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Stereoselectivity in the 1,3-Dipolar Cycloaddition of Nitrones to 1-Substituted 3,3-Methylene-5,5-dimethyl-2-pyrrolidinones

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Summary. The stereoselectivity of the nitrone cycloaddition with 1-substituted 3,3-methylene-5,5-dimethyl-2-pyrrolidinones **1** is discussed. C,N-Diarylnitrones give mixtures of diastereomeric spirocycloadducts **3** and **4**, in which **3** always dominates. In contrast, N-methylnitrones react under the formation of **4** as major products. Cycloaddition of C-benzoyl nitrones **7** with **1** affords exclusively single isoxazolidines **8**. Semi-empirical quantum mechanical methods (AM1) were used to rationalize the regio- and stereoselectivity of the reactions.

Keywords. 1,3-Dipolar cycloaddition of nitrones; Regio- and stereoselectivity of 1,3-dipolar cycloaddition; AM1 calculations.

Stereoselektivität der 1,3-dipolaren Cycloaddition von Nitronen an 1-substituierte 3,3-Methylen-5,5-dimethyl-2-pyrrolidinone

Zusammenfassung. Die Stereoselektivität der Cycloaddition von Nitronen mit 1-substituierten 3,3-Methylen-5,5-dimethyl-pyrrolidinonen (**1**) wird diskutiert. C,N-Diarylnitrone ergeben Mischungen der diastereomeren Spirocycloaddukte **3** und **4**, wobei **3** immer überwiegt. Im Gegensatz dazu entsteht bei der Reaktion von N-Methylnitronen **4** als Hauptprodukt. Die Cycloaddition von C-Benzoylnitronen (**7**) mit **1** liefert ausschließlich Isoxazolidine vom Typ **8**. Zum besseren Verständnis der Regio- und Stereoselektivität der Reaktionen wurden semiempirische quantenmechanische Berechnungen (AM1) durchgeführt.

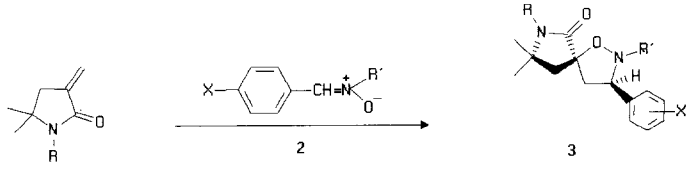
Introduction

The recent observation of the strong herbicidal activity of spiro cyclic lactams, coupled with the absence of toxicity to microorganisms [1] and also that some spiroisoxazolines occur naturally (Araplysillins are inhibitors of *ATP*ase [2]) stimulated our interest in the synthesis of other spirocyclic derivatives. In a continuation of our effort [3–6] to utilise heterocyclic compounds as dipolarophiles in 1,3-dipolar cycloaddition reactions, we have recently demonstrated that diarylnitrones react regioselectively with 3,3-methylene-5,5-dimethyl-2-pyrrolidinone (**1a**)

to give a mixture of diastereomeric spiro-cycloadducts **3** and **4**, in which **3** always dominates [4]. AM1 calculations showed that the regio- and stereochemistry of the nitrone cycloaddition seems to be controlled by steric effects. Since the reaction of **1** with 1,3-dipoles could be of some mechanistic interest regarding the pecularity of the regioselectivity pattern in electron deficient dipolarophiles in the 1,3-dipolar cycloadditions [7], we now report the cycloaddition of 1-substituted derivatives of pyrrolidinone **1** with nitrones, together with quantum mechanical calculations using the AM1 method.

Results and Discussion

1,3-Dipolar cycloadditions of C-(*X*-phenyl)-N-phenyl-nitrones **2** (where *X* is H, 4-Cl and 4-NO_2) and 1-substituted 3,3-methylene-5,5-dimethyl-2-pyrrolidinones **1b–g** (R = *n*-butyl, 1,1-dimethylethoxycarbonyl, 1-methylethenyl, allyl, methoxycarbonyl, and acetyl) in toluene at 110 °C afforded the isoxazolidines **3** and **4** as a mixture of diastereomers, with the predominance of the isomer **3**; the latter could be obtained in pure form (Scheme 1). The assignment of the regiochemistry in the isoxazolidines **3** and **4** was unequivocally possible on the basis of ^1H and ^{13}C NMR data of the isoxazolidine ring moiety and by comparison with the cycloadducts of **1a** [4]. NMR analysis of the crude reaction mixture permitted a determination of the ratio of the epimers **3** and 4 present in the original reaction mixture (Table 1). The comparison with the unsubstituted derivative **1a** shows a decrease of diastereoselectivity in the cycloaddition for the derivatives **1b–g** possessing a substituent at the nitrogen. The diastereomeric isoxazolidines **3** and **4** were formed *via* different planar complexes. A cycloaddition of nitrone **2** *via* an *exo* transition state (*exo* with respect to N-Ph and C=O groups) results in the formation of isoxazolidine **3**. Cycloaddition *via* the *endo* transition state yields the minor isomer **4**. The corresponding *exo* transition state is favorized, since the repulsions between the phenyl group on the nitrogen and the substituents on the dipolarophile **1** are minimized. The fact that the diastereoselectivity is controlled by steric effects was supported by the cycloaddition of C-phenyl-N-methylnitrone (**2t**) and **1f**, which furnished both diastereoisomers **3** and **4** in a ratio of 47:53 in favor of **4**. The cycloaddition of **1a,b**



1

2

3

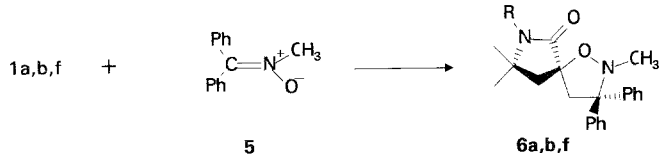
4

1a: R = H
1b: R = CH_2=$(CH_3)C$
1c: R = n-Bu
1d: R = Allyl
1e: R = $COCH_3$
1f: R = Boc
1g: R = $COOCH_3$

2t: R′ = CH_3, X = H
2u: R′ = Ph, X = H
2v: R′ = Ph, X = Cl
2x: R′ = Ph, X = NO_2

Scheme 1

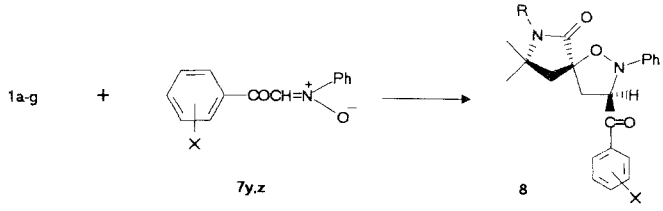
and **1f** with C,C-diphenyl-N-methylnitrone (**5**) proceeded analogously to give cycloadducts **6** (Scheme 2). On the other hand, cycloadditions of C-(*X*-benzoyl)-



Scheme 2

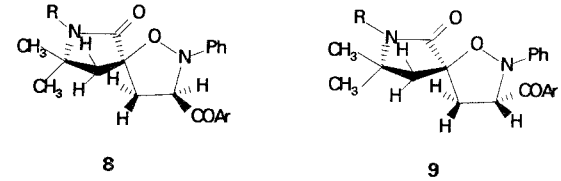
N-phenyl-nitrones **7y,z** (where *X* is H and 2,4-diCl) and **1** afforded exclusively the spiro-isoxazolidines **8** (Scheme 3). The corresponding diastereomer **9** as well as the regioisomeric diastereomers **10** and **11** could not be detected in the crude reaction mixture by NMR spectroscopy (Scheme 4). The stereochemical assignment of compounds **8** was based on nuclear *Overhauser* effect difference spectroscopy.

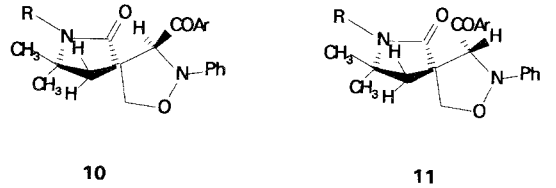
Irradiation of H-3 causes on NOE for H_B-4, which suggests that these protons are all on the same side of the molecule. Irradiation of H_A-4 (*cis* to 3-benzoyl) results in signal enhancement of H_B-9 of the pyrrolidine unit. Moreover, the irradiation of H_B-4 effects only H-3 and additionally, H_A-9 interacts with one of the methyl groups.



7y: X = H
7z: X = 2,4-Cl_2

Scheme 3





Scheme 4

Table 1. Ratio of diastereomers **3** and **4**; letters refer to substituents in Scheme 1

Comp.	**bu**	**bv**	**bx**	**cu**	**eu**	**ev**	**ex**	**ft**	**fu**	**fv**	**fx**	**gu**
3:4	83:17	72:28	82:18	82:18	77:23	78:22	85:15	47:53	83:17	85:15	86:14	78:22

In order to rationalize the high regio- and stereoselectivity of benzoylnitrone cycloadditions, quantum-chemical calculations of a model reaction (**1a** and C-benzoyl-N-phenylnitrone **7y**) were performed. The semiempirical method AM1 [8] was used to analyze electronic structures of reactants, energies of four possible products **8–11**, and activation barriers leading to these products. The frontier orbital energies of dipolarophile **1a** and dipole **7y** are as follows (values in eV):

$$E_{HOMO}(\mathbf{1a}) = -9.94 \qquad E_{HOMO}(\mathbf{7y}) = -9.40$$
$$E_{LUMO}(\mathbf{1a}) = 0.37 \qquad E_{LUMO}(\mathbf{7y}) = -0.94$$

The energy difference between LUMO-dipole and HOMO-dipolarophile (9.00 eV) is lower than between HOMO-dipole and LUMO-dipolarophile (9.77 eV). According to this data, the reaction should be controlled by the LUMO of dipole **7y**, but this orbital is delocalized throughout the whole π system with only minor contributions of the nitrone moiety. The HOMO of dipolarophile **1a** is localized on the ring nitrogen and has lone pair character. On the basis of this fact it seems that the reaction is controlled actually by the HOMO of dipole **7y** as most 1,3-dipolar cycloadditions of nitrones [9, 10]. Indeed, the LUMO of **1a** and the HOMO of **7y** are localized mostly on the reacting atoms, as may be seen from Figs. 1 and 2.

The HOMO molecular orbital coefficient of the nitrone carbon is 0.69, that of the oxygen −0.56. In the LUMO of dipolarophile **1a** the coefficient of the terminal methylene carbon is larger than that of the ring carbon (0.66 and −0.52, respectively). When these two orbitals are taken into account, a simple FMO analysis reveals that regioisomers with the oxygen of nitrone group bound to the spiro carbon (*i.e.* products **8** and **9**) should be preferred.

The thermodynamic stabilities of all four possible products **8–11** were calculated. Products **8–10** lie within the range of 4 kJ/mol, only product **11** is less stable (Table 2).

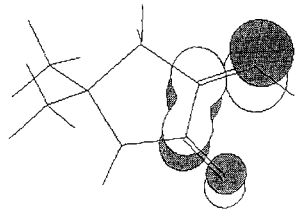


Fig. 1. LUMO of dipolarophile **1a** (AM1)

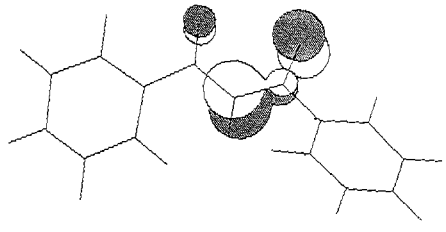


Fig. 2. HOMO of dipole **7y** (AM1)

Table 2. Energies of reactants (E) and transition states (E_T), thermodynamic stabilities of products (H) and activation barriers $\Delta E^{\neq}$ (data in kJ/mol)

Compound	$E(E_T)$	H	$\Delta E^{\neq}$
1a	−109.52	–	–
7y	229.89	–	–
8 (TS-1)	225.30	5.85	104.92
9 (TS-2)	233.24	4.59	112.86
10 (TS-3)	239.10	4.43	118.71
11	–	41.84	–

To obtain a closer look on factors controlling stereoselectivity, the transition states (TS) leading to the products were calculated. The structures of TS1 and TS2 are shown on Figs. 3 and 4, with respective energies listed in Table 2.

All transition states found are concerted ones. No attempts were made to localize biradical transition states which, according to *ab initio* MC SCF analysis of simple model compounds, are richer in energy by about 60 kJ/mol [11]. In agreement with results of simple FMO analyses, the activation barrier

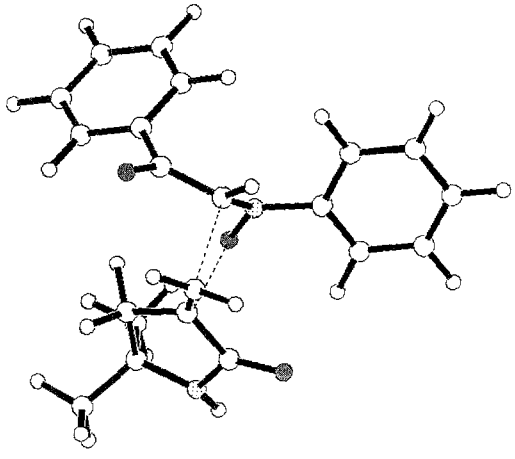


Fig. 3. TS-1 → cycloadduct **8** (AM1)

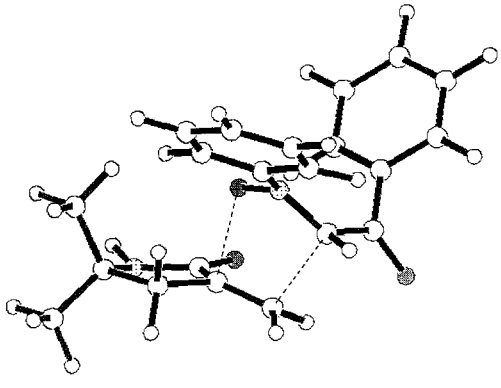


Fig. 4. TS-2 → cycloadduct **9** (AM1)

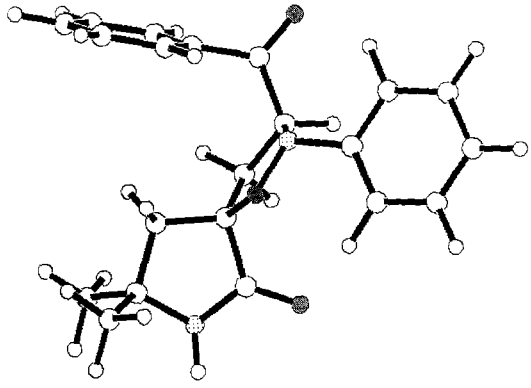


Fig. 5. Optimized geometry of the cycloadduct **8** (AM1)

leading to the "forbidden" product **10** is the highest (118.7 kJ/mol), while the lowest is the barrier leading to product **8** (104.9 kJ/mol). This may be compared with reported *ab initio* MC SCF results for the reaction of H_2CNHO with ethylene yielding a barrier 49.7 kJ/mol [11]. In our case, however, the steric interaction between phenyl groups may increase the reaction barrier considerably in comparison with this simple model system. Transition bond lengths in TS1 are 2.08 Å for the C–C bond, and 2.10 Å for the C–O bond. The imaginary frequency of TS1 is 648 cm^{-1}. The structure of the theoretically preferred product **8** is shown in Fig. 5.

The 1,3-dipolar cycloaddition of nitrones to alkenyl derivative **1b** proceeds fully chemoselective; only the cycloadducts to the exocyclic double bond were formed. The cycloadducts which could be formed by the attack of nitrones to the double bond of the alkenyl chain in **1b** have not been detected in the crude reaction mixture by NMR spectroscopy. This can be explained by the well known fact that angular strain in a dipolarophile increases its reactivity [12].

Experimental

Melting points were determined on a Kofler hot plate apparatus and are uncorrected. ^1H NMR spectra were recorded on Varian VXR 300 (300 MHz) and Tesla BS 487 C (80 MHz) spectrometers, ^{13}C NMR spectra (75 MHz) on a Varian VXR 300 spectrometer (*TMS* as internal standard, $CDCl_3$, δ in ppm, J in Hz). Quantum-chemical calculations were performed using the semiempirical method AM1 [8]. Geometries of reactants and all possible products were fully optimized using the PRECISE algorithm which increases the precision of the results by a factor of 10^2. Transition states were first roughly optimized by the reaction coordinate method, then by minimisation of gradients. All transition states were characterized as true transition states by the analysis of the force constant matrix.

The starting model compounds, namely **1a–g** (where R is H) were prepared according to Ref. [13].

Spiroisoxazolidines **3**, **4**, *and* **6**

N-Phenyl-C-aryl-nitrones **2** (10 mmol) and 1-substituted 3,3-methylene-5,5-dimethyl-2-pyrrolidinone **1** (10 mmol) in dry toluene (50 ml) were heated under reflux for 5–36 h (TLC). Evaporation of the solvent *in vacuo* and chromatography (silica gel) using chloroform or hexane-ethylacetate (4:1) gave the corresponding cycloadducts.

2-Methyl-3-phenyl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3at**)

Yield: 25%, m.p. 170–172 °C. $C_{15}H_{20}N_2O_2$ (260.3); calc.: C 69.23, H 7.69, N 10.76; found: C 69.56, H 7.92, N 10.48. ^1H NMR: 1.29 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.01 (d, 1H, H_B-9, $J_{AB} = 13.8$ Hz), 2.31

(dd, 1H, H_B-4, J_{AB} = 12.6 Hz, $J_{3,4B}$ = 8.4 Hz), 2.42 (d, 1H, H_A-9), 2.68 (s, 3H, N-CH_3), 3.02 (dd, 1H, H_A-4, $J_{3,4A}$ = 7.2 Hz), 3.99 (dd, 1H, H-3), 6.29 (s, 1H, NH), 7.27–7.39 (m, 5H, aromat. H). ^{13}C NMR: 29.93 (q, CH_3), 30.05 (q, CH_3), 43.86 (q, N–CH_3), 48.91, 49.36 (t, t, C-4, C-9), 53.88 (s, C-8), 72.98 (d, C-3), 84.29 (s, C-5), 127.55, 127.89, 128.60, 138.64 (aromat. C), 174.55 (s, C-6).

2-Methyl-3-phenyl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**4at**)

Yield: 15%, m.p. 210–212 °C. $C_{15}H_{20}N_2O_2$ (260.3); calc.: C 69.23, H 7.69, N 10.76; found: C 69.42, H 7.97, N 10.59. ^{1}H NMR: 1.30 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.12 (d, 1H, H_B-9, J_{AB} = 13.8 Hz), 2.28 (d, 1H, H_A-9), 2.44 (dd, 1H, H_B-4, J_{AB} = 12.3 Hz, $J_{3,4B}$ = 7.2 Hz), 2.57 (s, 3H, N–CH_3), 2.96 (dd, 1H, H_A-4), 3.50 (dd, 1H, H-3), 6.10 (s, 1H, NH), 7.27–7.49 (m, 5H, aromat. H).

2,3-Diphenyl-6-oxo-7-(1-methylethenyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3bu**)

Yield: 30%, m.p. 87–89 °C. $C_{23}H_{26}N_2O_2$ (362.5); calc.: C 76.24, H 7.18, N 7.73; found: C 76.45, H 7.34, N 7.72. ^{1}H NMR: 1.31 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.05 (d, 1H, H_B-9, J_{AB} = 13.5 Hz), 2.41 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 8.7 Hz), 2.44 (d, 1H, H_A-9), 3.14 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.5 Hz), 4.91 (s, 1H, vinyl. H), 5.03 (dd, 1H, H-3), 5.18 (s, 1H, vinyl. H), 6.89–7.51 (m, 10H, aromat. H). ^{13}C NMR: 21.86 (q, CH_3), 28.34 (q, CH_3), 28.66 (q, CH_3), 47.11, 47.67 (t, t, C-4, C-9), 59.87 (s, C-8), 70.19 (d, C-3), 83.86 (s, C-5), 115.46, 116.19, 122.33, 126.77, 127.60, 128.13, 128.84, 139.73, 141.17, 151.21 (aromat. and vinyl. C), 170.77 (s, C-6).

2-Phenyl-3-(4-chlorophenyl)-6-oxo-7-(1-methylethenyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3bv**)

Yield: 30%, m.p. 137–138 °C. $C_{23}H_{25}ClN_2O_2$ (396.9); calc.: C 69.59, H 6.34, N 7.05; found: C 69.42, H 6.40, N 7.04. ^{1}H NMR: 1.31 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 2.05 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 2.35 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 7.8 Hz), 2.41 (d, 1H, H_A-9), 3.12 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.5 Hz), 4.91 (s, 1H, vinyl. H), 5.02 (dd, 1H, H-3), 5.19 (s, 1H, vinyl. H), 6.92–7.45 (m, 9H, aromat. H). ^{13}C NMR: 21.76 (q, CH_3), 28.22 (q, CH_3), 28.54 (q, CH_3), 46.85, 47.38 (t, t, C-4, C-9), 59.82 (s, C-8), 69.41 (d, C-3), 83.81 (s, C-5), 115.48, 116.04, 116.08, 128.04, 128.11, 128.92, 133.18, 139.53, 150.93, (aromat. and vinyl. C), 170.53 (s, C-6).

2-Phenyl-3-(4-nitrophenyl)-6-oxo-7-(1-methylethenyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3bx**)

Yield: 33%, m.p. 149–150 °C. $C_{23}H_{25}N_3O_4$ (407.4); calc.: C 67.79, H 6.18, N 10.31; found: C 67.66, H 6.15, N 10.21. ^{1}H NMR: 1.38 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.12 (d, 1H, H_B-9, J_{AB} = 13.8 Hz), 2.43 (dd, 1H, H_A-4, J_{AB} = 12.6 Hz, $J_{3,4A}$ = 7.5 Hz), 2.45 (d, 1H, H_A-9), 3.24 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.5 Hz), 4.97 (s, 1H, vinyl. H), 5.26 (dd, 1H, H-3), 5.29 (s, 1H, vinyl. H), 6.94–8.30 (m, 9H, aromat. H). ^{13}C NMR: 21.76 (q, CH_3), 28.22 (q, CH_3), 28.59 (q, CH_3), 46.49, 47.05 (t, t, C-4, C-9), 59.94 (s, C-8), 69.26 (d, C-3), 84.08 (s, C-5), 115.69, 122.63, 124.14, 127.51, 128.60, 139.45, 147.41, 148.87, 150.73 (aromat. and vinyl. C), 170.30 (s, C-6).

2,3-Diphenyl-6-oxo-7-butyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3cu**)

Yield: 50%, oil. $C_{24}H_{30}N_2O_2$ (378.5). ^{1}H NMR: 0.94 (t, 3H, CH'_3), 1.28 (s, 3H, CH_3), 1.34 (m, 2H, H_2-3'), 1.44 (s, 3H, CH_3), 1.59 (m, 2H, H_2-2'), 1.97 (d, 1H, H_B-9, J_{AB} = 13.8 Hz), 2.40 (d, 1H, H_A-9), 2.37 (dd, 1H, H_A-4), 3.09–3.18 (m, 3H, H_B-4, H_2-1'), 5.03 (dd, 1H, H-3, $J_{3,4A}$ = 7.8 Hz, $J_{3,4B}$ = 8.1 Hz), 6.91–7.52 (m, 10H, aromat. H). ^{13}C NMR: 13.79 (q, C-4'), 20.52 (t, C-3'), 27.72 (q, CH_3), 28.09 (q, CH_3), 31.35 (t, C-2'), 39.83 (t, C-9), 46.73 (t, C-1'), 47.95 (t, C-4), 58.38 (s, C-8), 70.09 (d, C-3), 83.69 (s, C-5), 116.20, 122.19, 126.73, 127.51, 128.37, 128.79, 141.28, 151.25 (aromat. C), 171.46 (s, C-6).

2,3-Diphenyl-6-oxo-7-acetyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3eu**)

Yield: 30%, m.p. 121–122 °C. $C_{22}H_{24}N_2O_3$ (364.4); calc.: C 72.53, H 6.59, N 7.69; found: C 72.47, H 6.74, N 7.79. ^{1}H NMR: 1.55 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.00 (d, 1H, H_B-9, J_{AB} = 14.4 Hz), 2.38 (s, 3H, CH_3), 2.35 (d, 1H, H_A-9), 2.44 (dd, 1H, H_A-4, J_{AB} = 12.6 Hz, $J_{3,4A}$ = 7.5 Hz), 3.11 (dd, 1H, H_B-4, $J_{3,4B}$ = 8.1 Hz), 5.06 (dd, 1H, H-3), 6.88–7.48 (m, 10H, aromat. H). ^{13}C NMR: 26.39 (q, CH_3), 27.01 (q, CH_3), 28.34 (q, CH_3), 45.57, 47.32 (t, t, C-4, C-9), 60.69 (s, C-8), 69.82 (s, C-3), 83.81 (s, C-5), 115.07, 122.13, 126.51, 127.54, 128.43, 128.59, 140.92, 151.19 (aromat. C), 172.01, 174.09 (s, s, C-6, $COCH_3$).

2-Phenyl-3-(4-chlorophenyl)-6-oxo-7-acetyl-8,8dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3ev**)

Yield: 60%, m.p. 165–166 °C. $C_{22}H_{23}ClN_2O_3$ (398.9); calc.: C 66.33, H 5.78, N 7.04; found: C 66.35, H 5.90, N 6.94. ^{1}H NMR: 1.56 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 2.04 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 2.38 (s, 3H, CH_3), 2.37 (d, 1H, H_A-9), 2.44 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz. $J_{3,4A}$ = 7.5 Hz), 3.01 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.5 Hz), 5.06 (dd, 1H, H-3), 6.87–7.45 (m, 9H, aromat. H). ^{13}C NMR: 26.41 (q, CH_3), 27.05 (q, CH_3), 28.33 (q, CH_3), 45.51, 47.00 (t, t, C-4, C-9), 60.79 (s, C-8), 69.45 (s, C-3), 84.01 (s, C-5), 115.32, 122.69, 128.73, 129.15, 133.64, 138.94, 150.46 (aromat. C), 172.01, 173.92 (s, s, C-6, $COCH_3$).

2-Phenyl-3-(4-nitrophenyl)-6-oxo-7-acetyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3ex**)

Yield: 55%, m.p. 152–153 °C. $C_{22}H_{23}N_3O_5$ (409.4); calc.: C 64.53, H 5.66, N 10.26; found: C 64.43, H 5.67, N 10.19. ^{1}H NMR: 1.57 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 2.05 (d, 1H, H_B-9, J_{AB} = 14.7 Hz), 2.35 (s, 3H, CH_3), 2.37 (d, 1H, H_A-9), 2.40 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 7.8 Hz), 3.17 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.8 Hz), 5.06 (dd, 1H, H-3), 6.82–8.26 (m, 9H, aromat. H). ^{13}C NMR: 26.24 (q, CH_3), 26.96 (q, CH_3), 28.37 (q, CH_3), 45.03, 46.55 (t, t, C-4, C-9), 60.80 (s, C-8), 68.90 (s, C-3), 84.10 (s, C-5), 114.58, 122.45, 124.32, 127. 32, 128.78, 147.48, 148.51, 150.61 (aromat. C), 171.86, 173.64 (s, s, C-6, $COCH_3$).

2,8,8-Trimethyl-3-phenyl-6-oxo-7-(1,1-dimethoxycarbonyl)-1-oxa-2,7-diazaspiro[4,4]-nonane (**3ft**)

Yield: 15%, m.p. 215–216 °C. $C_{20}H_{28}N_2O_4$ (360.4); calc.: C 66.67, H 7.83, N 7.77; found: C 66.51, H 7.64, N 7.81. ^{1}H NMR: 1.45 (s, 3H, CH_3), 1.57 (s, 9H, CH_3), 1.58 (s, 3H, CH_3), 1.95 (d, 1H, H_B-9, J_{AB} = 13.5 Hz), 2.31 (dd, 1H, H_A-4), 2.37 (d, 1H, H_A-9), 2.68 (s, 3H, NCH_3), 3.01 (dd, 1H, H_B-4), 4.05 (dd, 1H, H-3), 7.20–7.40 (m, 5H, aromat. H). ^{13}C NMR: 27.29, 28.01, 28.07 (q, CH_3), 43.89 (q, NCH_3), 47.88, 48.64 (t, t, C-4, C-9), 59.96 (s, C-8), 72.74 (d, C-3), 82.84, 83.18 (s, s, C-5, C–*t*-Bu), 127.41, 127.81, 128.61, 138.18 (aromat. C), 150.10 (s, OCO), 173.28 (s, C-6).

2,8,8-Trimethyl-3-phenyl-6-oxo-7-(1,1-dimethoxycarbonyl)-1-oxa-2,7-diazaspiro[4,4]-nonane (**4ft**)

Yield: 20%, m.p. 185–186 °C. $C_{20}H_{28}N_2O_4$ (360.4); calc.: C 66.67, H 7.83, N 7.77; found: C 66.55, H 7.74, N 7.61. ^{1}H NMR: 1.49 (s, 3H, CH_3), 1.56 (s, 9H, CH_3), 1.58 (s, 3H, CH_3), 2.09 (d, 1H, H_B-9, J_{AB} = 13.8 Hz), 2.22 (d, 1H, H_A-9), 2.43 (dd, 1H, H_A-4, J_{AB} = 12.9 Hz, $J_{3,4A}$ = 7.8 Hz), 2.54 (s, 3H, NCH_3), 2.99 (dd, 1H, H_B-4), 3.48 (dd, 1H, H-3), 7.26–7.54 (m, 5H, aromat. H). 27.07, 28.12, 28.33 (q, CH_3), 43.19, 43.25 (t, t, C-4, C-9), 47.70 (q, NCH_3), 59.32 (s, C-8), 73.75 (d, C-3), 81.75, 83.03 (s, s, C-5, C–*t*-Bu), 128.15, 128.35, 128.50, 128.62, (aromat. C), 150.43 (s, OCO), 173.27 (s, C-6).

2,3-Diphenyl-6-oxo-7-(1,1-dimethoxycarbonyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3fu**)

Yield: 42%, m.p. 155–156 °C. $C_{25}H_{30}N_2O_4$ (420.6); calc.: C 71.09, H 7.10, N 6.63; found: C 69.89, H 6.96, N 6.65. ^{1}H NMR: 1.51 (s, 3H, CH_3), 1.54 (s, 9H, CH_3), 1.67 (s, 3H, CH_3), 1.98 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 2.36 (dd, 1H, H_A-4, J_{AB} = 12.6 Hz, $J_{3,4A}$ = 7.8 Hz), 2.37 (d, 1H, H_A-9), 3.11 (dd, 1H, H_B-4), 4.96 (dd, 1H, H-3), 6.91–7.43 (m, 10H, aromat. H). ^{13}C NMR: 27.28, 28.07, 28.39 (q, CH_3), 46.26 47.76 (t, t, C-4, C-9), 60.02 (s, C-8), 69.41 (d, C-3), 83.42, 83.47 (s, s, C-5, C–*t*-Bu), 116.54, 122.87, 126.78, 128.17, 128.57, 129.01, 133.48, 139.09 (aromat. C), 152.42 (s, OCO), 172.02 (s, C-6).

2-Phenyl-3-(4-chlorophenyl)-6-oxo-7-(1,1-dimethoxycarbonyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3fv**)

Yield: 77%, m.p. 147–148 °C. $C_{25}H_{29}ClN_2O_4$ (457.0); calc.: C 65.79, H 6.36, N 6.14; found: C 65.57, H 6.39, N 6.11. ^{1}H NMR: 1.51 (s, 3H, CH_3), 1.54 (s, 9H, CH_3), 1.67 (s, 3H, CH_3), 1.98 (d, 1H, H_B-9, J_{AB} = 13.8 Hz), 2.35 (dd, 1H, H_A-4, J_{AB} = 14.4 Hz, $J_{3,4A}$ = 7.5 Hz), 2.37 (d, 1H, H_A-9), 3.12 (dd, 1H, H_B-4), 4.96 (dd, 1H, H-3), 6.91–7.43 (m, 9H, aromat. H). ^{13}C NMR: 27.30, 28.10, 28.40 (q, CH_3), 46.30, 47.80 (t, t, C-4, C-9), 60.03 (s, C-8), 69.40 (d, C-3), 83.43, 83.47 (s, s, C-5, C–*t*-Bu), 116.50, 122.80, 128.20, 128.60, 129.10, 133.50, 139.10, 150.10 (aromat. C), 150.40 (s, OCO), 172.10 (s, C-6).

2-Phenyl-3-(4-nitrophenyl)-6-oxo-7-(1,1-dimethoxycarbonyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3fx**)

Yield: 86%, m.p. 165–166 °C. $C_{25}H_{29}N_3O_6$ (467.5); calc.: C 64.22, H 6.25, N 8.99; found: C 64.11, H 6.30, N 9.04. ^{1}H NMR: 1.52 (s, 3H, CH_3), 1.54 (s, 9H, CH_3), 1.69 (s, 3H, CH_3), 1.99 (d, 1H, H_B-9, J_{AB} = 14.4 Hz), 2.36 (d, 1H, H_A-9), 2.37 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 7.5 Hz), 3.90 (dd, 1H, H_B-4), 5.14 (dd, 1H, H-3), 6.80–8.25 (m, 9H, aromat. H). ^{13}C NMR: 27.30, 28.10, 28.40 (q, CH_3), 46.30, 47.80 (t, t, C-4, C-9), 60.03 (s, C-8), 69.40 (d, C-3), 83.43, 83.47 (s, s, C-5, C–*t*-Bu), 116.50, 122.80, 128.20, 128.60, 129.10, 133.50, 139.10, 150.10 (aromat. C), 150.40 (s, OCO), 172.10 (s, C-6).

2,3-Diphenyl-6-oxo-7-methoxycarbonyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**3gu**)

Yield: 65%, m.p. 97–98 °C. $C_{22}H_{24}N_2O_4$ (380.4); calc.: C 69.45, H 6.36, N 7.36; found: C 69.50, H 6.32, N 7.42. ^{1}H NMR: 1.25 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.97 (d, 1H, H_B-9, J_{AB} = 13.7 Hz), 2.39 (dd, 1H, H_A-4), 2.43 (d, 1H, H_A-9), 2.80 (s, 3H, OCH_3), 3.13 (dd, 1H, H_B-4, $J_{3,4B}$ = 4.8 Hz, J_{AB} = 12.2 Hz), 4.98 (dd, 1H, H-3), 6.94–8.42 (m, 10H, aromat. H). ^{13}C NMR: 24.55, (q, CH_3), 26.28 (q, CH_3), 27.11 (q, CH_3), 46.72, 48.23 (t, C-9, C-4), 57.55 (s, C-8), 70.08 (d, C-3), 83.88 (s, C-5), 115.56, 116.54, 121.72, 122.37, 126.83, 127.60, 128.43, 128.84, 130.97, 141.11, 150.97 (aromat. C), 171.27 (s, C-6).

2,3,3-Triphenyl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**6a**)

Yield: 45%, m.p. 250–251 °C. $C_{21}H_{24}N_2O_2$ (340.5); calc.: C 74.10, H 7.01, N 8.23; found: C 73.90, H 7.21, N 8.32. ^{1}H NMR: 1.14 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.45 (d, 2H, H_2-9, J_{AB} = 13.8 Hz), 2.56 (s, 3H, N–CH_3), 2.73 (d, 1H, H_B-4, J_{AB} = 12.3 Hz), 3.84 (d, 1H, H_A-4), 5.91 (s, 1H, NH), 7.19–7.57 (m, 10H, aromat. H). ^{13}C NMR: 29.92 (q, CH_3), 30.10 (q, CH_3), 42.89 (q, N–CH_3), 45.54 (t, C-4), 49.10 (t, C-9), 53.60 (s, C-8), 78.21 (s, C-3), 87.35 (s, C-5), 126.37, 126.99, 127.44, 127.99, 128.25, 128.45, 141.16, 146.14 (aromat. C), 175.06 (s, C-6).

2,3,3-Triphenyl-6-oxo-7-(1-methylethenyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**6b**)

Yield: 33%, m.p. 180–183 °C. $C_{24}H_{28}N_2O_2$ (376.5); calc.: C 76.58, H 7.44, N 7.44; found: C 76.57, H 7.52, N 7.36. ^{1}H NMR: 1.14 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.44 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 1.52 (d, 1H, H_A-9), 1.96 (s, 3H, CH_3), 2.58 (s, 3H, N–CH_3), 2.73 (d, 1H, H_B-4, J_{AB} = 12.0 Hz), 3.88 (d, 1H, H_A-4),

4.88 (s, 1H, vinyl. H), 5.17 (s, 1H, vinyl. H), 7.26–7.55 (m, 10H, aromat. H). ^{13}C NMR: 21.97 (q, CH_3), 28.40 (q, CH_3), 29.66 (q, CH_3), 42.85 (q, N–CH_3), 45.59, 49.03 (t, t, C-4, C-9), 59.58 (s, C-8), 78.19 (s, C-3), 86.25 (s, C-5), 114.99, 126.29, 126.94, 127.36, 128.23, 128.40, 140.04, 141.16, 146.21 (aromat. and vinyl. C), 172.33 (s, C-6).

2,3,3-Triphenyl-6-oxo-7(1,1-dimethylethoxycarbonyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**6f**)

Yield: 68%, m.p. 189–191 °C. $C_{26}H_{32}N_2O_4$ (436.7); calc.: C 71.56, H 7.34, N 6.42; found: C 71.38, H 7.45, N 6.48. ^{1}H NMR: 1.32 (s, 3H, CH_3), 1.39 (d, 2H, H_2-9, $J_{AB} = 14.1$ Hz), 1.40 (s, 3H, CH_3), 1.55 (s, 9H, $3 \times CH_3$), 2.56 (s, 3H, N–CH_3), 2.73 (d, 1H, H_B-4, $J_{AB} = 12.3$ Hz), 3.89 (d, 1H, H_A-4), 7.19–7.53 (m, 10H, aromat. H). ^{13}C NMR: 27.37 (q, CH_3), 28.12 (q, $3 \times CH_3$), 28.20 (q, CH_3), 42.93 (q, N–CH_3), 45.86, 48.05 (t, t, C-4, C-9), 59.85 (s, C-8), 78.33 (s, C-3), 83.21, 86.25 (s, s, *t*–Bu, C-5), 126.47, 126.94, 127.52, 128.04, 128.20, 128.51, 140.96 (aromat. C), 174.23 (s, C-6).

2-Phenyl-3-(X-benzoyl)-7-R-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonanes **8**

C-Aroyl-N-phenylnitrones **7a,b** (10 mmol) and the appropriate pyrrolidinone **1a–f** in benzene (50 ml) were warmed to 40–50 °C within 10 min and then stirred at room temperature for 4–24 h (TLC). The solvent was evaporated under reduced pressure and residue was purified on silica gel (hexane-ethylacetate, 4:1).

2-Phenyl-3-benzoyl-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8ay**)

Yield: 71%, m.p. 168–169 °C. $C_{21}H_{22}N_2O_3$ (350.4); calc.: C 71.97, H 6.33, N 7.99; found: C 71.82, H 6.32, N 7.94. ^{1}H NMR: 1.25 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 2.10 (d, 1H, H_B-9, $J_{AB} = 14.1$ Hz), 2.44 (d, 1H, H_A-9), 2.63 (dd, 1H, H_A-4, $J_{AB} = 12.3$ Hz, $J_{3,4A} = 6$ Hz), 3.09 (dd, 1H, H_B-4, $J_{3,4B} = 8.4$ Hz), 5.39 (dd, 1H, H-3), 6.84 (br.s, 1H, NH), 6.93–8.11 (m, 10H, aromat. H). ^{13}C NMR: 29.77 (q, CH_3), 29.89 (q, CH_3), 40.49 (t, C-4). 47.38 (t, C-9), 54.00 (s, C-8), 63.83 (d, C-3), 85.97 (s, C-5), 115.33, 122.39, 128.29, 128.64, 128.76, 128.94, 133.69, 133.88, 150.07 (aromat. C), 173.19 (s, C-6), 196.31 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8az**)

Yield: 63%, m.p. 143–144 °C. $C_{21}H_{20}Cl_2N_2O_3$ (419.3); calc.: C 60.15, H 4.81, N 6.68; found: C 59.90, H 4.81, N 6.69. ^{1}H NMR: 1.26 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.14 (d, 1H, H_B-9, $J_{AB} = 14.1$ Hz), 2.29 (d, 1H, H_A-9), 2.74 (dd, 1H, H_A-4, $J_{AB} = 12.3$ Hz, $J_{3,4A} = 3.3$ Hz), 2.96 (dd, 1H, H_B-4, $J_{3,4B} = 7.8$ Hz), 5.31 (dd, 1H, H-3), 6.87–7.45 (m, 8H, aromat. H). ^{13}C NMR: 29.79 (q, CH_3), 29.93 (q, CH_3), 37.55 (t, C-9), 47.97 (t, C-4), 53.82 (s, C-8), 72.49 (d, C-3), 86.78 (s, C-5), 115.05, 122.48, 127.30, 128.59, 130.12, 130.28, 131.58, 136.12, 137.33, 149.81 (aromat. C), 173.17 (s, C-6), 198.74 (s, C=O).

2-Phenyl-3-benzoyl-6-oxo-7-(1-methylethenyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8by**)

Yield: 50%, m.p. 141–142 °C. $C_{24}H_{26}N_2O_3$ (390.5); calc.: C 73.81, H 6.71, N 7.17; found: C 73.62, H 6.75, N 7.19. ^{1}H NMR: 1.31 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 2.13 (d, 1H, H_B-9, $J_{AB} = 14.1$ Hz), 2.49 (d, 1H, H_A-9), 2.58 (dd, 1H, H_A-4, $J_{AB} = 14.6$ Hz, $J_{3,4A} = 5.7$ Hz), 3.12 (dd, 1H, H_B-4, $J_{3,4B} = 8.1$ Hz), 4.91 (s, 1H, $=CH_A$), 5.19 (s, 1H, $=CH_B$), 5.46 (dd, 1H, H-3), 6.95–8.13 (m, 10H, aromat. H). ^{13}C NMR: 21.95 (q, CH_3), 28.20 (q, CH_3), 28.69 (q, CH_3), 40.50 (t, C-9), 46.93 (t, C-4), 60.07 (s, C-8), 70.07 (d, C-3), 84.76 (s, C-5), 115.42, 115.68, 122.56, 128.68, 128.74, 128.81, 128.98, 133.76, 134.95, 139.57, 150.30 (aromat. C), 170.34 (s, C-6), 196.43 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-7-(1-methylethenyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8bz**)

Yield: 50%, m.p. 155–156 °C. $C_{24}H_{24}Cl_2N_2O_3$ (459.3); calc.: C 62.75, H 5.27, N 6.10; found: C 62.74, H 5.27, N 6.13. ^{1}H NMR: 1.33 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 2.18 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 2.35 (d, 1H, H_A-9), 2.74 (dd, 1H, H_A-4, J_{AB} = 12.9 Hz, $J_{3,4A}$ = 3.9 Hz), 3.00 (dd, 1H, H_B-4, $J_{3,4B}$ = 8.1 Hz), 4.90 (s, 1H, =CH_A), 5.19 (s, =CH_B), 5.32 (dd, 1H, H-3), 6.93–7.49 (m, 8H, aromat. H). ^{13}C NMR: 21.83 (q, CH_3), 28.30 (q, CH_3), 28.65 (q, CH_3), 37.49 (t, C-4), 47.54 (t, C-9), 59.72 (s, C-8), 72.78 (d, C-3), 85.54 (s, C-5), 115.00, 115.59, 122.56, 127.30, 128.62, 130.17, 130.26, 131.63, 136.14, 137.34, 139.62, 150.05 (aromat. C), 170.14 (s, C-6), 199.83 (s, C=O).

2-Phenyl-3-benzoyl-6-oxo-7-butyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8cy**)

Yield: 60%, m.p. 130–131 °C. $C_{25}H_{30}N_2O_3$ (406.5); calc.: C 73.87, H 7.44, N 6.89; found: C 73.92, H 7.42, N 6.80. ^{1}H NMR: 0.94 (t, 3H, H-4′), 1.28 (s, 3H, CH_3), 1.32 (m, 2H, H-3′), 1.42 (s, 3H, CH_3), 1.58 (m, 2H, H-2′), 2.03 (d, 1H, H_B-9, J_{AB} = 13.8 Hz), 2.43 (d, 1H, H_A-9), 2.58 (dd, 1H, H_A-4, J_{AB} = 13.2 Hz, $J_{3,4A}$ = 6.3 Hz), 3.07–3.19 (m, 3H, H_B-4, H_2-1′), 5.43 (dd, 1H, H-3, $J_{3,4B}$ = 8.1 Hz), 6.94–8.12 (m, 10H, aromat. H). ^{13}C NMR: 13.82 (q, C-4′), 20.52 (t, C-3′), 27.67 (q, CH_3), 28.19 (q, CH_3), 31.31 (t, C-2′), 39.94 (t, C-9), 40.94 (t, C-1′), 46.66 (t, C-4), 58.34 (s, C-8), 70.25 (d, C-3), 84.61 (s, C-5), 115.50, 122.49, 128.65, 128.79, 128.99, 133.69, 135.06, 150.41 (aromat. C), 170.94 (s, C-6), 196.50 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-7-butyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8cz**)

Yield: 88%, m.p. 118–119 °C. $C_{25}H_{28}Cl_2N_2O_3$ (475.4); calc.: C 63.16, H 5.94, N 5.89; found: C 63.21, H 6.03, N 5.87. ^{1}H NMR: 0.92 (t, 3H, H-4′), 1.29 (s, 3H, CH_3), 1.26–1.37 (m, 2H, H-3′), 1.39 (s, 3H, CH_3), 1.51–1.62 (m, 2H, H-2′), 2.09 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 2.28 (d, 1H, H_A-9), 2.71 (dd, 1H, H_A-4, J_{AB} = 13.2 Hz, $J_{3,4A}$ = 3.9 Hz), 2.98 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.8 Hz), 3.14 (dd, 2H, 2H-1′), 5.30 (dd, 1H, H-3), 6.94–7.46 (m, 8H, aromat. H). ^{13}C NMR: 13.81 (q, C-4′), 20.49 (t, C-3′), 27.77 (q, CH_3), 28.16 (q, CH_3), 31.28 (t, C-2′), 37.91 (t, C-9), 39.99 (t, C-1′), 47.23 (t, C-4), 58.11 (s, C-8), 72.88 (d, C-3), 85.44 (s, C-5), 115.21, 122.56, 127.28, 128.61, 130.14, 130.24, 131.66, 136.21, 137.29, 150.17 (aromat. C), 170.78 (s, C-6), 199.76 (s, C=O).

2-Phenyl-3-benzoyl-6-oxo-7-allyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8dy**)

Yield: 85%, m.p. 56–57 °C. $C_{24}H_{26}N_2O_3$ (390.5); calc.: C 78.82, H 5.87, N 6.27; found: C 78.86, H 5.82, N 6.11. ^{1}H NMR: 1.28 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.06 (d, 1H, H_B-9, J_{AB} = 14.1 Hz), 2.45 (d, 1H, H_A-9), 2.59 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 6.3 Hz), 3.12 (dd, 1H, H_B-4, $J_{3,4B}$ = 8.1 Hz), 3.86 (dd, 2H, H-1′), 5.16 (m, 2H, H-3′), 5.43 (dd, 1H, H-3), 5.81 (m, 1H, H-2′), 6.96–7.59 (m, 10H, aromat. H). ^{13}C NMR: 27.64 (q, CH_3), 28.13 (q, CH_3), 40.85 (t, C-9), 42.28 (t, C-1′), 46.78 (t, C-4), 58.55 (s, C-8), 70.07 (d, C-3), 84.47 (s, C-5), 115.51, 117.01, 122.51, 128.61, 128.74, 128.92, 133.65, 133.99, 135.00, 150.22, (aromat. C), 170.83 (s, C-6), 196.36 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-7-allyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8dz**)

Yield: 65%, m.p. 76–78 °C. $C_{24}H_{24}Cl_2N_2O_3$ (459.4); calc.: C 62.75, H 5.27, N 6.10; found: C 62.77, H 5.24, N 6.08. ^{1}H NMR: 1.31 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.13 (d, 1H, H_B-9), J_{AB} = 14.1 Hz), 2.32 (d, 1H, H_A-9), 2.75 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 6.9 Hz), 3.01 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.8 Hz), 3.89 (dd, 2H, H-1′), 5.17 (m, 2H, H-3′), 5.34 (dd, 1H, H-3), 5.82 (m, 1H, H-2′), 6.96–7.48 (m, 8H, aromat. C). ^{13}C NMR: 27.74 (q, CH_3), 28.08 (q, CH_3), 37.82 (t, C-9), 42.30 (t, C-1′), 47.28 (t, C-4), 58.27 (s, C-8),

72.73 (d, C-3), 85.23 (s, C-5), 115.16, 116.99, 122.54, 127.22, 128.55, 129.03, 130.11, 130.20, 133.98, 135.34, 149.65 (aromat. C), 170.92 (s, C-6), 199.35 (s, C=O).

2-Phenyl-3-benzoyl-6-oxo-7-acetyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8ey**)

Yield: 50%, m.p. 140–141 °C. $C_{23}H_{24}N_2O_4$ (392.4); calc.: C 7.39, H 6.16, N 7.14; found: C 70.48, H 6.23, N 7.17. ^{1}H NMR: 1.57 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 2.13 (d, 1H, H_B-9, J_{AB} = 14.4 Hz), 2.35 (s, 3H, CH_3), 2.42 (d, 1H, H_A-9), 2.74 (dd, 1H, H_A-4, J_{AB} = 12.6 Hz, $J_{3,4A}$ = 5.4 Hz), 3.07 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.8 Hz), 5.52 (dd, 1H, H-3), 6.97–8.11 (m, 10H, aromat. H). ^{13}C NMR: 26.09 (q, CH_3), 27.00 (q, CH_3), 29.62 (q, CH_3), 38.77 (t, C-9), 45.77 (t, C-4), 60.82 (s, C-8), 69.16 (d, C-3), 85.10 (s, C-5), 114.47, 122.58, 128.80, 128.98, 133.79, 134.69, 149.81 (aromat. C), 171.94 (s, C-6), 173.79 (s, $COCH_3$), 195.83 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-7-acetyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8ez**)

Yield: 45%, m.p. 95–96 °C. $C_{23}H_{22}Cl_2N_2O_4$ (461.3); calc.: C 59.88, H 4.81, N 6.07; found: C 60.02, H 4.78, N 5.99. ^{1}H NMR: 1.57 (s, 3H, CH_3), 1.66 (s, 3H, CH_3), 2.12 (d, 1H, H_B-9, J_{AB} = 14.2 Hz), 2.28 (d, 1H, H_A-9), 2.33 (s, 3H, CH_3), 2.83 (dd, 1H, H_A-4, J_{AB} = 12.6 Hz, $J_{3,4A}$ = 3.6 Hz), 3.00 (dd, 1H, H_B-4, $J_{3,4B}$ = 7.8 Hz), 5.42 (dd, 1H, H-3), 6.86–7.45 (m, 8H, aromat. H). ^{13}C NMR: 26.16 (q, CH_3), 26.98 (q, CH_3), 28.66 (q, CH_3), 36.62 (t, C-9), 46.21 (t, C-4), 60.67 (s, C-8), 71.57 (d, C-3), 85.60 (s, C-5), 114.31, 122.67, 127.43, 128.84, 129.10, 130.14, 130.38, 131.60, 136.06, 137.53, 149.49 (aromat. C), 171.93 (s, C-6), 173.68 (s, $COCH_3$), 199.28 (s, C=O).

2-Phenyl-3-benzoyl-6-oxo-7-(1,1-dimethylethoxycarbonyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8fy**)

Yield: 62%, m.p. 146–147 °C. $C_{26}H_{30}N_2O_5$ (450.5); calc.: C 69.31, H 6.71, N 6.22; found: C 69.18, H 6.57, N 6.22. ^{1}H NMR: 1.54 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.70 (s, 9H, 3 × CH_3), 2.07 (d, 1H, H_B-9, J_{AB} = 14.4 Hz), 2.44 (d, 1H, H_A-9), 2.64 (dd, 1H, H_A-4, J_{AB} = 12.3 Hz, $J_{3,4A}$ = 6.0 Hz), 3.13 (dd, 1H, H_B-4, $J_{3,4B}$ = 8.1 Hz), 5.47 (dd, 1H, H-3), 6.98–8.10 (m, 10H, aromat. H). ^{13}C NMR: 27.01, 27.99, 28.56 (q, CH_3), 40.25 (t, C-9), 46.13 (t, C-4), 60.36 (s, C-8), 69.63 (d, C-3), 83.29 (s, C–*t*-Bu), 84.45 (s, C-5), 115.39, 122.69, 128.72, 128.76, 128.87, 133.74, 134.86, 149.70 (aromat. C), 150.02 (s, C–*t*-Bu), 171.64 (s, C-6), 195.95 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-7-(1,1-dimethylethoxycarbonyl)-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8fz**)

Yield: 77%, m.p. 46–47 °C. $C_{26}H_{28}Cl_2N_2O_5$ (519.4); calc.: C 60.12, H 5.43, N 5.39; found: C 60.21, H 5.45, N 5.41. ^{1}H NMR: 1.53 (s, 9H, 3 × CH_3), 1.56 (s, 3H, CH_3), 1.65 (s, 3H, CH_3), 2.11 (d, 1H, H_B-9, J_{AB} = 14.4 Hz), 2.32 (d, 1H, H_A-9), 2.76 (dd, 1H, H_A-4, J_{AB} = 10.2 Hz, $J_{3,4A}$ = 3.6 Hz), 3.02 (dd, 1H, H-4, $J_{3,4B}$ = 7.8 Hz), 5.35 (dd, 1H, H-3), 6.91–7.46 (m, 8H, aromat. H). ^{13}C NMR: 27.01, 27.91, 27.99 (q, CH_3), 37.31 (t, C-9), 46.59 (t, C-4), 59.76 (s, C-8), 72.22 (d, C-3), 83.26 (s, C–*t*-Bu), 85.19 (s, C-5), 114.91, 122.64, 127.28, 128.67, 130.08, 130.19, 121.53, 136.07, 137.36, 149.39 (aromat. C), 150.10 (s, C=O–Boc), 171.51 (s, C-6), 199.33 (s, C=O).

2-Phenyl-3-benzoyl-6-oxo-7-methoxycarbonyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8gy**)

Yield: 50%, m.p. 115–116 °C. $C_{23}H_{24}N_2O_5$ (408.4); calc.: C 67.63, H 5.92, N 6.86; found: C 67.54, H 5.88, N 6.99. ^{1}H NMR: 1.26 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.04 (d, 1H, H_B-9, J_{AB} = 14.2 Hz), 2.42

(d, 1H, H_A-9), 2.55 (dd, 1H, H_A-4, $J_{AB} = 12.1$ Hz, $J_{3,4A} = 6.1$ Hz), 2.79 (s, 3H, OCH_3), 3.12 (dd, 1H, H_B-4, $J_{3,4B} = 7.6$ Hz), 5.41 (dd, 1H, H-3), 6.96–8.11 (m, 10H, aromat. H). ^{13}C NMR: 24.64 (q, CH_3), 26.14 (q, CH_3), 27.21 (q, CH_3), 41.57, 46.57 (t, C-4, C-9), 57.64 (s, C-8), 70.13 (d, C-3), 84.81 (s, C-5), 115.76, 122.65, 128.69, 128.80, 128.96, 133.72, 135.08, 150.16 (aromat. C), 170.76 (s, C-6), 196.40 (s, C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-6-oxo-7-methoxycarbonyl-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]-nonane (**8gz**)

Yield: 75%, m.p. 142–143 °C. $C_{23}H_{22}Cl_2N_2O_5$ (477.3); calc.: C 57.87, H 4.65, N 5.87; found: C 57.77, H 4.64, N 5.82. ^{1}H NMR: 1.27 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 2.10 (d, 1H, H_B-9, $J_{AB} = 14.1$ Hz), 2.31 (d, 1H, H_A-9), 2.72 (dd, 1H, H_A-4, $J_{AB} = 12.6$ Hz, $J_{3,4A} = 3.6$ Hz), 2.78 (s, 3H, OCH_3), 2.99 (dd, 1H, H_B-4, $J_{3,4B} = 8.1$ Hz), 5.29 (dd, 1H, H-3), 6.94–7.46 (m, 8H, aromat. H). ^{13}C NMR: 24.39 (q, CH_3), 25.93 (q, CH_3), 26.85 (q, CH_3), 37.80, 46.79 (t, C-4, C-9), 57.07 (s, C-8), 72.58 (d, C-3), 85.37 (s, C-5), 115.10, 122.38, 128.33, 129.88, 129.97, 131.35, 135.93, 149.70 (aromat. C), 170.38 (s, C-6), 199.49 (s, C=O).

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