VERSITA

Cent. Eur. J. Chem. • 12(5) • 2014 • 586-593
DOI: 10.2478/s11532-014-0518-2

Central European Journal of **Chemistry**

Regio- and stereoselectivity of polar [2+3] cycloaddition reactions between (Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone and selected (E)-2-substituted nitroethenes§

Research Article

Radomir Jasiński[1*], Magda Ziółkowska[2], Oleh M. Demchuk[3], Agata Maziarka[1]

[1]*Cracow University of Technology, Institute of Organic Chemistry and Technology, 31-155 Cracow, Poland*

[2]*AGH University of Science and Technology, Faculty of Energy and Fuels, 30-059 Cracow, Poland*

[3]*Maria Curie-Sklodowska University, Department of Organic Chemistry, 20-614 Lublin, Poland*

Received 17 October 2013; Accepted 3 December 2013

Abstract: [2+3] Cycloaddition reactions of the highly reactive (Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone with (E)-2-R-nitroethenes proceed under mild conditions and yield mixtures of stereoisomeric 2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5-R-isoxazolidines. The effect of regiospecificity of the cycloadditions may be accounted for by the theory of electrophilicity indexes. Stereoselectivity, however, is determined by a compilation of steric and secondary orbital effects.

Keywords: *[2+3] cycloaddition • Nitrone • Nitroalkene • Regioselectivity • Stereoselectivity*

1. Introduction

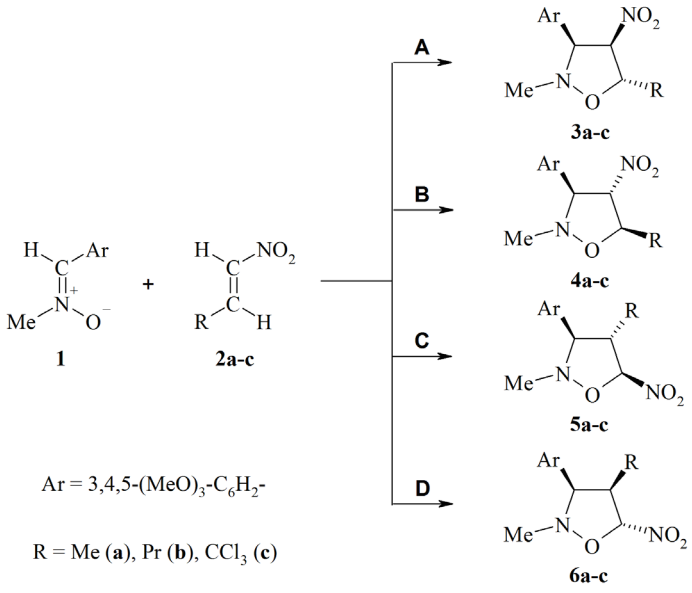
[2+3] Cycloaddition reactions are currently the most universal methods of synthesis of five-membered heterocyclic compounds [2-5]. Conjugated nitroalkenes are an interesting group of potential reactants in such reactions because the nitro group increases the biological activity of heterocyclic compounds [6-8]. Furthermore, the NO_2 group present in the molecule provides extensive possibilities for its further functionalisation towards carbonyl compounds [9-11], amines [10,12], hydroxylamines [10,13], oximes [10,12,13], esters and salts of nitronic acids [10,14,14b,14c], and many other compounds [10,15,16].

In this paper we continue our comprehensive studies of reactions between nitrones and conjugated nitroalkenes. We have already reported the experimental [17-19] and theoretical [20-22] details of the mechanistic aspects of cycloadditions involving (Z)-C,N-diarylnitrones, classified, according to Domingo [23,24], as strongly electrophilic reactants (ω=1.6÷2.11eV [19]). Now we intend to begin a comprehensive study of reactions involving moderately electrophilic nitrones activated by electron-donating substituents. No such studies have been carried out to date [2,3,25,26].

In our research we had studied regio- and stereochemistry of such a [2+3] cycloaddition. As the appropriate model substrates we selected moderately

* *E-mail: radomir@chemia.pk.edu.pl*

§ *Part 71 of the series " Synthesis and properties of azoles and their derivatives"; part 70 see [1]*



Scheme 1. Theoretically possible reaction paths of [2+3] cycloaddition between (Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone **1** and (E)-2-substituted nitroethenes **2a-c**.

electrophilic (Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone (**1**) and three (E)-2-substituted nitroethenes (**2a-c**) containing substituents of various sterical and electronic properties. These reactions, assuming a one-step mechanism, [4,27] may theoretically occur *via* four competing regio- and stereoisomeric pathways (Scheme 1).

For reactions **1**+**2a-c** we have planned to (i) determine the regio- and stereoselectivity of the cycloaddition, (ii) analyse the nature of intermolecular interactions in an elemental cycloaddition process, and (iii) identify the factors which determine the observed selectivity.

2. Experimental procedure

(Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone (**1**) and nitroalkenes (**2a-c**) were prepared according to the methods described in the literature: **1** – [28], **2a** – [29], **2b** – [30], **2c** – [31].

2.1. Synthesis of 2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5-R-isoxazolidines – general procedure

A mixture of 10 mmol of nitroalkene and 2.5 mmol of nitrone in 5 mL of dry toluene was stirred in the dark at room temperature for 24 h. The solvent was evaporated *in vacuo* and the residue was separated by semipreparative HPLC. Evaporation of the eluent from the fractions gave stereoisomeric 4-nitroisoxazolidines. The products were recrystallized from ethanol. Essential physical properties of obtained 2-methyl-3-(3,4,5-trimetoxyphenyl)-4-nitro-5-R-isoxazolidines are listed bellow:

2.2. 3,4-cis-4,5-trans-2,5-dimethyl-3-(3,4,5-trimethoxyphenyl)-4-nitroisoxazolidine (3a)

Yield 80%, colorless crystals, m.p. 124-125°C (ethanol). R_T (min): 2.6. IR, ν, cm^{-1}: 1549, 1370 (NO_2), 1184 (-C-N-), 1235, 1064 (CH_3-O-Ar), 853 (Ar). ^{1}H NMR, ppm (*J*, Hz): 6.55 (2H, s, $C_6\underline{H}_2$), 5.00 (1H, dd, *J* = 9.14, *J* = 5.67, H4), 4.96 (1H, dq, *J* = 5,67, *J* = 6.23, H5), 3.87 (1H, d, *J* = 9.14, H3), 3.86 (6H, s, m-OC$\underline{H}_3$), 3.85 (3H, s, p-OC$\underline{H}_3$), 2.67 (3H, s, N-C$\underline{H}_3$), 1.48 (3H, d, *J* = 6.23, C-C$\underline{H}_3$). ^{13}C NMR, ppm: 153.30, 138.43, 127.36, 105.09 (Ar), 98.15 (C4), 77.19 (C5), 76.77 (C3), 60.87 (p-O$\underline{C}H_3$), 56.12 (m-O$\underline{C}H_3$), 43.22 (N-$\underline{C}H_3$), 17.86 (C-$\underline{C}H_3$). Found, %: C 53.97; H 6.51; N 8.93. $C_{14}H_{20}N_2O_6$. Calculated, %: C 53.84; H 6.45; N 8.97. HR-MS: for $C_{14}H_{21}N_2O_6$ $(MH)^+$ calc. 313.1354 m/z, found 313.1350 m/z.

2.3. 3,4-trans-4,5-trans-2,5-dimethyl-3-(3,4,5-trimethoxyphenyl)-4-nitroisoxazolidine (4a)

Yield 14%, colorless crystals, m.p. 141-142 °C (ethanol). R_T (min): 3.5. IR, ν, cm^{-1}: 1554, 1373 (NO_2), 1180 (-C-N-), 1237, 1060 (CH_3-O-Ar), 843 (Ar). ^{1}H NMR, ppm

(*J*, Hz): 6.62 (2H, s, $C_6\underline{H}_2$), 4.82 (1H, dd, *J* = 5.90, *J* = 3.94, H4), 4.75 (1H, dq, *J* = 6.38, *J* = 5.90, H5), 3.89 (6H, s, m-OC$\underline{H}_3$), 3.88 (1H, d, *J* = 3.94, H3,), 3.87 (3H, s, p-OC$\underline{H}_3$), 2.74 (3H, s, N-C$\underline{H}_3$), 1.61 (3H, d, *J* = 6.38, C-C$\underline{H}_3$). ^{13}C NMR, ppm: 154.00, 138.54, 131.67, 104.94 (Ar), 100.93 (C4), 77.22 (C5), 77.04 (C3), 61.08 (p-OC$\underline{H}_3$), 56.46 (m-OC$\underline{H}_3$), 43.40 (N-C$\underline{H}_3$), 20.37 (C-C$\underline{H}_3$). Found, %: C 53.88; H 6.53; N 8.95. Calculated, %: C 53.84; H 6.45; N 8.97.

2.4. 3,4-cis-4,5-trans-2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5-propylisoxazolidine (3b)

Yield 73%, colorless crystals, m.p. 104-105°C (ethanol). R_T (min): 4.2. IR, ν, cm^{-1}: 1536, 1371 (NO_2), 1186 (-C-N-), 1244, 1071 (CH_3-O-Ar), 851 (Ar). ^{1}H NMR, ppm (*J*, Hz): 6.54 (2H, s, $C_6\underline{H}_2$), 5.02 (1H, dd, *J* = 8.35, *J* = 5.72, H4), 4.83 (1H, dq, *J* = 5.72, *J* = 6.18, H5), 3.84 (6H, s, m-OC$\underline{H}_3$), 3.83 (3H, s, p-OC$\underline{H}_3$), 3.79 (1H, d, *J* = 8.35, H3), 2.64 (3H, s, N-C$\underline{H}_3$), 1.73 (2H, m, C$\underline{H}_2$CH$_2$CH$_3$), 1.47 (2H, m, *J* = 8.18, CH$_2$C$\underline{H}_2$CH$_3$), 0.98 (3H, m, CH$_2$CH$_2$C$\underline{H}_3$). ^{13}C NMR, ppm: 153.42, 138.71, 127.40, 105.36 (Ar), 97.32 (C4), 80.67 (C5), 77.25 (C3), 60.83 (p-OC$\underline{H}_3$), 56.24 (m-OC$\underline{H}_3$), 43.24 (N-C$\underline{H}_3$), 34.71 (C$\underline{H}_2$CH$_2$CH$_3$), 18.77 (CH$_2$C$\underline{H}_2$CH$_3$), 13.85 (CH$_2$CH$_2$C$\underline{H}_3$). Found, %: C 56.48; H 7.25; N 8.20. Calculated, %: C 56.46; H 7.11; N 8.23. HR-MS: for $C_{16}H_{25}N_2O_6$ (MH)$^+$calc. 341.1707 m/z, found 341.1708m/z.

2.5. 3,4-trans-4,5-trans-2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5-propylisoxazolidine (4b)

Yield 17%, oil. R_T (min): 7.0. IR, ν, cm^{-1}: 1553, 1360 (NO_2), 1182 (-C-N-), 1238, 1066 (CH_3-O-Ar), 847 (Ar). ^{1}H NMR, ppm (*J*, Hz): 6.58 (2H, s, $C_6\underline{H}_2$), 5.02 (1H, dd, *J* = 6.58, *J* = 3.81, H4), 4.53 (1H, dq, *J* = 6.58, *J* = 8.80, H5), 3.87 (6H, s, m-OC$\underline{H}_3$), 3.85 (1H, d, *J* = 3.81, H3), 3.84 (3H, s, p-OC$\underline{H}_3$), 2.70 (3H, s, N-C$\underline{H}_3$), 1.86 (2H, m, C$\underline{H}_2$CH$_2$CH$_3$), 1.47 (2H, m, *J* = 8.18, CH$_2$C$\underline{H}_2$CH$_3$), 0.99 (3H, m, CH$_2$CH$_2$C$\underline{H}_3$). ^{13}C NMR, ppm: 153.80, 138.48, 131.35, 104.35 (Ar), 99.86 (C4), 80.75 (C5), 77.22 (C3), 60.80 (p-OC$\underline{H}_3$), 56.25 (m-OC$\underline{H}_3$), 43.18 (N-C$\underline{H}_3$), 36.27 (C$\underline{H}_2$CH$_2$CH$_3$), 18.92 (CH$_2$C$\underline{H}_2$CH$_3$), 13.88 (CH$_2$CH$_2$C$\underline{H}_3$). Found, %: C 56.50; H 7.27; N 8.19. Calculated, %: C 56.46; H 7.11; N 8.23.

2.6. 3,4-cis-4,5-trans-2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5 trichloromethylisoxazolidine (3c)

Yield 67%, colorless crystals, m.p. 131-132°C (ethanol). R_T (min): 5.0. IR, ν, cm^{-1}: 1554, 1369 (NO_2), 1185 (-C-N-), 1234, 1077 (CH_3-O-Ar), 852 (Ar). ^{1}H NMR, ppm (*J*, Hz): 6.55 (2H, s, $C_6\underline{H}_2$), 5.54 (1H, d, *J* = 4.33, H5), 5.46 (1H, dd, *J* = 4.33, *J* = 7.92, H4), 4.09 (1H, d, *J* = 7.92, H3), 3.88 (6H, s, m-OC$\underline{H}_3$), 3.87 (3H, s, p-OC$\underline{H}_3$), 2.78 (3H, s, N-C$\underline{H}_3$). ^{13}C NMR, ppm: 153.58, 138.95, 125.92, 104.82 (Ar), 95.23 (C$\underline{C}$l$_3$), 94.79 (C4), 88.82 (C5), 76.75 (C3), 60.82 (p-OC$\underline{H}_3$), 56.18 (m-OC$\underline{H}_3$), 43.33 (N-C$\underline{H}_3$). Found, %: C 40.42; H 3.96; N 6.69. $C_{14}H_{17}N_2O_6Cl_3$. Calculated, %: C 40.45; H 4.12; N 6.74. HR-MS: for $C_{14}H_{21}N_2O_6$ (MH)$^+$ calc. 415.0236 m/z, found 415.0225m/z.

2.7. 3,4-trans-4,5-trans-2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5 trichloromethylisoxazolidine (4c)

Yield 30%, colorless crystals, m.p. 158-159°C (ethanol). R_T (min): 7.2. IR, ν, cm^{-1}: 1560, 1363 (NO_2), 1180 (-C-N-), 1240, 1061 (CH_3-O-Ar), 837 (Ar). ^{1}H NMR, ppm (*J*, Hz): 6.52 (2H, s, $C_6\underline{H}_2$), 5.39 (1H, dd, *J* = 2.32, *J* = 4.85, H4), 5.23 (1H, d, *J* = 4.85, H5), 4.00 (1H, d, *J* = 2.32, H3), 3.88 (6H, s, p-OC$\underline{H}_3$), 3.87 (3H, s, m-OC$\underline{H}_3$), 2.66 (3H, s, N-C$\underline{H}_3$). ^{13}C NMR, ppm: 153.90, 139.06, 128.26, 104.38 (Ar), 97.99 (C$\underline{C}$l$_3$), 96.18 (C4), 88.66 (C5), 79.80 (C3), 60.84 (p-OC$\underline{H}_3$), 56.17 (m-OC$\underline{H}_3$), 43.21 (N-C$\underline{H}_3$). Found, %: C 40.33; H 3.93; N 6.68. Calculated, %: C 40.45; H 4.12; N 6.74.

Melting points were determined on a Boetius apparatus and are uncorrected. Elemental analyses were performed on a Perkin-Elmer PE-2400 CHN apparatus. IR spectra were recorded on a Bio-Rad spectrophotometer. ^{1}H NMR (500MHz) and ^{13}C NMR (125MHz) spectra were recorded on a Bruker AMX 500 spectrometer using $CDCl_3$ as a solvent. Liquid chromatography (HPLC) was done using a Knauer apparatus equipped with a UV-VIS detector. LiChrospher 18-RP 10 μm column (4×240 mm) and 70% methanol as the eluent at flow rate of 1.3 mL min^{-1} were used for monitoring of the reaction progress,. The separation of the post-reaction mixtures was performed at 20°C on the same Knauer apparatus, using a semipreparative column (LiChrospher 18-RP 10 μm, 16×240 mm) and 70% methanol as the eluent at flow rate of 10 mL min^{-1}. Shimadzu LCMS-IT-TOF instrument with ES ionization (heat bock and CDL temperature 200°C, nebulising gas flow 1.5 mL min^{-1}), connected to Shimadzu Prominence chromatograph two pumps LC-20AD equipped with Phenomenex Kinetex 2.6 μm C18 100A column (65% acetonitrile was used as the eluent) was used in all HPLC/MS experiments.

The quantum-chemical calculations were performed on a SGI-2800 computer in the Cracov Computing Center "CYFRONET". Hybrid B3LYP functional and 6-31G(d) basis set included within Gaussian 03 software

were applied [32]. For the simulation of the solvent effect (toluene), the polarisable continuum model (PCM) [33] was applied.

3. Results and discussion

In the first stage we analysed which of the plausible reaction paths **A-D** actually occur. We began by determining the regio- and stereochemistry of the [2+3] cycloaddition of nitrone **1** to (E)-1-nitroprop-1-ene **2a**. For this purpose, several experiments were conducted with varying reaction time, reagent molar ratio, solvent, and temperature. The most favourable conditions for the reaction **1**+**2a** were: room temperature, toluene as a solvent and 4-fold molar excess of the nitroalkene. The nitrone conversion in such conditions was completed after 24 hours. The HPLC analysis of the post-reaction mixture showed the presence of unreacted residual nitroalkene and two products of different retention times (R_T of 2.6 and 3.5 min respectively) in relation 5.9:1. The products were isolated by means of semipreparative HPLC, which yielded compounds of sufficient purity to conduct a full set of structural analyses.

Elemental analysis data gave the overall formula $C_{14}H_{20}N_2O_6$ for the isolated compounds. The absorption bands typical of the nitro group [16], ether bridges [34], 1,2,3,5-tetrasubstituted benzene ring [34], and isoxazolidine ring [35] were identified in the IR spectra. Next, we analysed the MS spectra of the products. Both compounds gave the pseudomolecular ion +313.1350 Da $(MH)^+$, which corresponded to the formula proposed on the basis of elemental analysis with tollerance of 1.92 ppm. Additionally the analysis of pseudomolecular ion fragmentation provided information about regioisomerism of both products. In particular, their fragmentation occurred via ion with m/e=240, which corresponded to the elimination of dimethyloxaziridine molecule. This confirmed that in both products the NO_2 group is in position 4.

Further information about the structure of the isolated compounds was obtained from the ^{1}H NMR spectra. In the compound with R_T=2.6 min the three signals of protons of the heterocyclic ring were identified along with those of the aromatic ring protons as well as methoxy and methyl groups. The H3 proton signal (a doublet) is in the strongest field, while the H4 and H5 proton signals are in weaker fields. The number of resonance lines in the respective multiplets confirmed that the CH_3 group is in position C5, while the nitro group is at C4. The values of the coupling constants $J_{3,4}$ and $J_{4,5}$ prove that protons H3 and H4 are located on the same side of the virtual plane of the heterocyclic ring, while protons H4 and H5 are located on opposite sides. Therefore the configuration of *3,4-cis-4,5-trans*-2,5-dimethyl-3-(3,4,5-trimethoxyphenyl)-4-nitroisoxazolidine **3a** may be assigned to the R_T=2.6 min compound.

The spin system in the ^{1}H NMR spectrum of the compound with R_T=3.5 min is very similar. Also in this case the H3 proton signal is found in a relatively stronger field, while those of H4 and H5 protons are in a weaker field. The multiplicity of the respective signals again shows that 4-nitro-5-methylisoxazolidine is the product. However the values of the coupling constants $J_{3,4}$ and $J_{4,5}$ indicate a *3,4-trans–4,5-trans* isomerism. Thus, the configuration *3,4-trans-4,5-trans*-2,5-dimethyl-3-(3,4,5-trimethoxyphenyl)-4-nitroisoxazolidine **4a** can therefore be assigned to the R_T=3.5 min compound.

We examined the outcome of the reactions **1+2b** and **1+2c** in a similar way. Stereoisomeric *3,4-cis*- and *3,4-trans*-4-nitro-5-R-isoxazolidines were shown to be the cycloaddition products in both cases.

We intended to explain the observed regioselectivity in terms of the recently widely promoted theory of electrophilicity indexes. This approach has been successfully applied to the interpretation of a number of bimolecular reactions [24,36], including [2+3] cycloadditions.

According to the theory of electrophilicity indexes concept [24], the [2+3] cycloaddition processes are considered to be the processes in which electrons are transferred from an addent with a lower global electrophilicity index value (ω) to the one with a higher value of the index. The index ω in this approach is defined as a quotient:

$$\omega=\mu^2/2\,\eta$$

where μ is the electronic chemical potential, and η is the chemical hardness of the substrates. At the same time the nucleophilicity (index N) is defined by the relationship [37]:

$$N=E_{HOMO(1,3\text{-dipole})}- E_{HOMO(TCNE)}$$

When the global reactivity index values (ω, N) are available, the respective local indexes can be determined, describing the electrophilicity (ω_k) [24] and nucleophilicity power (N_k) [38] of the reaction centres. For this purpose the following relationships are used:

$$\omega_k=f^+_k\omega$$

$$N_k=f_kN$$

Table 1. Global and local electronic properties of nitrone **1** nitroalkenes **2a-c**.

	Global properties				Local properties			
	η (a.u.)	μ (a.u.)	ω (eV)	N (eV)	ω_α (eV)	ω_β (eV)	N_C (eV)	N_O (eV)
1	0.1499	-0.1191	1.29	3.84			0.19	0.51
2a	0.2013	-0.1867	2.35		0.05	0.24		
2b	0.2009	-0.1851	2.32		0.05	0.23		
2c	0.1885	-0.2181	3.43		0.18	0.36		

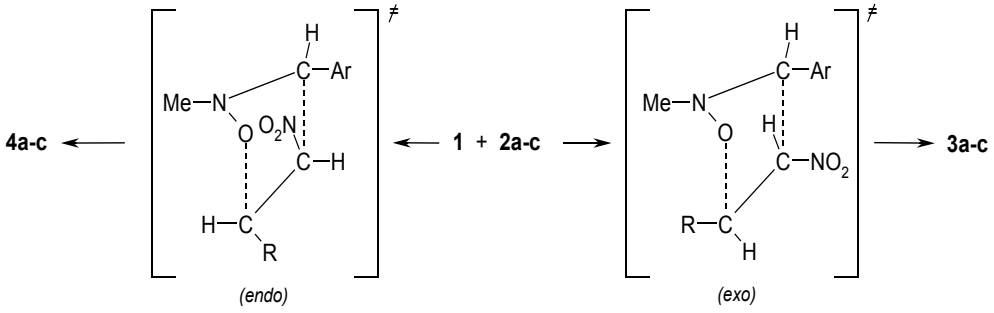


Figure 1. Transition complexes trajectories for formation of the stereoisomeric 2-methyl-3-(3,4,5-trimethoxyphenyl)-4-nitro-5-R-isoxazolidines.

The comparison of the electronic chemical potential μ values of the addents shows that the charge transfer in the elementary cycloaddition process should occur from nitrone **1** (μ = –0.1191 a.u.) to nitroalkene (μ = –0.1851 ÷ –0.2181 a.u.). The analysis of the global electrophilicity ω of the addents leads to a similar conclusion. In particular, the electrophilicities of nitroalkenes **2** are in the range of 2.35 ÷ 3.43 eV. Therefore, according to the scale proposed by Domingo [23], the nitroalkenes **2a-c** can be treated as strong electrophiles. On the other hand, the electrophilicity of nitrone **1** is only 1.29 eV. According to the theory of electrophilicity indexes terminology [23] nitrone **1** should be considered a moderate electrophile and therefore it will play the role of the nucleophile in the cycloaddition reactions with **2a-c**; Its global nucleophilicity N is equal to 3.84 eV.

As can be seen in Table 1, in all the cases the β carbon atom of the nitrovinyl moiety is the most electrophilic reaction centre of the nitroalkene (ω_k= 0.24 ÷ 0.36 eV). On the other hand, the most nucleophilic centre in the nitrone **1** molecule is the oxygen atom in the >C=N(O)- moiety (N_k = 0.51 eV). Hence, the reaction course should be controlled by the attack of one of the nucleophilic sites of the nitrone on the electrophilic site localized on the atom C_β in the nitrovinyl group of the corresponding nitroalkene. Interactions of this type favoured the reaction paths leading to 4-nitroisoxazolidines.

The stereoselectivity of the reactions can be accounted for when two competing effects are taken into consideration. One of these effects is the secondary, stabilising overlap (SOI [39]) of p_z orbitals of the phenyl ring carbon atoms and the nitro group oxygen atoms. This effect favours the transition complexes with the "*exo*" orientation of the nitro group. If this effect is dominant, the *3,4-cis* products predominate in the reaction mixture. On the other hand, steric interactions related to the orientation of the substituent R also affect the stereoselectivity. An increased volume of the substituent leads to the increased prevalence of the reactions which proceed through transition complexes with the "*endo*" orientation of the nitro group. Consequently the ratio of *3,4-cis* (**3**) and *3,4-trans* (**4**) stereoisomers for the cycloaddition **1**+**2a** is 5.9:1, for the cycloaddition **1**+**2b** it is 4.2:1, and for the cycloaddition **1**+**2c** it is 2.2:1.

Finally we have also performed the optimisation of transition complexes on the reaction paths leading to nitroisoxazolidines **3,4a-c**. It was found that all the transition complexes have an extremely assymetric nature (Fig. 2). However, a degree of assymetry is still not sufficient to enforce a zwitterionic, two-step mechanism [5]. On the other hand, a detailed analysis of the IRC trajectories for the reactions **1**+**2a-c** indicates that these processes should be considered "one-step – two-stage" cycloadditions [40].

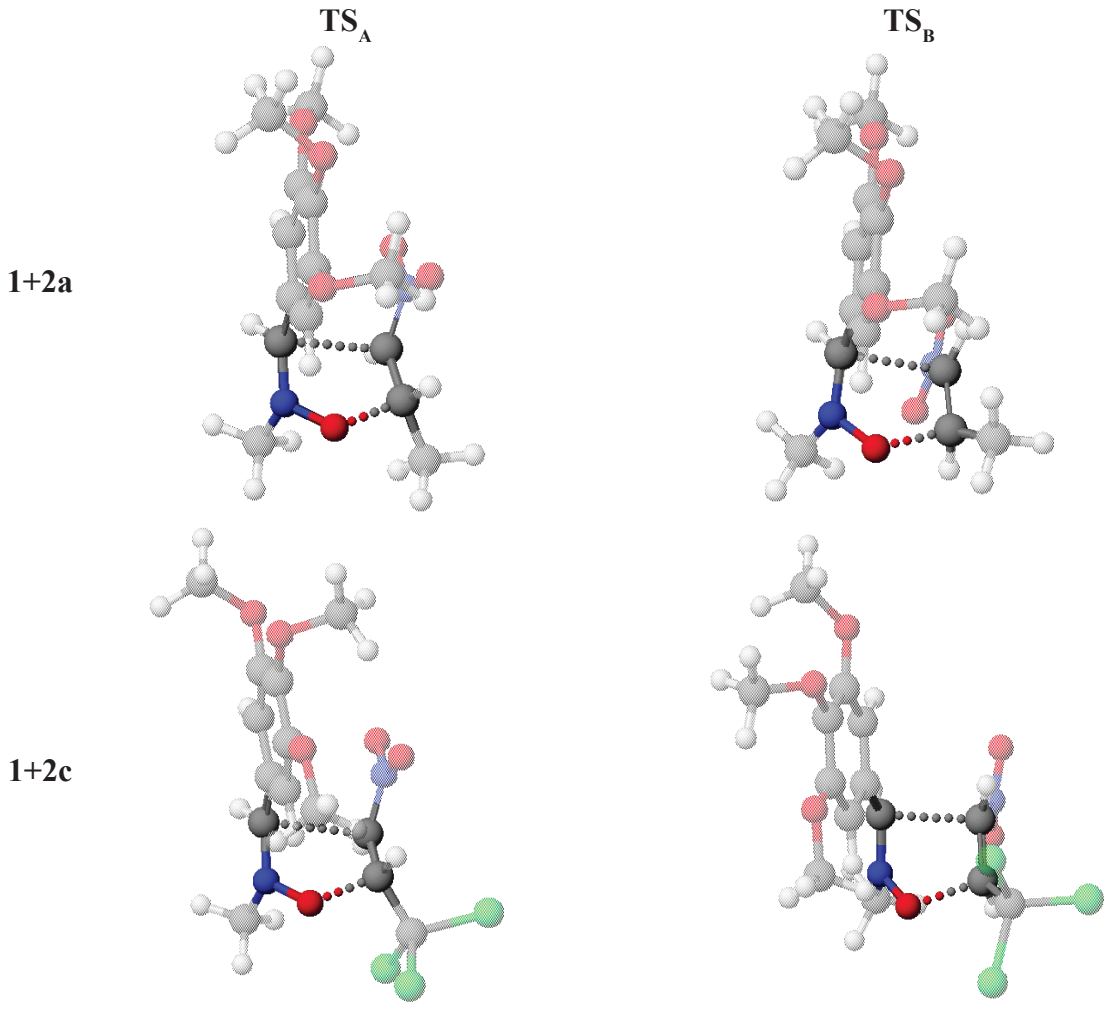


Figure 2. Transition complexes geometries for **1+2a** and **1+2c** [2+3] cycloaddition reactions.

4. Conclusion

In summary, reactions between (Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone **1** and (E)-2-substituted nitroethenes **2a-c** proceed in a regiospecific and stereoselective fashion. The formation of 4-nitroisoxazolidines during the reactions is determined by the characteristics of the local nucleophile-electrophile interactions. The regiochemistry of the reactions is identical as that of similar [2+3] cycloadditions involving highly electrophilic (Z)-C,N-diphenylnitrone [17], C,C,N-triphenylnitrone [21], as well as (for example) the [2+3] cycloaddition between moderately (**1**<ω<diphenylnitrone) electron-rich (Z)-C-phenyl-N-methylnitrone and (E)-3,3,3-trifluoro-1-nitroprop-1-ene [41]. On the other hand, the stereoselectivity is similar, but it depends on the nature of the substituent in position 2 of nitroethene. In particular, the ratio of isomeric *3,4-cis*/*3,4-trans* nitroadducts for the reaction of (Z)-C-(3,4,5-trimethoxyphenyl)-N-methylnitrone with the highly shielded and highly electrophilic (ω = 3.43 eV) (E)-3,3,3-trichloro-1-nitroprop-1-ene is 2.2:1, while that for the reactions involving the less shielded and less electrophilic (ω = 2.35 eV) (E)-1-nitroprop-1-ene is 5.9:1. In comparison, the steric effects have less influence on the reaction course in similar reactions involving (Z)-C,N-diphenylnitrone and their stereoselectivity is determined generally by polar interactions. In consequence, *3,4-cis* and *3,4-trans*-2,3-diphenyl-4-nitro-5-trichloromethylisoxazolidines are formed in a ratio of 14:1, while the ratio of *3,4-cis*- and *3,4-trans*-2,3-diphenyl-4-nitro-5-methylisoxazolidines is 4:1 [17].

Acknowledgements

The generous allocation of computing time by the regional computer center “Cyfronet” in Cracow (Grant No. MNil/SGI2800/PK/053/2003) and financial support from the Polish Ministry of Science and Higher Education (Grant No. C-2/175/DS/2012) are gratefully acknowledged.

References

[1] R. Jasiński, J. Heterocyclic Chem. 50 (2013) DOI: 10.1002/jhet.2020 (in press)
[2] T.B. Nguyen, A. Martel, C. Gaulon-Nourry, R. Dhal, G. Dujardin, Org. Prep. Proc. Int. 44, 1 (2012)
[3] A. Barański, R. Jasiński, E. Cholewka, In: Z. Kowalski (Ed.), Postępy w inżynierii i technologii chemicznej (Politechnika Krakowska, Kraków, 2011) (in Polish)
[4] A. Padwa, W.H. Pearson, Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products (Wiley & Sons, Hoboken, New Jersey, 2003)
[5] R. Huisgen, G. Mloston, In: A.A. Potekhin, R.R. Kostikov, M.S. Baird (Eds.), Modern Problems of Organic Chemistry (St. Petersburg University Press, St. Petersburg, 2004)
[6] G. Chauviere, B. Bouteille, B. Enanga, C. de Albuquerque, S.L. Croft, M. Dumas, J. Périé, J. Med. Chem. 46, 270 (2003)
[7] A.F. Oleinik, K.Yu. Novitskii, E.N. Dozorova, N.P. Solov’eva, L.M. Polukhina, N.A. Novitskaya, G. N. Pershin, Pharm. Chem. J. 14, 610 (1980)
[8] M.A. Iradyan, A.Kh. Ayvazyan, V.S. Mirzoyan, G.M. Paronikyan, T.P. Sarkisyan, G.M. Stepanyan, F.G. Arsenyan, B.T. Garibdzhanyan, Pharm. Chem. J. 21, 403 (1987)
[9] A.G.M. Barrett, G.G. Graboski, Chem. Rev. 86, 751 (1985)
[10] N. Ono, The nitro group in organic synthesis, (Wiley-VCH, Weinheim, 2001)
[11] R.Ballini, M. Petrini, Tetrahedron 60, 1017 (2004)
[12] G.W. Kabalka, L.H.M. Guindi, R.S. Varma, Tetrahedron 46, 7443 (1990)
[13] Z. Rappaport, J.F. Liebman, In: Z. Rappaport (Ed.), The Chemistry of functional groups (Wiley, Chichester, 2009) vol. 1
[14] (a) L.I. Belenkii, In: H. Feuer (Ed.), Nitrile oxides, nitrone and nitronates in orgnanic synthesis (Wiley, Chichester, New York, 2007); (b) V.Yu. Korotayev, A.Yu. Barkov, P.A. Slepukhin, M.I. Kodess, V.Ya. Sosnovskikh, Mendeleev Commun. 21, 112 (2011); (c) V.Yu. Korotayev, V.Ya. Sosnovskikh, M.A. Barabanov, A.Yu. Barkov, M.I. Kodess, Mendeleev. Commun. 17, (2010)
[15] J.P. Agrawal, R.D. Hodgson, Chemistry of explosives (Wiley, Chichester, Hoboken, 2007)
[16] C.C. Novikov, G.A. Shvekhgeimer, V.V. Sevastyanova, V.A. Shlaposhnikov, Khimiya alifaticheskikh i alitsiklicheskikh nitrosoedinenii (Izd. Khimya, Moscow, 1974) (in Russian)
[17] R. Jasiński, A. Barański, Polish J. Chem. 80, 1493 (2006)
[18] R. Jasiński, M. Mikulska, A. Barański, Acta Chim. Slov. 58, 41 (2011)
[19] R. Jasiński, M. Mikulska, A. Barański, Central Eur. J. Chem. 11, 1471 (2013)
[20] R. Jasiński, A. Lyubimcev, A. Ciężkowska, A. Barański, Chem. Heterocyclic Compd. 40, 206 (2004)
[21] R. Jasiński, O. Koifman, A. Barański, Mendeleev Commun. 21, 262 (2011)
[22] R. Jasiński, Tetrahedron 69, 927 (2013)
[23] P. Perez, L.R. Domingo, M.J. Aurell, R. Contreras, Tetrahedron 59, 3117 (2003)
[24] P. Perez, L.R. Domingo, A. Aizman, R. Contreras, In: A. Toro-Labbé (Ed.), Theoretical and Computational Chemistry (Elsevier, Amsterdam, Boston, 2007) vol. 1
[25] Barański, R. Jasiński, Wiad. Chem. 56, 829 (2002) (in Polish)
[26] A. Barański, V.I. Kelarev, Chem. Heterocyclic Compd. 26, 371 (1990)
[27] R. Huisgen, In: A. Padwa (Ed.), 1,3-Dipolar Cycloaddition Chemistry (Wiley Interscience, New York, 1984)
[28] G. Wagner, T. Garlan, Tetrahedron Lett. 49, 3596 (2008)
[29] G.D. Buckley, C.W. Scaife, J. Chem. Soc. 1417 (1947)
E. Schmidt, G. Rutz, Ber. Dtsch. Chem. Ges. 61,
[30] 2142 (1928)
[31] F. Brower, H. Burkett, J. Am. Chem. Soc. 75, 1082 (1953)

[32] M.J. Frisch , G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, T.Jr. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, Y. Nakajima, O. Honda, O. Kitao, H. Nakai, M. Klene, X Li, J.E. Knox, H.P. Hratchian, J.B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, M.C., Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D. J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez,. J.A. Pople, Gaussian 03, Revision B.04 (Gaussian, Inc., Pittsburgh PA, 2003)

[33] J. Tomasi, B. Mennucci, E. Cancès, J. Mol. Struct. (Theochem) 464, 211 (1999)

[34] E. Pretsch, P. Bullmann, C. Affolter, Structure Determination of Organic Compounds; Tables of Spectral Data (Springer-Verlag, Berlin, Heidelberg, 2000)

[35] P. Grunager, P. Vita-Finzi, In: A. Padwa (Ed.), The Chemistry of Heterocyclic Compounds (Wiley & Sons, New York, 1991) vol.49

[36] P.K. Chattaraj, S. Giri, S. Duley, Chem. Rev. 111, PR43 (2011)

[37] L.R. Domingo, E. Chamorro, P. Perez, J. Org. Chem. 73, 4615 (2008)

[38] P. Perez, L.R. Domingo, M. Duque-Norena, E. Chamorro, J. Mol. Struct. (TheoChem), 895, 86 (2009)

[39] D. Ginsburg, Tetrahedron 39, 2095 (1983)

[40] L.R. Domingo, J.A. Saez, Org. Biomol. Chem. 7, 3576 (2009)

[41] K. Tanaka, T. Mori, K. Mitsuhashi, Bull. Chem. Soc. Japan 66, 263 (1993)