1,3-DIPOLAR CYCLOADDITION
OF C-BENZOYL-N-PHENYLNITRONE WITH DIHYDROFURAN
DERIVATIVES. INVESTIGATION OF *endo-exo* STEREOSELECTIVITY*

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C-Benzoyl-N-phenylnitrone (*Ia*) reacts with dihydrofuran derivatives (2,3-dihydro- and 2,5-di-hydrofuran, 2,5-dimethoxy- and 2,5-diacetoxy-2,5-dihydrofuran) *via* 1,3-dipolar cycloaddition to give diastereoisomeric pair of *exo-* and *endo-*cycloadducts. The *endo-exo* stereoselectivity of the reaction is discussed. Cycloaddition of C,N-diphenylnitrone (*Ib*) with 2,3-dihydrofuran is also described. The cycloaddition kinetics have been studied with the nitrone *Ia* and non--substituted dihydrofurans.

1,3-Dipolar cycloaddition of nitrones *I* with olefins produces regioisomeric isoxazolidines due to two possible orientations of the reactants[1]. Each orientation can give two diastereoisomeric isoxazolidines on the basis of two possible *endo-* and *exo-*arrangements of the transition states[2,3]. In previous reports[4-7] we dealt with 1,3-dipolar cycloaddition of C-benzoyl-N-phenylnitrone (*Ia*) with furan derivatives; *Ia* reacted with high degree of regioselectivity and stereospecificity to give the *endo*-monoadduct *IIa* only (Scheme 1, the indexes *a* and *b* denote $R^1 = C_6H_5CO$ and C_6H_5, respectively; for *V* and *VI* it is $R^2 = H$; for *VII* and *VIII* it is $R^2 = OCOCH_3$; for *IX – XII* it is $R^2 = OCH_3$). The present paper deals with 1,3-dipolar cyclo-additions of nitrones *Ia* and *Ib* with 2,3- and 2,5-dihydrofuran, 2,5-dimethoxy-and 2,5-diacetoxy-2,5-dihydrofuran. In the case of 2,3- and 2,5-dihydrofurans the cycloaddition kinetics was also followed.

Physical and analytical data of the newly prepared derivatives are given in Table I. Elemental analysis, mass spectra, UV and IR spectra indicate formation of the cycloadducts. Their stereochemical structure was determined from ${}^1H$ NMR and

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^{13}C NMR spectra, chemical shifts and coupling constants. The chemical shifts and coupling constants of the monoadducts prepared as well as denotation of the protons in tetrahydrofurans are given in Table II and Scheme 1. The following results were obtained.

a, R^1 = C$_6$H$_5$CO, b, R^1 = C$_6$H$_5$
V, VI, R^2 = H
VII, $VIII$, R^2 = OCOCH$_3$
IX – XII, R^2 = OCH$_3$
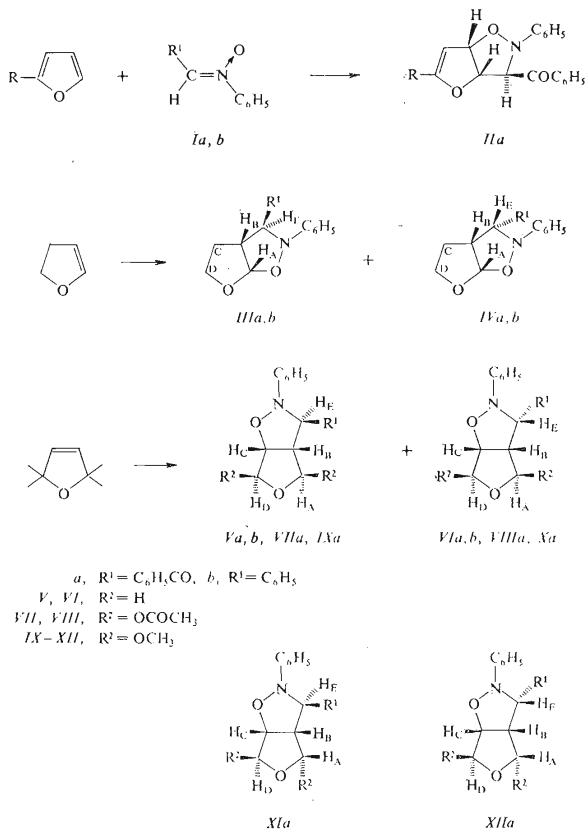
SCHEME 1

2,3-*Dihydrofuran*: The ^{1}H NMR spectrum of the compound *IVa* shows a distinct doublet with high value δ 5·92 ppm and a therewith coupled multiplet at δ 3·65 ppm, which indicates formation of the head-to-head regioisomer. Signals of the bridge protons in the mono-adduct *IIa* (head-to-tail) were found at almost the same values δ 5·91 and 5·57 ppm. In case of identical regioisomerism of the isolated adduct with the monoadduct *IIa* the both bridge protons had to be found at lower δ values due to loss of shielding of double bond. The found very different values of chemical shifts of the tetrahydrofuran bridge protons δH_B at 3·65 ppm and δH_A at 5·92 ppm

TABLE I

Physical properties and elemental analyses of the compounds prepared

Compound	Formula (mol. mass)	M.p., °C (yield %)	IR $\nu(CO)$ cm^{-1}	UV λ_{max} (log ε)	Calculated/Found		
					% C	% H	% N
IVa	$C_{18}H_{17}NO_3$ (295·3)	183—185 (51)	1 698	249 (4·30)	73·20 73·43	5·80 5·55	4·74 4·85
IIIa	$C_{18}H_{17}NO_3$ (295·3)	151—153 (47)	1 693	245 (4·42)	73·20 73·16	5·80 5·61	4·74 4·73
IIIb	$C_{17}H_{17}NO_2$ (267·3)	71—72 (18)	1 698	245 (3·92)	76·38 76·52	6·41 6·40	5·24 5·40
IVb	$C_{17}H_{17}NO_2$ (267·3)	103—105 (71)	1 698	247 (3·79)	76·38 76·50	6·41 6·30	5·24 5·43
IVa	$C_{18}H_{17}NO_3$ (295·3)	98—100 (17)	1 694	248 (4·42)	73·20 72·95	5·80 4·79	4·74 4·85
VIa	$C_{18}H_{17}NO_3$ (295·3)	142—144 (57)	1 694	246 (4·42)	73·20 73·19	5·80 5·62	4·74 4·71
VIIa	$C_{22}H_{21}NO_7$ (411·4)	171—172 (42)	1 692 1 654	242 (4·29)	64·22 64·36	5·15 5·06	3·40 3·72
VIIIa	$C_{22}H_{21}NO_7$ (411·4)	162—164 (18)	1 698 1 654	247 (4·28)	64·22 64·32	5·15 5·05	3·40 3·65
IXa	$C_{20}H_{21}NO_5$ (355·4)	138—140 (17)	1 697	248 (4·28)	67·59 67·52	5·96 5·91	3·94 4·05
Xa	$C_{20}H_{21}NO_5$ (355·4)	110—112 (16)	1 697	245 (4·35)	67·59 67·64	5·96 6·08	3·94 4·11
XIa	$C_{20}H_{21}NO_5$ (355·4)	106—107 (48)	1 697	245 (4·35)	67·59 67·51	5·96 5·68	3·94 4·07

(the high value of chemical shift δH_A is caused by shielding due to two heteroatoms of oxygen) indicate, according to expectation, the opposite regioisomerism of the 1,3-dipolar cycloaddition of Ia to 2,3-dihydrofuran as compared with furan. In a previous paper[7] we determined values of the frontier orbitals of nitrone Ia ($\varepsilon_{HOMO} = -849 \cdot 05$ kJ mol^{-1} and $\varepsilon_{LUMO} = -84 \cdot 90$ kJ. mol^{-1}) which, together with the values by Houk and Caramella[8] for 2,3-dihydrofuran ($\varepsilon_{HOMO} = -820 \cdot 11$ kJ mol^{-1}

TABLE II
Chemical shifts and coupling constants (δ, ppm, J, Hz)

Compound	H_A (J_{AB})	H_B (J_{BC})	H_C (J_{CD})	H_D	H_E (J_{BE})	Aromatic[a] (m)
$IIIa$	6·01 d (5·5)	3·75 m	1·95—2·33 m	3·38—4·01 m	5·03 d (2·0)	7·03—8·09
$IIIb$	6·00 d (4·8)	3·87 m	1·95—2·33 m	3·77—4·00 m	4·48 d (3·1)	6·85—7·45
IVa	5·92 d (5·5)	3·50—4·41 m	1·62—1·92 m	3·50—4·41 m	4·94 d (7·7)	7·00—7·95
IVb	5·89 d (5·6)	3·27—3·67 m	1·47—1·85 m	3·86—4·25 m	4·50 d (7·9)	6·81—7·26
Va	2·23—4·18 m	3·61 m (6·0)	5·02 d,d (4·1)	2·23—4·18 m	4·77 d (4·3)	6·91—8·11
VIa	3·48—4·22 (5·5)	—	4·90—5·15 m (1·5 and 4·2)	3·48—4·22 m	5·14 d (8·2)	6·96—7·97
$VIIa$	6·26 d (1·5)	3·90 m (6·9)	4·99 d (0·0)	6·45 s	5·57 d (1·9)	6·95—8·05
$VIIIa$	6·25 d (1·0)	3·80 m (6·5)	5·02 d (0·0)	6·54 s	5·08 d (7·5)	7·01—8·11
IXa	5·28 s (0·0)	3·75 m (6·5)	4·95 d (0·0)	5·10 s	4·88 d (2·5)	6·96—8·11
Xa	5·19 s (0·0)	3·71—3·86 m (6·6)	4·92 d (0·0)	5·12 s	5·16 d (5·5)	6·96—8·08
XIa	5·20 d (5·7)	3·65—3·87 m (7·5)	4·73 d (0·0)	5·08 s	5·75 d (2·5)	6·88—8·08

[a] VIa $J_{DD}' = 10 \cdot 5$ Hz, $VIIa$ CH_3 (1·98 and 2·03), $VIIIa$ CH_3 (1·87 and 2·07), IXa CH_3 (3·15 and 3·42), Xa CH_3 (3·32 and 3·37), XIa CH_3 (3·32 and 3·47).

and $\varepsilon_{\text{LUMO}} = 231 \cdot 56$ kJ mol^{-1}), indicate that the given 1,3-dipolar cycloaddition is controlled (as in the case of furan) by the frontier orbital interaction LUMO (Ia)/ /HOMO(2,3-dihydrofuran). In contrast to furan the atomic orbital coefficients in HOMO(2,3-dihydrofuran) have the greatest values at β-carbon atom[8], which results in formation of the opposite head-to-head regioisomer. The coupling constant $J_{\text{AB}} = 5 \cdot 5$ Hz proves cis-stereospecificity[4] of 1,3-dipolar cycloaddition of the nitrone Ia. The ^{1}H NMR spectrum contains still another doublet at δ 4·94 ppm with the coupling constant $J_{\text{BE}} = 7 \cdot 7$ Hz, which is also coupled with the multiplet H$_B$ which was assigned to the isoxazolidine proton H$_E$.

The derivatives $IIIa$ and IVa are rigid systems, which enabled determination of stereochemistry of the mono-adducts being formed by means of coupling constants[9]. The dihedral angles H$_B$–C–C–H$_E$ were determined from the Dreiding models within the limits $120-130°$ and $5-15°$ for $IIIa$ and IVa, respectively, which corresponds to the calculated vicinal coupling constants J_{BE} $2 \cdot 0-3 \cdot 0$ Hz or $7 \cdot 5-8 \cdot 5$ Hz from the Karplus equation[10] $J_{\text{vic}} = k \cdot \cos^2 \varphi$, where φ means the dihedral angle, and k means a constant[11,12]. On the basis of coupling constant $J_{\text{BE}} = 7 \cdot 7$ Hz of compound IVa we can assign this compound the structure of exo-diastereoisomer with syn-arrangement of the isoxazolidine proton H$_E$ with respect to the bridge protons H$_A$ and H$_B$.

Signals of the bridge protons H$_A$ (6·01 ppm) and H$_B$ (3·75 ppm) in the $endo$-diastereoisomer $IIIa$ absorb at lower field than those in IVa due to their being shielded by benzoyl group assuming syn-arrangement with the mentioned protons in $IIIa$. The coupling constant J_{BE} of the doublet for the isoxazolidine proton H–E at δ 5·03 ppm $J_{\text{BE}} = 2 \cdot 0$ Hz agrees well with the already mentioned coupling constant obtained from the Dreiding model by means of the Karplus equation for the $endo$-diastereoisomer $IIIa$. The both monoadducts IV and $IIIa$ are formed at a ratio $52 : 48$ in favour of the $endo$-cycloadduct $IIIa$. The given ratio was obtained from ^{1}H NMR spectrum of the reaction mixture.

In contrast to furan derivatives[4], 2,3-dihydrofuran reacted by 1,3-dipolar cycloaddition also with C,N-diphenylnitrone (Ib). The exo-cycloadduct IVb has syn-arrangement of the isoxazolidine proton H$_E$ with the bridge tetrahydrofuran protons H$_A$ and H$_B$, which follows from the values of the coupling constant $J_{\text{BE}} = 7 \cdot 9$ Hz. According to expectation, substitution of phenyl for benzoyl group caused an upfield shift of the H$_B$ and H$_E$ protons signals as compared with monocycloadduct, H$_B$ $(3 \cdot 27-3 \cdot 67$ ppm) and H$_E$ (4·50 ppm). Their assignement was accomplished by decoupling of the signal with frequency at 273·3 Hz which corresponds to H$_B$ resonance, whereafter the doublets at δ 5·89 ppm (H$_A$) and 4·50 ppm (H$_E$) reduced to singlets, and the multiplet H$_C$ was simplified.

In the ^{1}H NMR spectrum of the $endo$-cycloadduct $IIIb$ there appear two doublets for the H$_A$ proton at δ 6·00 ppm with coupling constant $J_{\text{AB}} = 4 \cdot 8$ Hz and a doublet for the isoxazolidine proton H$_E$ at δ 4·48 ppm with coupling constant $J_{\text{BE}} = 3 \cdot 1$ Hz

determining the *endo*-arrangement of the formed cycloadduct *IIIb*. Ratio of the *endo-exo* isomers is 22 : 78.

2,5-Dihydrofuran: As with symmetrically substituted 2,5-dihydrofuran derivatives no regioisomerism is possible, the problem of stereochemistry of the formed cycloadducts was simplified to that of configuration of the isoxazolidine proton H_E. From the Dreiding models the following dihedral angles were estimated (the calculated values of coupling constants are given in brackets): H_A–C–C–H_B 15–25° $(J = 6.5-7.5 \text{ Hz})$, $H_{A'}$–C–C–H_B 110–120°. $(J = 1.0-2.0 \text{ Hz})$, H_B–C–C–H_C 5–10° $(J = 8.0-8.5 \text{ Hz})$, H_B–C–C–H_E 5–15° $(J = 7.5-8.5 \text{ Hz})$, and H_B–C–C–H_E, 120–130° $(J = 2.0-3.0 \text{ Hz})$. In the ^{1}H NMR spectrum of the compound *VIa* there is a doublet at δ 5·14 ppm (H_E) with coupling constant $J_{BE} = 8.2$ Hz. Decoupling experiment at the frequency 327·1 Hz which corresponds to resonance of the H_D, proton made it possible to analyze the multiplet of the H_C proton with the following coupling constants: $J_{BC} = 5.5$ Hz, $J_{DD'} = 10.5$ Hz, $J_{CD'} = 1.5$ Hz, and $J_{CD} = 4.2$ Hz. In the ^{1}H NMR spectrum of the *endo*-cycloadducts *Va* there is a doublet at δ 4·77 ppm belonging to the isoxazolidine proton H_E and separated from the doublet for the H_C proton. The coupling constant $J_{BE} = 4.3$ Hz indicates that the adduct is *endo*-diastereoisomer. By decoupling of the signal at the frequency 288·4 Hz (H_B) the doublet (H_E) was reduced to singlet, and the doublet-doublet (H_C) was reduced into doublet with coupling constant $J_{CD} = 4.1$ Hz, $J_{CD'}$ being equal to zero. The coupling constants $J_{BC} = 6.0$ Hz (*Va*) and 5·5 Hz (*VIa*) confirm *cis*-stereospecificity of the 1,3-dipolar cycloaddition. The found ratio of *endo*- and *exo*-diastereoisomers is 44 : 56 without separation.

2,5-Diacetoxy-2,5-dihydrofuran: Analysis of ^{1}H NMR spectrum of the compound *VIIa* ($R^2 = OCOCH_3$) can assign it the structure of *endo*-cycloadduct with *cis*-arrangement of acetoxyl groups and *anti*-arrangement of the isoxazolidine proton H_E with the bridge tetrahydrofuran protons H_B and H_C. The found coupling constants $J_{AB} = 1.5$ Hz ($\delta H_A = 6.26$ ppm), $J_{BC} = 6.9$ Hz ($\delta H_B = 3.90$ ppm and $\delta H_C = 4.99$ ppm), $J_{BE} = 1.9$ Hz ($\delta H_E = 5.57$ ppm) agree well with those from the Karplus equation. Signal of the proton H_D appears in the spectrum as a singlet at δ 6·45 ppm similar to the signals of CH_3COO groups at the value 1·98 and and 2·03 ppm.

Signal of the isoxazolidine proton H_E of the compound *VIIIa* appears in the ^{1}H NMR spectrum as a doublet at δ5·08 ppm with the coupling constant $J_{BE} = 7.5$ Hz, which means that the isolated compound is a diastereoisomeric pair to *VIIa*, viz *exo*-cycloadduct. The *cis*-arrangement of acetoxyl groups is confirmed by character of splitting of signals of α-protons of tetrahydrofuran skeleton. Signal of the H_A proton is found in the spectrum as a doublet at δ 6·25 ppm with small coupling constant $J_{AB} = 1.0$ Hz, and signal of the H_D protons appears as a singlet at δ 6·54 ppm. Value of the coupling constants $J_{BC} = 6.5$ Hz is similar to that

of *VIIa*. Although we carried out the cycloaddition of *Ia* with 2,5-diacetoxy-2,5-di-hydrofuran, which represented a 1 : 1 mixture of *cis-* and *trans*-isomers, we only isolated the cycloaddition products of the *cis*-derivative. The respective *endo* (*VIIa*) and *exo* (*VIIIa*) diastereoisomers are present in the reaction mixture before separation at a ratio 70 : 30.

2,5-Dimethoxy-2,5-dihydrofuran: We obtained the cycloadducts *IXa*, *Xa*, and *XIa* in the yields 17, 16, and 48%, respectively. The *trans*-arrangement of α-hydrogen atoms of tetrahydrofuran skeleton in the compound *XIa* is determined by the coup-

TABLE III
Mass spectra

Compound	m/z (rel. int.)
IIIa	295, $M^{+ \cdot}$ (9), 191 (18), 19 (100), 174 (5), 173 (23), 172 (7), 156 (5), 144 (17), 144 (17), 130 (16), 122 (14), 106 (5), 105 (44), 104 (17), 93 (5), 78 (6), 77 (50), 51 (20), 50 (5), 43 (5), 41 (8), 39 (7)
IVa	295, $M^{+ \cdot}$ (4), 249 (4), 191 (5), 190 (30), 174 (5), 173 (25), 172 (10), 162 (8), 156 (9), 145 (5), 144 (30), 143 (5), 130 (25), 122 (17), 120 (6), 117 (10), 115 (6), 106 (8), 105 (62), 104 (17), 93 (7), 91 (6), 81 (6), 78 (12), 77 (100), 76 (7), 74 (5), 65 (5), 52 (7), 51 (47), 50 (15), 43 (5), 41 (12), 39 (16)
VIa	295, $M^{+ \cdot}$ (9), 191 (12), 190 (100), 174 (9), 173 (18), 172 (7), 160 (4), 156 (4), 147 (7), 145 (6), 144 (25), 143 (6), 132 (7), 131 (6), 130 (34), 122 (18), 117 (7), 106 (9), 105 (53), 104 (37), 93 (8), 91 (6), 81 (6), 78 (12), 71 (5), 70 (7), 69 (8), 57 (15), 56 (11), 55 (15), 51 (37), 50 (10), 43 (18), 42 (10), 41 (37), 39 (18)
VIIo	411, $M^{+ \cdot}$ (6), 351 (4), 308 (6), 307 (6), 247 (5), 246 (24), 226 (8), 205 (4), 204 (21), 188 (19), 187 (19), 186 (20), 176 (19), 171 (6), 170 (10), 158 (9), 147 (8), 146 (50), 130 (19), 122 (10), 105 (100), 104 (15), 93 (6), 91 (4), 78 (16), 77 (70), 76 (5), 60 (24), 57 (9), 55 (7), 51 (21), 50 (6), 45 (24), 43 (89), 42 (6), 41 (10), 39 (8)
VIIIa	411, $M^{+ \cdot}$ (1), 351 (4), 306 (5), 291 (4), 248 (5), 246 (9), 204 (6), 188 (16), 187 (7), 186 (12), 170 (5), 158 (5), 146 (30), 130 (9), 122 (7), 106 (10), 105 (100), 104 (14), 93 (5), 78 (6), 77 (51), 74 (5), 50 (25), 59 (6), 57 (10), 56 (6), 55 (8), 51 (15), 45 (27), 43 (77), 42 (6), 41 (12), 39 (7)
XIa	355, $M^{+ \cdot}$ (21), 324 (4), 251 (20), 250 (95), 226 (6), 190 (23), 174 (4), 166 (11), 163 (9), 162 (62), 160 (9), 158 (11), 146 (7), 131 (7), 130 (46), 129 (8), 122 (17), 106 (10), 105 (69), 104 (69), 99 (53), 94 (6), 93 (16), 91 (8), 87 (34), 85 (5), 84 (6), 83 (18), 82 (34), 81 (6), 78 (16), 77 (100), 74 (27), 71 (18), 69 (11), 67 (11), 59 (46), 57 (20), 56 (12), 55 (19), 51 (27), 50 (10), 45 (74), 43 (20), 42 (10), 41 (41), 39 (20)

ling constant $J_{AB} = 5.7$ Hz and by the fact that the H_D proton is shown in the spectrum as a singlet at δ 5·08 ppm. The *endo*-arrangement of the isoxazolidine proton H_E with the bridge protons H_B and H_C in *XIa* follows from values of the coupling constants $J_{BE} = 2.5$ Hz and $J_{BC} = 7.5$ Hz. The cycloadducts *IXa* (*endo*) and *Xa* (*exo*) represent a diastereoisomeric pair formed by cycloaddition of the nitrone *Ia* to *cis*-2,5-dimethoxy-1,5-dihydrofuran as it follows from interpretation of the ^{1}H NMR spectrum (Table II). The found *endo : exo* ratio is 54 : 46 and is given in Table III along with the other derivatives.

The *endo-exo* isomerism is an important aspect of 1,3-dipolar cycloaddition to which not much attention has been paid so far. The *endo-exo* nomenclature[13] used in the present paper is applied to relative orientation of bent 1,3-dipoles, *i.e.* also nitrones *Ia* and *Ib*, with respect to the substituted double bond. The *endo-exo* stereospecificity is due to secondary orbital interactions or steric effects[13,14]. In our previous papers dealing with the cycloadditions of nitrone *Ia* to furan derivatives we always detected the presence of the *endo*-cycloadduct *IIa* only. The steric hindrance favouring the adduct formation through the *endo* transition state cannot be considered in the case of furan. Therefore, better stabilization in the *endo* transition state can be explained by secondary overlap between the LUMO of nitrogen in 1,3-dipole and the HOMO *i.e.* π orbital of the second double bond in furan (Scheme 2). Geometry

endo   *exo*
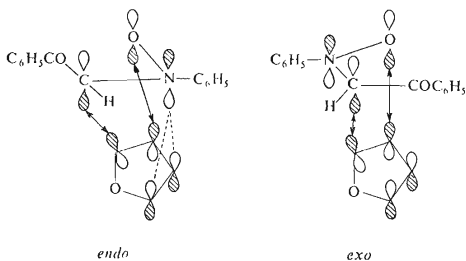
SCHEME 2

of the transition states in cycloadditions of nitrone *Ia* is deduced from the found structures of the final cycloadducts and on the basis of the known *E* configuration of nitrone *Ia* which is not changed during the concerted 1,3-dipolar cycloaddition. In case of cycloadditions with 2,3-dihydro- and 2,5-dihydrofurans the second double bond is absent, the secondary orbital interactions cannot operate, and, therefore, the *endo-exo* adducts are formed at a ratio almost equal to 1 : 1.

Cycloaddition to E (*trans*) 2,5-dimethoxy-2,5-dihydrofuran again produces the *endo* diastereoisomer *XIa* only. Stabilization of *endo*-arrangement of the transition state (following from the Dreiding model) can be explained by interaction between free electron pair at oxygen atom of methoxy-group and electrophilic terminal carbon atom of 1,3-dipole–nitrone *Ia* (Scheme 3).
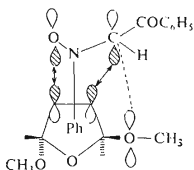
SCHEME 3

In case of 2,3-dihydrofuran and 2,5-dihydrofuran we also investigated the cyclo-addition kinetics with the nitrone *Ia* at 40°C under conditions of pseudomono-molecular reaction using the method described in ref.[7]. According to expectation, these compounds are more reactive than furan derivatives with comparable IP value (Table IV), 2,3-dihydrofuran being only $2·21 \times$ more reactive than 2,5-di-hydrofuran.

The values of chemical shifts obtained from ^{13}C NMR spectra confirm the as-signement of *endo*- and *exo*-stereochemistry to the prepared cycloadducts *IIIa*, *IVa*, *Va*, *VIa*, *VIIa*, *VIIIa* (Table V). In case of the adducts of 2,3-dihydrofuran pseudo-axial benzoyl group in the *endo*-derivative *IIIa* produces a γ effect on $C_{(5)}$ atom

TABLE IV
The *endo* : *exo* stereoselectivity ratio determined from ^1H NMR spectra of the reaction mixtures

| Olefin	*endo* : *exo*	k_2, l mol^{-1} s^{-1}
Furan	100 : 0	
2,3-Dihydrofuran	52 : 48 (22 : 78)[a]	$3·34 . 10^{-4}$
2,5-Dihydrofuran	44 : 56	$1·51 . 10^{-4}$
cis-2,5-Diacetoxy-2,5-dihydrofuran	70 : 30	—
cis-2,5-Dimethoxy-2,5-dihydrofuran	54 : 46	—
trans-2,5-Dimethoxy-2,5-dihydrofuran	100 : 0	—

[a] For C,N-diphenylnitrone.

TABLE V
^{13}C NMR Chemical shifts of the derivatives prepared[a]

endo IIIa		exo IVa		endo Va		exo VIa		endo VIIa		exo VIIIa	
ppm	assignment	ppm	assignment	ppm	assignment	ppm	assignment	ppm	assignment	ppm	assignment
30·90	5	29·69	5	53·67	4	52·94	4	21·15	CH$_3$	21·03	CH$_3$
50·12	4	51·03	4	71·81	5	68·78	5	56·45	4	57·33	4
68·04	6	69·60	6	72·86	7	72·15	7	69·68	3	71·68	3
73·63	3	72·85	3	75·32	3	73·97	3	86·56	8	85·12	8
108·69	8	105·05	8	83·45	8	83·31	8	101·22	7	100·18	7
114·14	2'	118·56	2'	116·80	2'	115·75	2'	103·69	5	101·74	5
121·55	4'	124·14	4'	123·35	4'	122·89	4'	114·85	2'	117·39	2'
		128·30		128·85		128·60		123·15	4'	124·33	4'
128·69	2",3",3'	128·56	2",3",3'	129·08	2",3",3'	128·86	2",3",3'	128·86	3'	128·69	3'
		129·08						129·25	2",3"	128·95	2",3"
133·36	4"	134·14	4"	133·88	4"	133·79	4"	133·92	4"	134·20	1",4"
134·79	1"	135·44	1"	135·29	1"	135·87	1"	134·70	1"		
149·34	1'	148·43	1'	148·62	1'	149·89	1'	147·68	1'		
195·69	C=O	194·01	C=O	196·13	C=O	195·44	C=O	168·98		168·75	OCOCH$_3$
								169·74	OCOCH$_3$		
								194·14	C=O	193·61	C=O

[a] For numbering see Scheme 4.

($\Delta\delta = 2\cdot21$ ppm) and $C_{(8)}$ atom ($\Delta\delta = 3\cdot64$ ppm) as compared with pseudoequato-
rial benzoyl group in the *exo*-derivative *IVa*. High value of chemical shift for $C_{(8)}$
atom (δ 105·05 and 108·69 ppm for *IVa* and *IIIa*, respectively), which is due to de-
shielding effect of two oxygen heteroatoms, confirms the regioisomerism of the
1,3-dipolar cycloaddition of nitrone *Ia* to 2,3-dihydrofuran.

IIIa, IVa

Va, VIa, R = H
VIIa, VIIIa, R = OCOCH₃
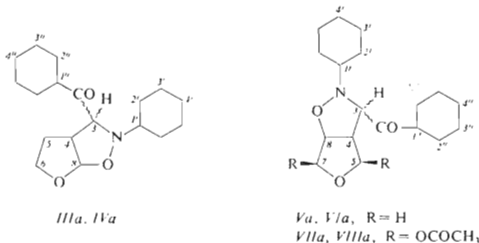
SCHEME 4

In case of the monoadducts derived from 2,5-dihydrofuran the γ effect on $C_{(5)}$
atom in *Va* is observed ($\Delta\delta = 3\cdot03$ ppm) as compared with *VIa*. Also the value
for the α-atom ($C_{(3)}$) is different, $\Delta = 1\cdot35$ ppm. In the adducts derived from 2,5-
diacetoxy-2,5-dihydrofuran γ is observed on $C_{(5)}$ atom ($\Delta\delta = 1\cdot95$ ppm).
An opposite effect exerts the acetoxy group at $C_{(5)}$ atom by the γ effect on $C_{(3)}$
atom in the *exo*-adduct *VIIIa* as compared with the *endo*-adduct *VIIa* ($\Delta\delta = 2\cdot0$ppm).
The given deshielding effects of benzoyl group in pseudoaxial arrangement agree
with literature data[15] for cyclic systems.

EXPERIMENTAL

The yields, uncorrected melting points, and analytical data of the compounds synthetized are
given in Table I. The IR spectra were measured in the region 700 to 3 800 cm⁻¹ using a UR-20
spectrophotometer (Zeiss, Jena) in saturated chloroform solution (0·6 mm NaCl cell). The ¹H
NMR spectra were measured in deuteriochloroform using a BS-487C apparatus (80 MHz,
Tesla Brno), δ scale, tetramethylsilane as internal standard (Table II). The mass spectra (Table III)
were measured with a MS 902S apparatus (AEI Manchester) using a direct inlet system at an
electron energy of 70 eV. The UV spectra were measured with a UV VIS spectrophotometer
in methanol solutions. The reaction course and purity of the compounds were checked by TLC
using Silufol plates (detection in UV₂₅₄ light). 2,3- and 2,5-Dihydrofurans were prepared ac-
cording to ref.¹⁴. The column chromatography was carried out using silica gel and cyclohexane-
-ethyl acetate as eluent (4 : 1, 8 : 1, 2 : 1, and 6 : 1 for 2,3-, 2,5-dihydrofuran, 2,5-diacetoxy-
and 2,5-dimethoxy-2,5-dihydrofuran, respectively).

The cycloadditions were carried out in a sixfold excess of the dihydrofuran derivative to nitrone *Ia* in toluene under the following conditions: 2,3-dihydrofuran (40°C, 8 h), 2,5-dihydrofuran (40°C, 20 h), 2,5-diacetoxy-2,5-dihydrofuran (40°C, 40 h), and 2,5-dimethoxy-2,5-dihydrofuran (55°C, 30 h); with nitrone *Ib* 2,3-dihydrofuran (70°C, 24 h). The kinetic measurements were carried out at 40°C by the procedure given in ref.[7].

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