselectivity in the 1,3-Dipolar Cycloaddition of Nitrile Oxides to 3,3-Methylene-5,5-dimethyl-2-pyrrolidinone**

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Summary. Nitrile oxides add regioselectively to the carbon-carbon double bond of 3,3-methylene-5,5-dimethyl-2-pyrrolidinone (**1**), giving exclusively spiro-isoxazolines: 3-aryl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-enes **3a–l**. The regiochemistry of the 1,3-dipolar cycloaddition to **1** seems to be controlled by the steric effect of the methyl groups at the ring junction and by frontier orbital interactions.

Keywords. 1,3-Dipolar cycloaddition of nitrile oxides; Regioselective 1,3-dipolar cycloaddition; AM 1 calculations.

Regioselektivität bei der 1,3-dipolaren Cycloaddition von Nitriloxid an 3,3-Methylen-5,5-dimethyl-2-pyrrolidinon

Zusammenfassung. Additionsreaktionen von Nitriloxiden an die C=C-Doppelbindung von 3,3-Methylen-5,5-dimethyl-2-pyrrolidinon (**1**) verlaufen regioselektiv, wobei ausschließlich Spiro-ixoxazoline entstehen: die 3-Aryl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene **3a–l**. Die Regiochemie der 1,3-dipolaren Cycloaddition scheint von den sterischen Effekten der Methylgruppen an der Ringverknüpfung und von den Frontorbital-Wechselwirkungen gesteuert zu werden.

Introduction

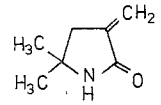
The high synthetic versatility of 2-isoxazolines (4,5-dihydroisoxazoles) is based on their potential to serve as flexible synthetic equivalents of β-hydroxy ketones [1], γ-amino alcohols [2], enamino aldehydes [3] and other related functions [4]. One of the most general preparation methods of 2-isoxazolines involves cycloaddition of nitrile oxides [5]. Particular attention has been focused on the factors influencing the stereo- and regio-selectivity. In the framework of our project [3, 6–10] on the utilization of heterocyclic compounds as dipolarophile components in 1,3-dipolar cycloadditions we have chosen 3,3-methylene-5,5-dimethyl-2-pyrrolidinone (**1**) as a model system. Only its formation [11]) and some aspects of its chemistry [12] have been investigated, its potential as a reactive dipolarophile has so far been neglected. Regarding the peculiarity of the regioselectivity pattern in electron de-

** Part XXV in the series 1,3-Dipolar Cycloaddition on Heterocycles. Part XXIV Ref. [10]

ficient dipolarophiles in 1,3-dipolar cycloaddition [5], the reaction of **1** with 1,3-dipoles should be of some mechanistic interest. In continuation of this study the present report describes the first 1,3-dipolar cycloadditions of aryl nitrile oxides **2** with **1**, with the aim to probe the origin of regioselectivity [13] together with quantum mechanical calculations using the AM 1 method. Moreover, the synthesized spiro-lactams could be used as potential precursor for the synthesis of various substituted isoxazolines.

Results and Discussion

3,3-Methylene-5,5-dimethyl-2-pyrrolidinone (**1**) was prepared by the established literature procedure [11] involving treatment of 2,2,6,6-tetramethyl-4-piperidone in chloroform with 50% aqueous NaOH under catalysis of *TEBA* and piperidine. When *X*-substituted benzenenitrile oxides **2** (where *X* is H, 2-Cl, 4-Cl, 2,4-diCl, 2-F, 4-F, 2-Br, 2-NO_2, 3-NO_2, 4-NO_2, 4-CH_3, and 2,4,6-triCH_3) were generated from the corresponding benzohydroxamoyl chlorides and triethylamine in diethyl ether in the presence of pyrrolidinone **1**, the cycloadducts **3 a–l** were formed in high yields, the remainder being the recovered starting material **1** and small amounts of 3,4-diarylfuroxan, the nitrile oxide dimer. Regioisomer **4** have not been detected in the crude reaction mixture by NMR spectroscopy. The carbon-carbon double bond of **1** seems to be a rather reactive dipolarophile; since unstable nitrile oxides, such as **p**- and **m**-substituted benzenenitrile oxides added to it very fast, only small amounts of the dimers of nitrile oxides were formed.



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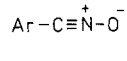

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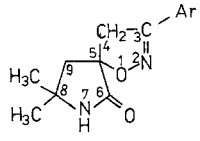

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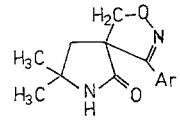

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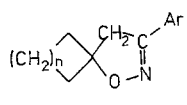

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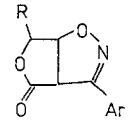

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R = H, OH, OEt, $OCOCH_3$, OCOPh

The structural assignment of the isolated spiro-isoxazolines, 3-aryl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-enes (**3**) is based on the chemical shifts of the methylenic CH_2 dublets for H_B-9 and H_A-9, (δ 2.04–2.33 ppm and δ 2.48–2.78 ppm, triplets of C-9, δ 48.69–49.09 ppm) and of the adjacent spiro-C (C-5, δ 87.63–89.64 ppm) indicating a strong shielding influence of the spiroheterocyclic ring on the 5-position of the isoxazoline, together with the expected value for C-4. The chemical shift of the methylene carbon C-4 in the isoxazoline ring is δ 42.11–46.89 ppm. A similar regioselectivity was observed in the cycloaddition of nitrile oxides to methylenecycloalkanes [14–19]. In all cases the reactivity of methylenecycloalkanes toward nitrile oxides was very high, for example the 1,3-dipolar cycloaddition of benzenenitrile oxide with methylenecyclobutane [15] has been reported to give quantitatively the cycloadduct **5**. The reactions [14–19] appeared to be completely regioselective, also as a result of the preferred approach of the dipole from the less hindered face of the dipolarophile.

We have shown that the ^1H and ^{13}C NMR spectra indicate the regiochemistry of the [3 + 2] cycloadducts **3a–l** which are formed by the attack of the carbon of the nitrile oxide at the CH_2 terminus of the α,β-unsaturated moiety. This is in contrast with the opposite mode of addition reported earlier by us for the heterocyclic compounds possessing an α,αb-unsaturated skeleton such as the reaction of arylnitrile oxide with 2(5*H*)-furanone [7, 8], 5-alkoxy- and 5-acetoxy-2(5*H*)-furanones [9, 10], as well as by other enones [20, 21]. In all the above mentioned cases the oxygen of the nitrile oxides is attached to the β-carbon of the enone unit of the furanone (cycloadducts of the type **7**). The lack of any report on 1,3-dipolar cycloadditions with **1** did not allow any prediction on the regioselectivity obtained in the cycloaddition. The regioselective formation of **3** and **7** requires a FMO treatment, in order to rationalize the contrary modes of addition to **1** and **6**.

Therefore we have performed an FMO analysis of calculated (AM1) [22] frontier orbitals. Optimized geometries of reactants, together with the most important bond lengths and atomic charges are shown in Fig. 1. The results of the calculations are summarized in Tables 1 and 2.

The reaction site in both dipolarophiles is the carbon-carbon double bond; in **6** it is part of a heterocycle, in **1** it is an exocyclic double bond. Differences in the chemical environment were, however, not reflected in the respective electronic

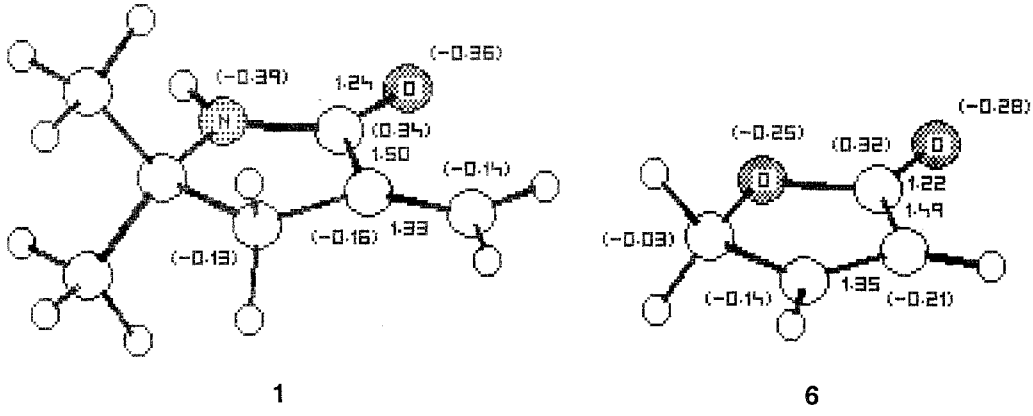

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Fig. 1. Bond lengths and charge distribution of **1** and **6** from AM1 calculations

Table 1. 3-(*X*-Phenyl)-6-oxo-8,8-dimethyl-l-oxa-2,7-diazaspiro[4.4]-non-2-enes **3**

Compound **3**	*X*	m.p. (°C)	Yield (%)	Formula[a]	M.w.
a	H	243–244	77	$C_{14}H_{16}N_2O_2$	244.29
b	2-Cl	162–163	82	$C_{14}H_{15}N_2O_2Cl$	278.73
c	4-Cl	247–248	52	$C_{14}H_{15}N_2O_2Cl$	278.73
d	2,4-Cl_2	211–212	72	$C_{14}H_{14}N_2O_2Cl_2$	313.18
e	2-F	214–216	76	$C_{14}H_{15}N_2O_2F$	262.28
f	4-F	213–215	38	$C_{14}H_{15}N_2O_2F$	262.28
g	2-Br	164–166	76	$C_{14}H_{15}N_2O_2Br$	323.19
h	2-NO_2	157–158	52	$C_{14}H_{15}N_3O_4$	289.28
i	3-NO_2	243–245	86	$C_{14}H_{15}N_3O_4$	289.28
j	4-NO_2	240–242	76	$C_{14}H_{15}N_3O_4$	289.28
k	4-CH_3	248–249	85	$C_{15}H_{18}N_2O_2$	258.31
l	2,4,6-triCH_3	234–236	70	$C_{17}H_{22}N_2O_2$	286.37

[a] Satisfactory microanalyses obtained: C ± 0.30, H ± 0.25, N ± 0.21

Table 2. Relevant electronic parameters of **1**, **2**, and **6** calculated with AMl

Compd.	E_{HOMO}	E_{LUMO}	HOMO		LUMO		Net charges	
			C/Cα	O/Cβ	C/Cα	O/Cβ	C/Cα	O/Cβ
2	−9.38	−0.50	0.37	−0.49	0.23	0.21	−0.21	−0.31
1	−9.94	0.38	0.18	0.21	0.52	−0.67	−0.16	−0.14
6	−10.88	−0.42	0.57	0.49	0.54	−0.66	−0.21	−0.14

structures. Much more prominent was the effect on the stereochemistry of dipolarophiles, specifically on the accessibility of the double bond. Molecules of **1** and **6** differ in their electronic structure due to conjugation of the α, β-unsaturated carbonyl moiety with the heteroatom (nitrogen in **1**, oxygen in **6**) of the ring. This is also reflected in the character of HOMO, and in marked differences in energies of frontier orbitals of **1** and **6** (Fig. 2). Both dipolarophiles differ in charge distribution as well; while in **1** both carbons of the double bond carry approximately the same charge, in **6** the bond is polarized towards the α carbon.

Now, if the cycloadditions with **2** are judged by electrostatic interactions alone, the negatively charged oxygen terminus in **2** would be expected to attack the β-carbon in **6**, while in the reaction with **1** the electrostatic interaction for both ways should have roughly the same energy.

A more detailed analysis of the regioselectivity is furnished by FMO arguments [23, 24]. Frontier orbital energies and coefficients are given in Table 1. Inspection of energy levels shows that the interaction **2**–**6** and its 5-substituted derivatives [8–10] is governed by the $HOMO_{DIPOLE}$

$$E_{LUMO\,6} - E_{HOMO\,2} = 8.96\,eV, \qquad E_{LUMO\,2} - E_{HOMO\,6} = 10.38\,eV$$

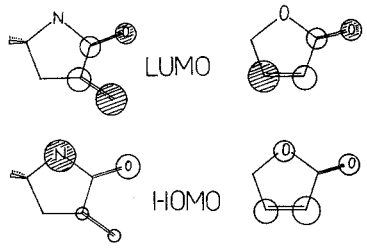

Fig. 2. Schematic drawings of HOMO and LUMO of **1** and **6**

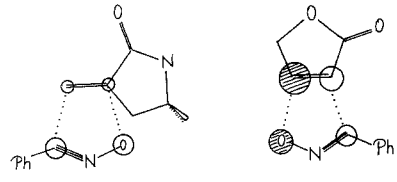

Fig. 3. Schematic drawings of interactions of $HOMO_1$ with $LUMO_2$ and $LUMO_6$ with $HOMO_2$

while the reaction of **2** with **1** is a $LUMO_{DIPOLE}$

$$E_{LUMO\,2} - E_{HOMO\,1} = 9.44\,eV\,, \qquad E_{LUMO\,1} - E_{HOMO\,2} = 9.76\,eV\,.$$

The energies differ only slightly, the small difference being due to the different heteroatoms in the respective dipolarophiles. Moreover, the HOMO of **6**, located at the α, β-unsaturated bond, has mostly π character, in **1** the pz orbital of nitrogen is only weakly conjugated (small contributions from both α and β carbons) and lies almost 1 eV higher. There is an energy difference in the LUMO energies of **1** and **6**, $LUMO_6$ being 0.8 eV lower than that of **1**.

According to the FMO theory, regioselectivity is governed predominantly by orbitals coefficients at the double bond and by those at terminal atoms of the dipole. In the HOMO of **1** the methylenic carbon has a larger orbital coefficient and would be expected to interact with the carbon terminus of the nitrile oxide (Fig. 3). In 5 *H*-furanones the LUMO have bigger coefficient at the β carbon, hence it is expected to couple with the oxygen of **2** possessing itself a bigger coefficient in HOMO (Fig. 3).

The present simple FMO arguments based on calculations of electronic structures of the reactants predict the correct regioselectivity: the preferential attack of dipole oxygen at the β-carbon in the LUMO-controlled 1,3-dipolar cycloadditions of **2** and **1**, as well as the formation of 5-substituted isoxazolines, resulting from the $HOMO_{DIPOLE}$ controlled cycloaddition. The regiochemistry of **3** is also favourable for a steric reason. The van der Waals nonbonded interaction energies should be very large in the second regioisomer **4** compared to the adduct **3**. From Dreiding models it is obvious that the bulky methyl group at the 5-position of **1** prevents the attack to give spiro-isoxazoline **4**. The arrangement of the aryl moiety of **2** suggests a steric effect between the bulky aryl group and the two methyl groups at 5-position. In conclusion, the regiochemistry of the 1,3-dipolar cycloaddition of the exocyclic double bond of **1** seems to be controlled by the steric effect of the methyl groups at the ring junction and the frontier orbital interaction.

Experimental Part

Melting points were determined on a Kofler hot plate m.p. apparatus and are uncorrected. ^1H- and ^{13}C-NMR spectra (in $CDCl_3$) were recorded on Varian VXR 300 (300 MHz) spectrometer. Chemical

shifts are given in ppm/**TMS.** UV spectra were obtained on a M-40 (Carl Zeiss, Jena) spectrometer in methanol (nm/log ε). Chlorides of benzenehydroximic acids were prepared by chlorination of the corresponding benzaldoximes in chloroform according to [25], 2,4,6-trimethylbenzenenitrile oxide was synthesized as described [26]. 3,3-Methylene-5,5-dimethyl-2-pyrrolidinone (**1**) was prepared according to [11].

3-(X-Phenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-enes **3**

Dry triethylamine (11 mmol) in dry ether (30 ml) was added dropwise at 0°C to a stirred cooled solution of the corresponding benzenehydroxime acid chloride (10 mmol) and **1** (1.25 g, 10 mmol) in dry ether (30 ml) during 2 h. After stirring overnight at room temperature, the precipitated triethylammonium chloride was removed by filtration and the filtrate was concentrated in vacuo. The products were triturated with methanol and purified by crystallization from methanol or methanol-chloroform. The cycloaddition of 2,4,6-trimethylbenzenenitrile oxide was performed in the following way: The nitrile oxide (10 mmol) and dipolarophile **1** (1.25 g, 10 mmol) in dry benzene (30 ml) were heated to 80°C for 4 h. After cooling, the mixture was concentrated and worked up as described above.

3-Phenyl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3 a**)

UV: 263 (3.30). ^{1}H-NMR: 1.64 (s, 3 H, CH_3), 1.74 (s, 3 H, CH_3), 2.33 (d, 1 H, H_B-9, J = 14.1), 2.78 (d, 1 H, H_A-9), 3.48 (d, 1 H, H_B-4, J = 16.8), 4.22 (d, 1 H, H_A-4), 6.78 (s, 1 H, NH), 7.53 – 7.94 (m, 5 H, aromat. H). ^{13}C-NMR: 29.85 (q, CH_3), 29.95 (q, CH_3), 42.99 (t, C-4), 49.04 (t, C-9), 54.18 (s, C-8), 88.41 (s, C-5), 126.85, 128.72, 129.03, 130.26 (aromat. C), 155.81 (s, C-3), 172.62 (s, C-6).

3-(2-Chlorophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3 b**)

UV: 258 (2.93). ^{1}H-NMR: 1.36 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.07 (d, 1 H, HB-9, J = 14.1), 2.52 (d, 1 H, H_A-9), 3.43 (d, 1 H, H_B-4, J = 17.4), 4.01 (d, 1 H, H_A-4), 6.88 (s, 1 H, NH), 7.28 – 7.70 (m, 4 H, aromat. H). ^{13}C-NMR: 29.94 (q, CH_3), 45.36 (t, C-4), 48.83 (t, C-9), 54.18 (s, C-8), 89.13 (s, C-5), 127.08, 128.42, 130.64, 130.82, 131.01, 132.86 (aromat. C), 155.72 (s, C-3), 172.49 (s, C-6).

3-(4-Chlorophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3 c**)

UV: 269 (3.34). ^{1}H-NMR: 1.36 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.06 (d, 1 H, H_B-9, J = 13.8), 2.50 (d, 1 H, H_A-9), 3.17 (d, 1 H, H_B-4, J = 16.5), 3.90 (d, 1 H, H_A-4), 6.60 (s, 1 H, NH), 7.38, and 7.60 (d, d, 4 H, aromat. H). ^{13}C-NMR: 29.84 (q, CH_3), 29.93 (q, CH_3), 42.78 (t, C-4), 48.98 (t, C-9), 54.24 (s, C-8), 88.80 (s, C-5), 127.58, 128.08, 129.02, 136.23 (aromat. C), 154.89 (s, C-3), 172.65 (s, C-6).

3-(2,4-Dichlorophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3 d**)

UV: 264 (3.13). ^{1}H-NMR: 1.35 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.07 (d, 1 H, H_B-9, J = 13.8), 2.51 (d, 1 H, H_A-9), 3.41 (d, 1 H, H_B-4, J = 17.1), 3.99 (d, 1 H, H_A-4), 6.79 (s, 1 H, NH), 7.27 – 7.65 (m, 3 H, aromat. H). ^{13}C-NMR: 29.89 (q, CH_3), 45.00 (t, C-4), 48.70 (t, C-9), 54.22 (s, C-8), 89.30 (s, C-5), 126.95, 127.47, 130.44, 131.56, 133.48, 136.43 (aromat. C), 154.83 (s, C-3), 172.29 (s, C-6).

3-(2-Fluorophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3 e**)

UV: 262 (3.14). ^{1}H-NMR: 1.35 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 2.07 (d, 1 H, H_B-9, J = 14.1), 2.48 (d, 1 H, H_A-9), 3.33 (d, 1 H, H_B-4, J = 17.4), 3.99 (d, 1 H, H_A-4), 6.92 (d, 1 H, NH), 7.08 – 7.90 (m, 4 H, aromat. H). ^{13}C-NMR: 29.89 (q, CH_3), 44.73 (t, C-4), 48.97 (t, C-9), 54.15 (s, C-8), 88.73 (s, C-5), 116.38, 117.15, 124.49, 129.18, 131.94, 160.36 (aromat. C), 152.55 (s, C-3), 172.72 (s, C-6).

3-(4-Fluorophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3f**)

UV: 262 (3.19). ^{1}H-NMR: 1.35 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 2.05 (d, 1H, H_B-9, J = 14.1), 2.49 (d, 1H, H_A-9), 3.18 (d, 1H, H_B-4, J = 17.1), 3.91 (d, 1H, H_A-4), 6.88 (s, 1H, NH), 7.06–7.12 and 7.63–7.68 (d, d, 4H, aromat. H). ^{13}C-NMR: 29.80 (q, CH_3), 29.86 (q, CH_3), 42.99 (t, C-4), 48.95 (t, C-9), 54.26 (s, C-8), 88.62 (s, C-5), 115.88, 125.30, 128.80, 163.80 (aromat. C), 154.82 (s, C-3), 172.49 (s, C-6).

3-(2-Bromophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3g**)

^{1}H-NMR: 1.36 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 2.08 (d, 1H, H_B-9, J = 14.1), 2.52 (d, 1H, H_A-9), 3.44 (d, 1H, H_B-4, J = 17.1), 3.96 (d, 1H, H_A-4), 7.44 (s, 1H, NH), 7.25–7.64 (m, 4H, aromat. H). ^{13}C-NMR: 29.86 (q, CH_3), 29.92 (q, CH_3), 45.53 (t, C-4), 48.88 (t, C-9), 54.24 (s, C-8), 89.31 (s, C-5), 121.90, 127.56, 130.58, 131.10, 133.69 (aromat. C), 156.74 (s, C-3), 172.61 (s, C-6).

3-(2-Nitrophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3h**)

UV: 263 (3.16). ^{1}H-NMR: 1.35 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 2.13 (d, 1H, H_B-9, J = 14.1), 2.59 (d, 1H, H_A-9), 3.19 (d, 1H, H_B-4, J = 17.1), 3.71 (d, 1H, H_A-4), 7.20 (s, 1H, NH), 7.59–8.11 (m, 4H, aromat. H). ^{13}C-NMR: 29.85 (q, CH_3), 29.95 (q, CH_3), 4.35 (t, C-4), 48.91 (t, C-9), 54.37 (s, C-8), 89.64 (s, C-5), 124.84, 125.18, 130.80, 131.40, 133.82, 147.72 (aromat. C), 154.88 (s, C-3), 172.24 (s, C-6).

3-(3-Nitrophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3i**)

UV: 260 (3.47). ^{1}H-NMR: 1.41 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.15 (d, 1H, H_B-9, J = 13.8), 2.57 (d, 1H, H_A-9), 3.29 (d, 1H, H_B-4, J = 16.5), 3.99 (d, 1H, H_A-4), 5.91 (s, 1H, NH), 7.61–8.45 (m, 4H, aromat. H). ^{13}C-NMR: 29.85 (q, CH_3), 29.88 (q, CH_3), 42.28 (t, C-4), 48.69 (t, C-9), 54.19 (s, C-8), 89.10 (s, C-5), 114.81, 121.66, 124.73, 129.84, 130.87, 132.33 (aromat. C), 154.17 (s, C-3), 171.79 (s, C-6).

3-(4-Nitrophenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspira[4.4]non-2-ene (**3j**)

UV: 308 (3.32). ^{1}H-NMR: 1.39 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 2.11 (d, 1H, H_B-9, J = 13.8), 2.54 (d, 1H, H_A-9), 3.23 (d, 1H, H_B-4, J = 17.1), 3.96 (d, 1H, H_A-4), 5.98 (s, 1H, NH), 7.83, and 8.27 (d, d, 4H, aromat H). ^{13}C-NMR: 29.85 (q, CH_3), 29.97 (q, CH_3), 42.11 (t, C-4), 48.74 (t, C-9), 54.25 (s, C-8), 89.40 (s, C-5), 124.00, 124.02, 127.55, 135.08 (aromat. C), 154.30 (s, C-3), 171.76 (s, C-6).

3-(4-Methylphenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspira[4.4]non-2-ene (**3k**)

UV: 267 (3.20). ^{1}H-NMR: 1.35 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 2.04 (d, 1H, H_B-9, J = 13.8), 2.38 (s, 3H, CH_3), 2.48 (d, 1H, H_B-9), 3.18 (d, 1H, H_B-4, J = 16.8), 3.92 (d, 1H, H_A-4), 6.91 (s, 1H, NH), 7.20, and 7.55 (d, d, 4H, aromat. H). ^{13}C-NMR: 21.47 (q, CH_3), 29.82 (q, CH_3), 29.88 (q, CH_3), 43.18 (t, C-4), 49.09 (t, C-9), 54.19 (s, C-8), 88.31 (s, C-5), 126.21, 126.78, 129.39, 140.47 (aromat. C), 155.74 (s, C-3), 172.85 (s, C-6).

3-(2,4,6-Trimethylphenyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4.4]non-2-ene (**3l**)

^{1}H-NMR: 1.35 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 2.28 (d, 1H, H_B-9, J = 14.1), 2.29 (s, 9H, CH_3), 2.54 (d, 1H, H_A-9), 2.98 (d, 1H, H_B-4, J = 17.4), 3.73 (d, 1H, H_A-4), 6.65 (s, 1H, NH), 6.90 (s, 2H, aromat. H). ^{13}C-NMR: 19.69 (q, CH_3), 21.09 (q, CH_3), 29.90 (q, CH_3), 46.89 (t, C-4), 48.74 (t, C-9), 54.09 (s, C-8), 87.63 (s, C-5), 125.60, 128.44, 136.84, 138.92 (aromat. C), 156.90 (s, C-3), 172.71 (s, C-6).

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