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Cycloaddition of Bifunctional Nitrones to Monosubstituted Alkenes, I

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Cycloaddition of bifunctional nitrones **1** containing a nitrone function as part of the 1,4-diazabutadiene system to electron-rich monosubstituted alkenes has been investigated. The nitrone group manifested predominant 1,3-dipolar reactivity compared with that of the 1,3-heterodiene system leading to isoxazolidine derivatives **2** and **3**. An atypical assistance of the 1,4-diazabutadiene system was demonstrated by a reverse regioselectivity of cycloadditions to allyl alcohol yielding bicyclic heterocycles **2** via 3,4-disubstituted isoxazolidines. Cycloadditions with allyl halides gave 3,5-disubstituted isoxazolidines **3** showing common regioselectivity for the nitrone function. The mechanism and configuration of the products are discussed.

Cycloaddition von bifunktionellen Nitronen an monosubstituierte Alkene, I

Die Cycloaddition der bifunktionellen Nitrone **1**, die die Nitronfunktion als Teil eines 1,4-Diazabutadien-Systems enthalten, an elektronenreiche monosubstituierte Alkene wurde untersucht. Gegenüber dem 1,3-Heterodiensystem wies die Nitrongruppe eine bevorzugte 1,3-dipolare Reaktivität auf, wobei die Isoxazolidinderivate **2** und **3** entstanden. Eine atypische Beteiligung des 1,4-Diazabutadiensystems zeigte sich durch eine umgekehrte Regioselektivität der Cycloadditionen an Allylalkohol, die bicyclische Heterocyclen **2** über 3,4-disubstituierte Isoxazolidine ergaben. Cycloadditionen mit Allylhalogeniden führten gemäß der üblichen Regioselektivität der Nitrofunktion zu 3,5-disubstituierten Isoxazolidinen **3**. Der Mechanismus sowie die Konfiguration der Produkte werden diskutiert.

Although 1,3-dipolar cycloadditions of simple nitrones with alkenes have widely been studied[1)], well recognized[2)], and utilized for organic syntheses[3)], such reactions of bifunctional nitrones possessing a nitrone function incorporated into a 1,3-heterodiene skeleton have hardly been investigated. Those which were reported[4,5)], concerned exclusively on bifunctional nitrones containing the 1-oxa-4-azabutadiene system. Our attention has been directed towards cycloaddition of such bifunctional nitrones in which a nitrone group is a part of the 1,4-diazabutadiene system. This system can be considered as an efficient "masked" 1,3-dipol regarding a number of reactions with aryl isothio- and isocyanates[6)]. The bifunctional 1,4-diazabutadiene-nitrones **1** were readily available via condensation of acetophenone anils with nitrosobenzenes[7,8)].

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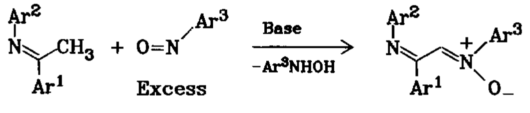


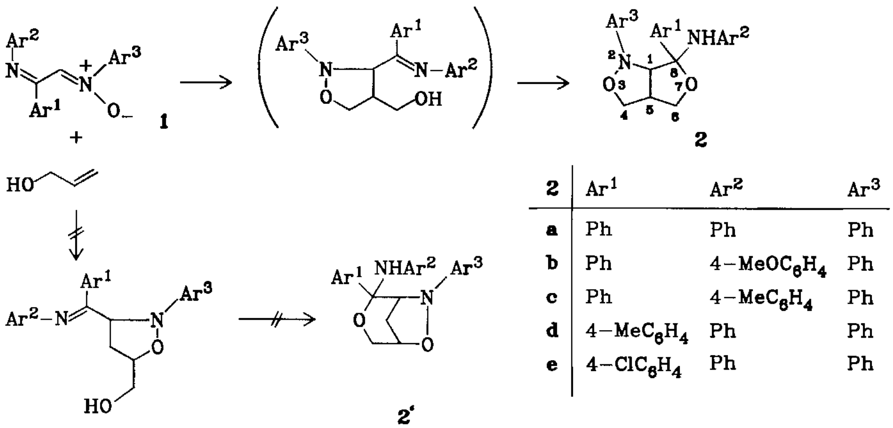
1

Cycloaddition to Allyl Alcohol

The compounds 1 were treated with an excess of allyl alcohol in dichloromethane at room temperature. After 48 h standing crystalline 1:1 adducts were isolated with yields about 80%. Spectroscopic behaviour of these products indicated participation of both nitrone and 1,3-heterodiene functions in cycloaddition.

The IR spectra showed a strong NH absorption at approximately 3400 cm^{-1} but not bands for hydroxyl, azomethine, and nitrone groups. The ^{1}H NMR spectra confirmed the presence of the amino group in the adduct molecule revealing broad singulets at approximately 5.6 ppm. A bunch of signals between 3.5 and 4.5 ppm was ascribed to six protons probably attached to iso- or *n*-butane skeleton. The ^{13}C NMR spectra supported this arrangement of aliphatic carbon atoms showing two closely positioned triplets and two doublets originating from two methylene and two methine groups. These signals indicated that both methylene groups were joined to oxygen (68.8 ppm, $^1J_{CH}$ = 150.0 Hz, 70.2 ppm, $^1J_{CH}$ = 145.0 Hz), whereas one of the methine groups (49.8 ppm, $^1J_{CH}$ = 135.0 Hz) seemed to be bonded only to carbon atoms. Another (83.2 ppm, $^1J_{CH}$ = 146.0 Hz) could be attached to nitrogen. A signal belonging to a quaternary carbon was also observed (93.4 ppm).

The electron impact spectra of the products suggested a bond between a quaternary carbon and oxygen revealing prominent peaks of benzanilide-type radical ions. Furthermore, this carbon bore both aryl and arylamino substituents. On the other hand the parent isoxazolidine-type ions responsible for peaks at m/z = 161 ejected a neutral formaldehyde molecule (m^*) proving that at least one of the methylene groups was bonded to oxygen.



2	Ar¹	Ar²	Ar³
a	Ph	Ph	Ph
b	Ph	4-MeOC$_6$H$_4$	Ph
c	Ph	4-MeC$_6$H$_4$	Ph
d	4-MeC$_6$H$_4$	Ph	Ph
e	4-ClC$_6$H$_4$	Ph	Ph

All these spectral evidences indicated that cycloaddition products possessed rather a tetrahydrofuran-isoxazolidine structure 2 than that represented by a tetrahydropyran-isoxazolidine **2'**. Then the virtual 1,3-dipolar cycloaddition of the nitrone group to the monosubstituted alkene yielded a 3,4-disubstituted isoxazolidine instead of the common 3,5-disubstituted one[1,4]. The other five-membered ring resulted from an ordinary addition of the hydroxyl group to the carbon-nitrogen double bond[9].

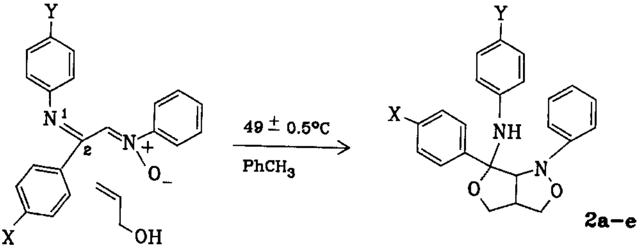
Mechanistic Aspects

The regioselective formation of tetrahydrofuran-isoxazolidines **2** is connected with one inter- and one intramolecular more or less independent processes. Kinetic measurements exposed second order kinetics proving that the intermolecular process controlled the reaction rate and the intramolecular reaction was either a rapid one or synchroneous with the intermolecular reaction. However, this intermolecular process could be the 1,3-cycloaddition of the nitrone group to the double bond or addition of the hydroxy group to the C=N double bond. Differentiation between these intermolecular steps was made with the help of activation parameters. Thus, activation enthalpy ΔH^{+} was found to be 44.4 ± 2.1 $kJ \cdot mol^{-1}$ and activation entropy ΔS^{+} equal to -186.2 ± 6.6 $J \cdot mol^{-1} \cdot deg^{-1}$. The first reflects well the second order kinetics[10] whereas the latter expresses a cyclic transition state relating more to a 1,3-cycloaddition than to a common addition. Such a low activation entropy for a non-cyclic transition state would be found only if it were more polar compared with any of the reactants[11]. On the contrary, the rate constant became smaller along with an increase of solvent polarity exposing lower polarity of the transition state than at least of one of the reagents. In conclusion, the virtual 1,3-cycloaddition controlls the formation of the products. The solvent effect upon the rate constant of formation of **2c** is exemplified below.

Solvent	Dielectric Constant ε (25 °C)[12]	$10^{-6} \cdot k$ (dcm^3 mol^{-1} s^{-1}) (Reaction Temp. 49 ± 0.5 °C)
toluene	2.4	206 ± 6.7
chlorobenzene	5.6	191 ± 4.5
dichloromethane	8.9	78.2 ± 0.8
benzonitrile	25.0	30.9 ± 1.4
n-octanol	—	18.9 ± 0.5
n-propanol	(24.0)	7.1 ± 0.1

Strong effect of both protic solvents impeding the reaction rate might express competition between intramolecular addition of an hydroxy group to the C=N double bond and intermolecular N,O-acetal formation with the alcohol used.

According to expectations substituents located in the aryl ring at C-2 of the 1,4-diazabutadiene N^4-oxide moiety in **1** did not affect at all the reaction rate. This was fully consistent with perpendicular orientation of this ring in relation to the 1,3-heterodiene π-orbital system[13]. In contrast, substituents located in the aryl ring attached to N-1 affected visibly the rate constant supporting its coplanar arrangement.



	Substituent X	Y	$10^{-6} \cdot k$ (dcm^3 mol^{-1} s^{-1})
2b	H	OMe	218 ± 4.0
c	H	Me	206 ± 6.7
a	H	H	93.2 ± 4.3
d	Me	H	97.7 ± 2.5
e	Cl	H	89.3 ± 1.9

Configuration of the Tetrahydrofuran-isoxazolidines 2

^{13}C NMR spectra evidenced a high diastereoselectivity of the 1,3-cycloaddition (chirality at C-1 and C-8 in **2**) suggesting that only one transition state was prac-

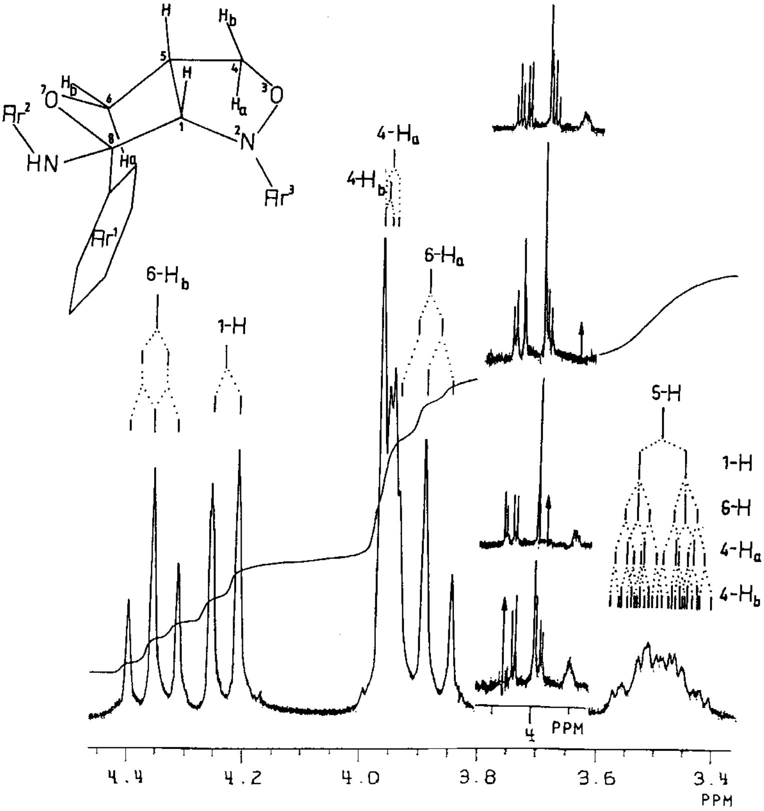


Figure 1. The region from 3.4 to 4.4 ppm of the 200 MHz ^{1}H NMR spectrum (CDCl$_3$) of 8-anilino-2,8-diphenyl-3,7-dioxa-2-azabicyclo[3.3.0]octane (**2a**) and its selective decoupling. Arrows point out a place of irradiation

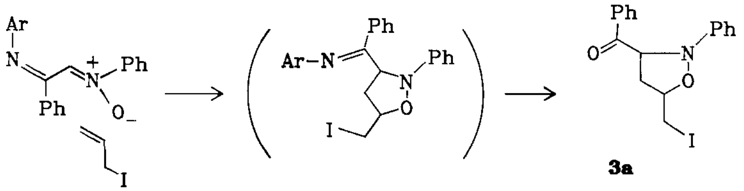
tically involved leading to a C-1/C-5 *cis*-configuration (compare formula in Fig. 1). The 200 MHz ^{1}H NMR spectra permitted to establish the configuration.

Triplets at 4.35 and 3.89 ppm were ascribed to the C-6 methylene protons. Difference in their chemical shift seemed to be due to a through space effect of pseudo-axially oriented aryl ring at C-8, deshielding the proton 6-H_a and ultimately provoking geminal coupling with the proton 6-H_b. Accidentally the geminal coupling constant was equal to the vicinal coupling constant characterizing coupling with 5-H (ABM spin system $J_{6_a,6_b} = J_{6_a,5} = J_{6_b,5} = 8.4$ Hz). This also reflected rather synclinal conformation of 6-H_a, 6-H_b, and 5-H. The doublet at 4.23 ppm corresponded to 1-H ($J_{1,5} = 9.2$ Hz). This coupling constant indicated practically *syn*-periplanar orientation of 1-H in relation to 5-H (angle of torsion close to 10°)[14]. Two closely positioned doublets at 3.94 and 3.96 ppm were from 4-H_a and 4-H_b and expressed vicinal coupling with 5-H. Both coupling constants were slightly different because of difference of torsion angle in this synclinal-type conformation ($J_{4_a,5} = 4.7$, $J_{4_b,5} = 4.9$ Hz). The multiplet at 3.49 ppm was produced by 5-H. Such assignment of the signals was fully supported by decoupling (Figure 1).

Thus the 200 MHz ^{1}H NMR spectra proved the 8-(arylamino)-2,8-diaryl-3,7-dioxa-2-azabicyclo[3.3.0]octane structure of **2**.

Cycloaddition to Allyl Halides

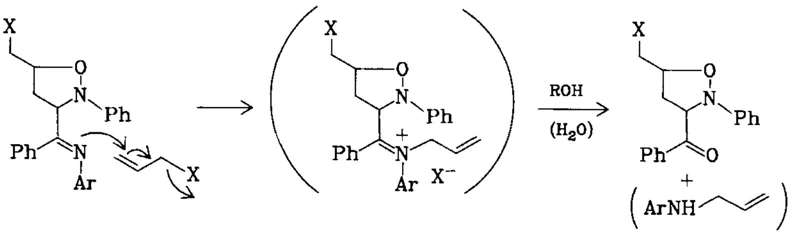
Three bifunctional nitrones **1** differently substituted in the aryl ring linked to N-1 were first used for cycloaddition to allyl iodide but in all the cases the same product was obtained. This suggested loss of the arylimino fragment during the process. Combustion analysis confirmed it. The IR spectrum of the product isolated showed strong carbonyl absorption at 1685 cm^{-1}. The ^{1}H NMR spectrum contained a multiplet of ten aromatic protons at 7.0 to 8.3 ppm, a four line signal at 5.2, a pentet at 4.5, a doublet at 3.4, and a multiplet at 2.7 ppm. Such a pattern fitted well the 3-benzoyl-5-(iodomethyl)-2-phenylisoxazolidine structure **3a**. The ^{13}C NMR spectrum confirmed this structure exposing a singlet at 196.2 ppm (CO), a triplet at 4.8 ppm ascribed to the iodomethyl group[14] ($J_{CH} = 153.1$ Hz), and a triplet at 36.2 ppm ($J_{CH} = 137.2$ Hz). The C-3 and C-5 methine groups produced doublets at 77.6 and 69.3 ppm, respectively ($J_{C\text{-}3,H} = 151.2$ and $J_{C\text{-}5,H} = 143.8$ Hz). The mass spectrum showed the molecular peak at $m/z = 393$. The most prominent peak in the spectrum was due to loss of the benzoyl radical ($M^+ - PhCO$, $m/z = 288$, 100%). Then cycloaddition with allyl iodide reflected the common regioselectivity of the nitrone group yielding a 5-substituted isoxazolidine **3a** in contrast to the analogous reaction with allyl alcohol producing 4-substituted isoxazolidines **2**. The difference of regioselectivity can be explained by an assistance of the 1,4-diazabutadiene fragment in cycloaddition with allyl alcohol. The azo-



3a

methine group anchors the hydroxyl group perhaps via hydrogen bonding, fixing in this way preorientation of the alkene double bond. Such an anchoring effect is obviously impossible in the case of allyl iodide. However, the formal hydrolysis of the imino group was rather an obscure process.

Also cycloadditions with allyl bromide and allyl chloride produced 3-benzoyl-5-(halomethyl)-2-phenylisoxazolidines **3**. As a tentative explanation it was assumed that this hydrolysis was promoted by alkylation of N-1 because of an excess of the allyl halide used (arylamines were in fact detectable in the reaction mixtures).



	X
3a	I
b	Br
c	Cl

Configuration of 3-Benzoyl-5-(halomethyl)-2-phenylisoxazolidines 3

Cycloaddition to allyl halides showed also diastereoselectivity. The correct configuration of **3** was established with the help of the 200 MHz ^1H NMR spectra.

A four line signal in **3a** at 5.25 ppm (AXX' three spin system) was ascribed to 3-H ($J_{3,4_{ax}} = 9.4$ and $J_{3,4_{eq}} = 4.2$ Hz). 5-H caused a pentet-like multiplet at 4.53 ppm (AM_2XX' with $J_{AM} = J_{AX} < J_{AX'}$). The AM_2 coupling described spin interactions of 5-H and the isochronic CH_2-Hal protons whereas the AX coupling corresponded to those of 5-H and 4-H in more synclinal conformation ($J_{5,CH_2} = J_{5,4_{eq}} = 7.3$ Hz). The AX' coupling related to interactions of 5-H with the pseudo-axial 4-H ($J_{5,4_{ax}} = 9.3$ Hz). The diastereotopic ring methylene protons caused two triplets at 2.56 and 2.62 ppm and two quartets at 2.72 and 2.78 ppm. The triplets were ascribed to the pseudo-axial proton 4-H forming an AMX-type spin system ($J_{5,4} = J_{5,3} = 9.3$ Hz). The quartets were produced by the pseudo-equatorial 4-H due to coupling with 3-H and 5-H. This indicated the pseudo-equatorial location of both substituents at C-3 and C-5. The protons 3-H, 4-H_{ax}, and 5-H seemed to be arranged in antiperiplanar configuration with a torsion angle between 150 and 180°. 4-H_{eq} was then oriented between 3-H and 5-H forming dihedral angles about 60° and 30°, respectively (Figure 2).

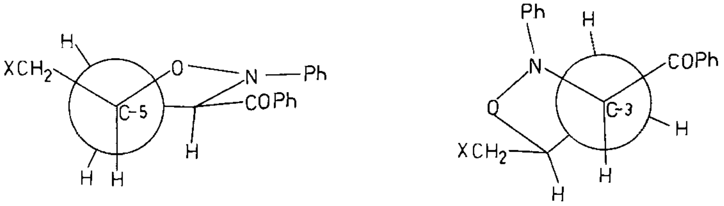


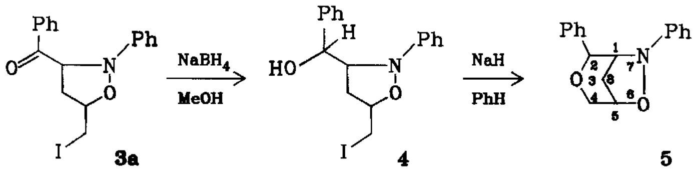
Figure 2. Conformation of vicinal protons attached to C-4, C-5 and C-3, C-4 of 3-benzoyl-5-(halomethyl)isoxazolidines **3a – c**

The halomethylene protons in **3a – c** produced doublets at 3.38 (CH_2I), 3.56 (CH_2Br), and 3.69 ppm (CH_2Cl). The coupling constants were as expected for rapidly rotating vicinal protons[14], i. e., 7.2 to 7.4 Hz.

2,7-Diphenyl-3,6-dioxa-7-azabicyclo[3.2.1]octane (5)

Pseudo-equatorial location of the benzoyl and halomethyl groups in **3** suggested a possibility of a six-membered ring closure leading to a bicyclic isoxazolidine **5**, an alternative product of cycloaddition of bifunctional nitrones **1** to allyl alcohol. Comparison of both compounds **2** and **5** could be the final proof for their structure and cyclisation mechanism.

Reduction of 3-benzoyl-5-(iodomethyl)-2-phenylisoxazolidine (**3a**) by means of sodium borohydride in methanol yielded nearly quantitatively 3-(hydroxyphenylmethyl)-5-(iodomethyl)-2-phenylisoxazolidine (**4**) which cyclized to the desired product **5** after short reflux in benzene in the presence of sodium hydride.



3a **4** **5**

The ^{13}C NMR spectrum revealed essential differences compared to that of **2a**. A triplet of the bridged methylene group (C-8) appeared at 34.1 ppm (J_{CH} = 148.9 Hz). Three methine carbons C-1, C-2, and C-5 produced doublets at 73.5, 80.3, and 69.4 ppm, respectively. The proper assignment of these signals was facilitated by the coupling constants ($J_{C\text{-}1,H}$ = 146.3, $J_{C\text{-}2,H}$ = 152.8, and $J_{C\text{-}5,H}$ = 143.2 Hz). Electron impact induced fragmentation of **5** was based on ejection of a neutral molecule of benzaldehyde from the molecular ion. This resembled fragmentation of the compounds **2**. However, further pathways manifested structural differences between both bicyclic isoxazolidines **2** and **5**. Thus, loss of a benzanilide molecule by the molecular ions of **2** led to 4-substituted isoxazolidine radical ions whereas loss of benzaldehyde by the molecular ion of **5** produced 5-substituted isoxazolidine radical ions. From the former a formaldehyde molecule is detached yielding aziridine-type radical ions causing the most prominent peak in the spectrum ($m/z = 131$). Such a fragmentation was hardly possible for 5-substituted isoxazolidine radical ion and a peak at $m/z = 131$ was negligible. On the other hand fragmentation of the 5-substituted isoxazolidine radical ion suggested a number of skeletal and hydrogen rearrangements facilitating detachment of an acetyl and an hydroxyl radical that caused appearance of the prominent peaks at m/z = 146, 144, and 143 which were not observed in the spectra of the compounds **2**.

Configuration of 5 was established on the basis of the 200 MHz ^1H NMR spectrum.

The C-8 methylene protons produced a triplet-like signal at 2.21 ppm (ABM spin system). The coupling constants ($J_{8,5}$ = 2.4 and $J_{8,1}$ = 2.6 Hz) indicated the synclinal conformations of 8-H, 5-H and 8-H, 1-H. A triplet at 4.75 ppm was ascribed to 1-H vicinally coupled only with 8-H. The proton 2-H adopted perpendicular orientation in relation to 1-H ($J_{1,2}$ = 0). It produced a slightly broadened singlet at 4.65 ppm. The C-4 methylene protons were seen as a pair of doublets at 3.86 and 3.74 ppm ($J_{5,4_{eq}}$ = 4.3, $J_{5,4_{ax}}$ = 11.2 Hz). Geminal coupling was not observed. Difference in chemical shift seemed to result from through space effect of isoxazolidine oxygen deshielding the pseudo-equatorial 4-H. As expected 5-H produced a complex multiplet at 4.14 ppm ($ABMX_2$ spin system with $J_{AM} > J_{AB} \gg J_{AX}$).

In conclusion, the six-membered ring of 2,7-diphenyl-3,6-dioxa-7-azabicyclo-[3.2.1]octane (**5**) adopts a twisted chair-type conformation.

Experimental Part

IR spectra: Perkin-Elmer 257 and Zeiss IR-71 spectrophotometers; KBr pills or Nujol/Hexachlorobutadiene mulls. – UV spectra: UV/Vis Zeiss and VSU-2P Zeiss spectrophotometers; in 0.2 cm silica transmission cells using spectrally pure ethanol. – Mass spectra: LKB-9000S and MICROMAS spectrometers; direct inlet system, 70 eV, 3.5 and 8 kV, 150 to 250°C (IS). – ^1H NMR spectra: Hitachi-Perkin Elmer 24B, Jeol-100, and Nicolet 200 spectrometers; $CDCl_3$ as solvent, TMS as internal standard. – ^{13}C NMR spectra: Nicolet 200 or Varian XL-100 spectrometers; $CDCl_3$ as solvent, reference TMS. The coupling constants $^1J_{CH}$ of aromatic carbons varied from 161 to 163.5 Hz and were not specified unless stated otherwise. The multiplicity of the long range coupling J_{CH} was designated by a star (*). – Melting points: not corrected. – Combustion analyses: Regional Laboratory of Physicochemical and Structural Research, Cracow, Poland.

Kinetic Measurements: In order to determine the rate constants and activation parameters several series of solutions of a corresponding nitrone **1** and allyl alcohol were prepared in a concentration of 0.005 and 0.5 M, respectively. Samples of these solutions mixed in a ratio 1:1 were placed into an U1 MLW thermostat to maintain a constant temperature within 0.2°C. Concentration changes of the nitrone were measured spectroscopically (λ_{max} 400 nm) in 10 to 30 min intervals for 300 min (20 measuring points). Activation parameters were evaluated for formation of **2c**. The reaction rate was measured at 29.0, 39.7, and 49.0°C within 0.2°. The rate constants $k \cdot 10^{-6}$ were 64.0 ± 1.1, 124.4 ± 1.6, and 205.7 ± 6.7 $dm^3\ mol^{-1}\ s^{-1}$, respectively. Rate constants and activation parameters were calculated on an ODRA-1305 computer (ICI 1900) using the average data taken from three sets of independent measurements.

8-Anilino-2,8-diphenyl-3,7-dioxa-2-azabicyclo[3.3.0]octane (**2a**): Typical procedure: To a solution of 0.50 g (1.7 mmol) of 1,2,4-triphenyl-1,4-diaza-1,3-butadiene N^4-oxide (**1**, $Ar^1 = Ar^2 = Ar^3 = Ph$) in 0.5 ml of dichloromethane 0.35 g (6.0 mmol) of pure allyl alcohol in 0.5 ml of dichloromethane was added. The mixture was left at room temp. for 48 h. Then the solvent was removed under reduced pressure and the oily residue was purified by column chromatography (Al_2O_3 Brockmann 90, II/III; CH_2Cl_2/*n*-pentane 1:1) and repeated crystallization from ethanol. 0.49 g (80%) of colourless prisms were obtained, m. p. 141–142°C. – IR (KBr): 3420 (NH), 2980, 2930 (aliphat CH), 2800 (OC–H), 1045, 1028 ($O-CH_2$) cm^{-1}. – ^1H NMR (60 MHz): δ = 7.6–6.4 (m, 15H), 5.8 (s, 1H), 4.25 (t, 1H, $^2J_{HH}$ = 8.8 Hz), 4.12 (d, 1H, $^3J_{HH}$ = 9.1 Hz), 3.9–3.6 (m, 3H), 3.55–3.2 (m, 1H). – ^{13}C NMR ($CDCl_3$): C-1 δ = 83.2 (dd*, $^1J_{CH}$ = 147.2, $^2J_{CH}$ = 5.2 Hz), C-4 70.2 (t, $^1J_{CH}$ = 145.3 Hz), C-5 49.8 (d, $^1J_{CH}$ = 136.2 Hz), C-6 68.8 (t, $^1J_{CH}$ = 151.0 Hz), C-8 91.4 (d*, $^2J_{CH}$ = 6.0 Hz), 2-phenyl: C-1 143.1 (s), C-2,6 116.2 (d), C-3,5 129.0 (d), C-4 121.9 (d), 8-phenyl: C-1 137.4 (s), C-2,6 127.6 (d), C-3,5 127.6 (d), C-4 126.3 (d), aniline: C-1 149.8 (s), C-2,6 113.7 (d), C-3,5 129.3 (d), C-4 117.5 (d). – MS: *m/z* = 358 (1.8%, M^+), 359 (0.4), 266 (8.0, M – PhNH), 236 (0.5, M – PhNH – CH_2O), 197 (22.7, PhNHCOPh), 180 (6.1, PhN≡CPh), 161 (7.3, M – PhNHCOPh), 160 (7.0), 162 (4.2), 131 (100, M – PhNHCOPh – CH_2O), 130 (64.9), 132 (45.2), 118 (2.0), 117 (4.0), 116 (2.6), 105 (80.3, PhCO), 104 (22.1, PhNCH), 77 (83.5, Ph), 28 (18.8, CO). – UV (ethanol, λ_{max}, ε_{max}): 208 (15800), 243 (17300), 283 nm (1690).

$C_{23}H_{22}N_2O_2$ (358.5) Calcd. C 77.1 H 6.2 N 7.8 Found C 77.0 H 6.2 N 7.7

8-(4-Methoxyanilino)-2,8-diphenyl-3,7-dioxa-2-azabicyclo[3.3.0]octane (**2b**): Analogous to **2a** from 0.50 g (1.5 mmol) of 1-(4-methoxyphenyl)-2,4-diphenyl-1,4-diazabutadiene N^4-oxide

(**1**, Ar^1 = Ar^3 = Ph, Ar^2 = 4-$CH_3OC_6H_4$) and trifold molar excess of allyl alcohol. 0.48 g (83%) of colourless prisms from ethanol; m. p. 142 – 143°C. – IR (KBr): 3400 (NH), 2990, 2930 (aliphat. CH), 2800 (OC – H), 1238 (C – OMe), 1038, 1029 cm^{-1}. – ^{1}H NMR (60 MHz): δ = 6.4 – 7.6 (m, 14H), 5.6 (s, 1H), 4.3 (t, 1H, $^2J_{HH}$ = 8.2 Hz), 4.15 (d, 1H, $^3J_{HH}$ = 9.3 Hz), 3.9 – 3.7 (m, 3H), 3.6 (s, 3H), 3.55 – 3.3 (m, 1H). – ^{13}C NMR ($CDCl_3$): C-1 δ = 83.1 (dd*, $^1J_{CH}$ = 146.0, $^2J_{CH}$ = 5.0 Hz), C-4 70.2 (t, $^1J_{CH}$ = 145.0 Hz), C-5 49.7 (d, $^1J_{CH}$ = 135.0 Hz), C-6 68.8 (t, $^1J_{CH}$ = 150.0 Hz), C-8 93.5 (d*, $^2J_{CH}$ = 6.2 Hz), 2-phenyl: C-1 142.9 (s), C-2,6 117.0 (d), C-3,5 129.0 (d), C-4 121.9 (d), 8-phenyl: C-1 137.2 (s), C-2,6 and C-3,5 127.5 (d), C-4 126.0 (d), methoxyaniline: C-1 149.7 (s), C-2,6 113.9 (d), C-3,5 113.7 (d), C-4 151.8 (s), CH_3O 55.2 (q, $^1J_{CH}$ = 144.0 Hz). – MS: *m/z* = 388 (3.2%, M$^+$), 389 (0.9), 266 (M – MeOPhNH), 227 (65.0, MeOPhNHCOPh), 210 (4.5 MeOPhN≡CPh), 161 (M – MeOPhNHCOPh), 160 (2.7), 131 (14.1, M – MeOPhNHCOPh – CH_2O), 130 (31.9), 132 (12.7), 117 (5.5), 105 (100, PhCO), 104 (34.2, PhNCH), 91 (6.8, PhN), 77 (85.4, Ph). – UV (ethanol, λ_{max}, ε_{max}): 210 (14490), 242 (16080), 307 nm (1770).

$C_{24}H_{24}N_2O_3$ (388.5) Calcd. C 74.2 H 6.2 N 7.2 Found C 74.3 H 6.2 N 7.2

8-(4-Methylanilino)-2,8-diphenyl-3,7-dioxa-2-azabicyclo[3.3.0]octane (**2c**): Similar to **2a** from 0.50 g (1.6 mmol) of 1-(4-methylphenyl)-2,4-diphenyl-1,4-diazabutadiene *N*^{4}-oxide (**1**, Ar^2 = 4-$CH_3C_6H_4$, Ar^1 = Ar^3 = Ph) and 0.28 g (4.8 mmol) of allyl alcohol. 0.51 g (86%) of colourless prisms from ethanol, m. p. 147 – 148°C. – IR (KBr): 3405 (NH), 2880, 2940 (aliphat. CH), 1318 (N – O), 1035, 1025 cm^{-1} (O – CH_2). – ^{1}H NMR (200 MHz): δ = 7.68 (d, 2H, $^3J_{HH}$ = 7.0 Hz), 7.39 (q_{AB}, 2H, $^3J_{HH}$ = 7.2 Hz), 7.26 (m, 3H), 7.12 (d, 2H, $^3J_{HH}$ = 8.1 Hz), 6.96 (t, 1H, $^3J_{HH}$ = 7.2 Hz), 6.84 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 6.59 (d, 2H, $^3J_{HH}$ = 8.1 Hz), 5.84 (s, 1H), 4.35 (t, 1H, $^3J_{HH}$ = 8.6 Hz), 4.21 (d, 1H, $^3J_{HH}$ = 9.3 Hz), 3.92 (d, 1H, $^3J_{HH}$ = 2.3 Hz), 3.96 (d, 1H, $^3J_{HH}$ = 3.6 Hz), 3.88 (t, 1H, $^3J_{HH}$ = 8.6 Hz), 3.39 – 3.58 (m, 1H), 2.42 (s, 3H). – MS: *m/z* = 372 (3.3%, M$^+$), 373 (0.8), 266 (12.0, M – MePhNH), 211 (84.3, MePhNHCOPh), 212 (15.0), 194 (5.7, MePhN≡CPh), 161 (6.4, M – MePhNHCOPh), 160 (5.6), 131 (41.5, M – MePhNHCOPh – CH_2O), 130 (43.1), 132 (29.2), 117 (6.4), 116 (3.1), 106 (19.5, MePhNH), 105 (100, PhCO), 104 (33.1, PhNCH), 91 (9.1), 77 (53.7, Ph), 28 (9.6, CO). – UV (ethanol, λ_{max}, ε_{max}): 210 (15830), 243 (16760), 288 nm (1860).

$C_{24}H_{24}N_2O_2$ (372.5) Calcd. C 77.4 H 6.5 N 7.5 Found C 77.1 H 6.6 N 7.5

8-Anilino-8-(4-methylphenyl)-2-phenyl-3,7-dioxa-2-azabicyclo[3.3.0]octane (**2d**): Analogous to **2a** from 0.50 g (1.6 mmol) of 2-(4-methylphenyl)-1,4-diphenyl-1,4-diazabutadiene *N*^{4}-oxide (**1**, Ar^1 = 4-$CH_3C_6H_4$, Ar^2 = Ar^3 = Ph) and 0.28 g (4.8 mmol) of allyl alcohol. 0.48 g (82%) of colourless prisms from ethanol, m. p. 172 – 173°C. – IR (KBr): 3398 (NH), 2930, 2880 (aliphat. CH), 1315 (N – O), 1035, 1020 cm^{-1} (O – CH_2). – ^{1}H NMR (60 MHz): δ = 7.5 – 6.4 (m, 14H), 5.8 (s, 1H), 4.2 (t, 1H, $^3J_{HH}$ = 8.3 Hz), 4.1 (d, 1H, $^3J_{HH}$ = 9.6 Hz), 3.9 – 3.6 (m, 3H), 3.5 – 3.2 (m, 1H), 2.40 (s, 3H). – ^{13}C NMR ($CDCl_3$): C-1 δ = 83.6 (dd*, $^1J_{CH}$ = 148.2, $^2J_{CH}$ = 5.6 Hz), C-4 70.2 (t, $^1J_{CH}$ = 145.8 Hz), C-5 50.0 (d, $^1J_{CH}$ = 139.8 Hz), C-6 68.9 (t, $^1J_{CH}$ = 151.8 Hz), C-8 93.1 (d*, $^2J_{CH}$ = 5.3 Hz), 2-phenyl: C-1 143.5 (s), C-2,6 115.9 (d), C-3,5 129.1 (d), C-4 122.1 (d), 8-methylphenyl: C-1 139.8 (s), C-2,6 125.9 (d), C-3,5 128.4 (d), C-4 137.2 (s), CH_3 21.0 (q, $^1J_{CH}$ = 126.5 Hz), aniline: C-1 149.7 (s), C-2,6 113.8 (d), C-3,5 129.4 (d), C-4 117.5 (d). – MS: *m/z* = 372 (3.1%, M$^+$), 373 (0.9), 280 (14.2, M – PhNH), 250 (1.0), 211 (34.8, PhNHCOPhMe), 212 (9.5), 194 (11.0, PhN≡CPhMe), 161 (4.2, M – PhNHCOPhMe), 160 (4.4), 131 (66.8, M – PhNHCOPhMe – CH_2O), 130 (77.2), 132 (35.8), 118 (7.9), 117 (11.2), 116 (4.8), 119 (100, MePhCO), 104 (32.1, PhNCH), 93 (7.0, $PhNH_2$), 92 (7.8, PHNH), 91 (32.3), 28 (1.2, CO). – UV (ethanol, λ_{max}, ε_{max}): 209 (16360), 243 (18220), 283 nm (2070).

$C_{24}H_{24}N_2O_2$ (372.5) Calcd. C 77.4 H 6.5 N 7.5 Found C 77.0 H 6.4 N 7.4

8-Anilino-8-(4-chlorophenyl)-2-phenyl-3,7-dioxa-2-azabicyclo[3.3.0]octane (**2e**): Similar to **2a** from 0.50 g (1.5 mmol) of 2-(4-chlorophenyl)-1,4-diphenyl-1,4-diazabutadiene N^4-oxide (**1**, Ar^1 = 4-ClC_6H_4, Ar^2 = Ar^3 = Ph) and 0.25 g (4.3 mmol) of allyl alcohol. 0.45 g (79%) of colourless prisms from ethanol; m. p. 189 – 190°C. – IR (KBr): 3398 (NH), 2938, 2982 (aliphat. CH), 1315 (N – O), 1090 (C – Cl), 1035, 1015 cm^{-1} (O – CH_2). – ^1H NMR (60 MHz): δ = 7.6 – 6.4 (m, 14H), 5.8 (s, 1H), 4.3 (t, 1H, $^3J_{HH}$ = 8.6 Hz), 4.1 (d, 1H, $^3J_{HH}$ = 9.4 Hz), 4.0 – 3.8 (m, 2H), 3.8 (t, 1H, $^3J_{HH}$ = 8.6 Hz), 3.7 – 3.2 (m, 1H). – MS: *m/z* = 392 (1.2%, M^+), 394 (0.4), 300 (9.3, M – PhNH), 302 (3.2), 231 (10.2, PhNHCOPhCl), 233 (3.5), 214 (4.0, PhN$\equiv$CPhCl), 216 (1.7), 161 (5.2, M – PhNHCOPhCl), 160 (5.6), 131 (100, M – PhNHCOPhCl – CH_2O), 130 (77.6), 132 (53.2), 118 (2.1), 117 (3.8), 139 (56.7, ClPhCO), 141 (18.2), 111 (19.4, ClPh), 113 (6.1), 104 (25.6, PhNCH), 93 (6.3, $PhNH_2$), 77 (18.1, Ph), 28 (1.3, CO). – UV (ethanol, λ_{max}, ε_{max}): 210 (13880), 224 (12880), 243 (16390), 284 nm (2070).

$C_{23}H_{21}ClN_2O_2$ (392.9) Calcd. C 70.3 H 5.4 Cl 9.0 N 7.1
Found C 70.2 H 5.3 Cl 8.9 N 7.0

3-Benzoyl-5-(iodomethyl)-2-phenylisoxazolidine (**3a**) was obtained from 0.60 g (2.0 mmol) of 1,2,4-triphenyl-1,4-diazabutadiene N^4-oxide or 0.66 g (2.0 mmol) of 1-(4-methoxyphenyl)-2,4-diphenyl-1,4-diazabutadiene N^4-oxide or 0.66 g (2.0 mmol) of 1-(4-chlorophenyl)-2,4-diphenyl-1,4-diazabutadiene N^4-oxide and 0.84 g (5.0 mmol) of freshly distilled allyl iodide. 0.49 to 0.38 g (52 to 40%) of colourless needles from CH_2Cl_2/*n*-pentane (1:2); m. p. 162 – 163°C (dec). – IR (KBr): 1685 (CO), 1490, 1450 (def CH_2), 1260, 1220 cm^{-1} (N – O – CH_2). – ^1H NMR (200 MHz): δ = 8.12 (d, 2H, $^3J_{HH}$ = 7.1 Hz), 7.59 (t, 1H, $^3J_{HH}$ = 6.8 Hz), 7.55 (q_{AB}, 2H, $^3J_{HH}$ = 7.1, $\Delta\nu$ = 7.8 Hz), 7.39 (t, 2H, $^3J_{HH}$ = 7.2 Hz), 7.18 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 7.09 (t, 1H, $^3J_{HH}$ = 7.0 Hz), 5.25 (2 × d, 1H, $^3J_{HH}$ = 9.4, $^3J_{HH}$ = 4.2 Hz), 4.53 (pentet, 1H, $^3J_{HH}$ = 7.3 Hz), 3.38 (d, 2H, $^3J_{HH}$ = 7.3 Hz), 2.53 – 2.80 (m, 2H). – ^{13}C NMR ($CDCl_3$): isoxazolidine: C-3 δ = 77.6 (d, $^1J_{CH}$ = 151.2 Hz), C-4 36.2 (t, $^1J_{CH}$ = 137.2 Hz), C-5 69.3 (d, $^1J_{CH}$ = 143.8 Hz), ICH_2 4.8 (t, $^1J_{CH}$ = 153.1 Hz), benzoyl: CO 196.2 (s), C-1 135.1 (s), C-2,6 and C-3,5 128.2 (d), C-4 132.7 (d), 2-phenyl: C-1 149.7 (s), C-2,6 113.9 (d), C-3,5 128.7 (d), C-4 121.7 (d). – MS: *m/z* = 393 (3.6%, M^+), 394 (0.8), 288 (100, M – PhCO), 161 (2.0, M – PhCO – I), 146 (2.2, M – PhCO – CH_2I), 143 (4.5), 132 (3.0), 119 (7.4, MeCH$\equiv$NPh), 118 (13.7), 105 (26.9, PhCO), 104 (11.1, PhNCH), 91 (9.1), 77 (45.8, Ph), 28 (6.3, C_2H_4).

$C_{17}H_{16}INO_2$ (393.0) Calcd. C 51.9 H 4.1 I 32.3 N 3.6
Found C 51.9 H 4.1 I 32.1 N 3.5

3-Benzoyl-5-(bromomethyl)-2-phenylisoxazolidine (**3b**): From 0.60 g (2.0 mmol) of 1,2,4-triphenyl-1,4-diazabutadiene N^4-oxide and 0.61 g (5.0 mmol) of freshly distilled allyl bromide. 0.41 g (48%) of colourless needles; m. p. 144 – 145°C (dec). – IR (KBr): 1678 (CO), 1485, 1450 (def CH_2), 1258, 1235, 1218 cm^{-1} (N – O – CH_2). – ^1H NMR (60 MHz): δ = 8.2 (d, 2H, $^3J_{HH}$ = 7.1 Hz), 7.7 – 7.0 (m, 8H), 5.1, 5.2 (dd, 1H, $^3J_{HH}$ = 9.7, $^3J_{HH}$ = 4.7 Hz), 4.5 (pentet, 1H, $^3J_{HH}$ = 7.3 Hz), 3.56 (d, 2H, $^3J_{HH}$ = 7.3 Hz), 2.8 – 2.6 (m, 2H). – MS: *m/z* = 345 (1.7%, M^+), 347 (1.6), 240 (92.9, M – PhCO), 242 (87.4), 160 (1.2, M – PhCO – HBr), 145 (7.6, M – PhCO – CH_3Br), 144 (8.6), 143 (14.1), 132 (1.1), 119 (19.6, MeCH$\equiv$NPh), 118 (28.4), 105 (45.6, PhCO), 104 (17.7, PhNCH), 91 (20.5, PhN), 77 (100, Ph), 28 (4.6, C_2H_4).

$C_{17}H_{16}BrNO_2$ (345.0) Calcd. C 59.1 H 4.7 Br 23.2 N 4.1
Found C 59.1 H 4.6 Br 23.0 N 4.2

3-Benzoyl-5-(chloromethyl)-2-phenylisoxazolidine (**3c**): From 0.60 g (2.0 mmol) of 1,2,4-triphenyl-1,4-diazabutadiene N^4-oxide and 0.38 g (5.0 mmol) of freshly distilled allyl chloride.

0.29 g (38%) of colourless needles from ethanol; m. p. 165–166°C. – IR (KBr): 1678 (CO), 1482, 1442 (def CH_2), 1262, 1238, 1218 cm^{-1} ($N-O-CH_2$). – ^1H NMR (60 MHz): δ = 8.0 (d, 2H, $^3J_{HH}$ = 7.1 Hz), 7.6–6.9 (m, 8H), 5.2, 5.1 (dd, 1H, $^3J_{HH}$ = 9.6, $^3J_{HH}$ = 4.5 Hz), 4.4 (pentet, 1H, $^3J_{HH}$ = 7.3 Hz), 3.69 (d, 2H, $^3J_{HH}$ = 7.0 Hz), 2.7–2.3 (m, 2H). – MS: *m/z* = 301 (3.8%, M^+), 303 (1.3), 196 (93.7, M – PhCO), 198 (31.2), 160 (2.8, M – PhCO – HCl), 145 (1.9, M – PhCO – CH_3Cl), 144 (6.2), 143 (9.7), 132 (1.3), 119 (23.7, MeCH≡NPh), 118 (17.8), 104 (22.8, PhNCH), 91 (25.1, PhN), 77 (100, Ph), 28 (5.4, C_2H_4).

$C_{17}H_{16}ClNO_2$ (301.1) Calcd. C 67.8 H 5.4 Cl 11.6 N 4.7
Found C 67.7 H 5.3 Cl 11.8 N 4.6

5-(Iodomethyl)-α,2-diphenyl-3-isoxazolidinemethanol (**4**): Reduction of 0.80 g (2.0 mmol) of **3a** using 5-fold excess of sodium borohydride (0.20 g) in methanol (15 ml) leads to 0.79 g (97%) of colourless prisms from methanol; m. p. 121–124°C (dec.). – IR (KBr): 3570 (free OH), 3420–3510 (bonded OH), 1485, 1455 (def CH_2), 1260, 1200 ($N-O-CH_2$), 1026 cm^{-1} (C–O). – ^1H NMR (60 MHz): δ = 6.9–7.7 (m, 10H), 4.9–4.6 (2 × d, 1H, $^3J_{HH}$ = 7.8, $^3J_{HH}$ = 4.9 Hz), 4.1–3.9 (m, 1H), 4.3–3.8 (m, 1H), 3.4 (d, 2H, $^3J_{HH}$ = 7.3 Hz), 2.5–1.5 (m, 3H).

$C_{17}H_{18}INO_2$ (395.0) Calcd. C 51.6 H 4.6 I 32.1 N 3.5
Found C 51.4 H 4.3 I 31.9 N 3.7

2,7-Diphenyl-3,6-dioxa-7-azabicyclo[3.2.1]octane (**5**): The solution of 0.79 g (2.0 mmol) of **4** in benzene (10 ml) was refluxed for 15 min in the presence of sodium hydride (0.10 g, 4.0 mmol). 0.50 g (93%) of colourless prisms from CH_2Cl_2/*n*-pentane (1:2); m. p. 144–145°C. – IR (KBr): 1490, 1450 (def CH_2), 1215, 1170, 1095 cm^{-1} ($N-O-CH_2$). – ^1H NMR (200 MHz): 7-phenyl: δ = 6.72 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 7.17 (t, 2H, $^3J_{HH}$ = 7.2 Hz), 6.86 (t, 1H, $^3J_{HH}$ = 7.0 Hz), 2-phenyl: 7.51 (d, 2H, $^3J_{HH}$ = 6.8 Hz), 7.88 (q_{AB}, 2H, $^3J_{HH}$ = 6.9, $\Delta\nu$ = 8.5 Hz), 7.85 (t, 1H, $^3J_{HH}$ = 6.8 Hz), other data see text. – ^{13}C NMR ($CDCl_3$): 7-phenyl: C-1 δ = 152.3 (s), C-2,6 115.6 (d), C-3,5 128.3 (d), C-4 121.9 (d), 2-phenyl: C-1 140.2 (s), C-2,6 127.7 (d), C-3,5 128.3 (d), C-4 126.7 (d), others see text. – MS: *m/z* = 267 (16.9%, M^+), 268 (3.5), 161 (4.4, M – PhCHO), 146 (33.8, M – PhCHO – Me), 144 (15.5, M – PhCHO – OH), 143 (33.5, M – PhCHO – H_2O), 132 (23.8), 119 (73.2, MeCH=NPh), 118 (26.5), 117 (19.3), 115 (22.8), 106 (23.5, PhCHO), 105 (32.6, PhCO), 104 (34.1, PhNCH), 92 (11.7, PhNH), 91 (89.1), 77 (100, Ph), 43 (8.7), 27 (5.4).

$C_{17}H_{17}NO_2$ (267.2) Calcd. C 76.4 H 6.4 N 5.2 Found C 76.4 H 6.3 N 5.2

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