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A DFT study on the regioselectivity and molecular mechanism of nitroethene [2+3] cycloaddition to (*Z*)-*C*,*N*-diphenylnitrone and *C*,*C*,*N*-triphenylnitrone

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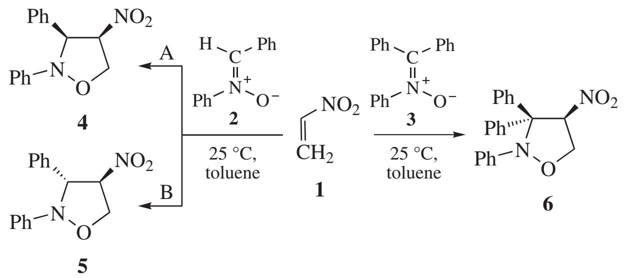
Global and local reactivity indexes indicate a polar character of the [2+3] cycloaddition of nitroethene to (*Z*)-*C*,*N*-diphenylnitrone and *C*,*C*,*N*-triphenylnitrone. The regioselectivity of the reactions is determined by the attack of an oxygen-centred nucleophilic site of the nitrone on the β-carbon atom in nitroethene, which is confirmed by B3LYP/6-31G(d) simulations of the reaction pathways. Although the transition complexes are considerably asymmetric and polar, the reactions proceed *via* a concerted mechanism.

This work is a continuation of our studies[1–9] on the [4+2] π-electron cycloaddition involving conjugated nitroalkenes. Previously, we found experimentally[3,4] that [2+3] cycloadditions of nitroethene **1** to (*Z*)-*C*,*N*-diphenylnitrone **2** and *C*,*C*,*N*-triphenylnitrone **3** are regiospecific, yielding the respective 4-nitroisoxazolidines as the only reaction products (Scheme 1). Due to the high nitroethene π-deficiency,[10,11] the reactions can proceed according to either a concerted[12] or zwitterionic mechanism.[13,14]



Scheme 1

We explained the regiospecificity phenomenon with respect to the widely promoted theory of reactivity indexes[10] and performed B3LYP/6-31G(d) simulations of the reaction pathways under the conditions resembling those used in the experiment.[†] Recently, a similar approach was used to analyze the [2+3] cycloaddition of (*Z*)-*C*,*N*-diarylnitrones to 2-nitroprop-1-ene,[7] (*E*)-2-phenylnitroethene,[9] (*E*)-3,3,3-trichloro-1-nitropropene[9] and other π-deficient dipolarophiles,[19,20] and good correlations between theoretical and experimental data were found.

A comparison of the chemical potentials (μ) of addents suggests that charge transfer during the cycloaddition reactions occurs from nitrone [μ(**2**) = –0.1312 a.u.; μ(**3**) = –0.1256 a.u.] to nitroethene **1** [μ(**1**) = –0.1958 a.u.]. The global electrophilicity (ω) of nitroethene **1** is 2.61 eV. Hence, according to published data,[17] **1** can be considered as a strong electrophile. Nitrones **2** and **3** are in the same group, despite their electrophilicity is slightly lower [ω(**2**) = 1.67 eV; ω(**3**) = 1.56 eV]. Therefore, they act as nucleophiles in the test reactions. The nucleophilicity index N describes their nucleophilic strength, which is 3.64 eV for nitrone **2** and 3.83 eV for nitrone **3**. The electrophilicity difference ($\Delta\omega$) of the reagent pairs **1**+**2** and **1**+**3** is ~1 eV. Therefore, the reactions can be considered as polar processes.[10] The regioselectivity of such reactions can be forecast[17] using local electrophilicity (ω_k) and nucleophilicity (N_k) indexes.

The values of ω_k suggest that the strongest electrophilic centre in the nitroethene molecule is located on the β-carbon of the nitrovinyl moiety [ω_β(**1**) = 0.26 eV]. However, in nitrones **2** and **3**, the most nucleophilic centres are located on the oxygen atoms of the >C=N(O) moiety [N_O(**2**) = 0.57 eV; N_O(**3**) = 0.60 eV]. If the regioselectivity of the reactions is determined by electrophile–nucleophile interactions, the products should be 4-nitroisoxazolidines **4**–**6** (Scheme 1). Experimental studies have clearly confirmed the regioselectivity predictions.[3,4]

The analysis of ω_k and N_k indexes provides no information on the reaction mechanism. Therefore, we performed B3LYP/6-31G(d) calculations of the reaction energy profiles to clarify this issue.

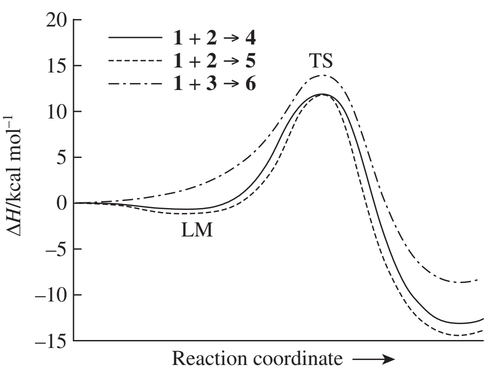


Figure 1 Reaction profiles for [2+3] reactions between nitroethene **1** and nitrones **2**, **3** in a toluene solution.

[†] The global (μ, ω, N) and local (ω_k, N_k) reactivity indexes for reactants **1**–**3** were estimated according to the equations recommended by Domingo (see ref. 15). The critical points on the potential energy surface were localised in a similar manner as in the case of the previously analysed reaction of 2-nitroprop-1-ene with (*Z*)-*C*,*N*-diphenylnitrone,[7] using the hybrid B3LYP functional and the 6-31G(d) basis set.[16] The presence of toluene as a solvent was taken into account in the calculations. For this purpose, the polarizable continuum model (PCM)[17] with full geometry optimizations was applied. All calculations were performed for T = 298 K and p = 1 atm. The bond advancement indexes l were calculated according to the equation described previously.[7] Charge transfer (t) was calculated according to the expression given by Leroy *et al.*[18] Consistently with previously[7,9] used convention, in this paper, the letters LM and TS denote pre-reaction complexes and transition states, respectively.

The calculations were carried out in the presence of toluene as a reaction medium, which was previously used as a solvent in experimental studies.[3,4]

The energy profiles of the reactions **1** + **2** → **4** and **1** + **2** → **5** are similar (Figure 1). In both cases, only one transition state TS, preceded by a shallow local minimum of the pre-reaction complex LM, occurs between the product and substrate minima. This is conclusively confirmed by IRC calculations.

LM formation is related to the system enthalpy reduced by 0.5 kcal mol^{-1} for pathway A and by 1.4 kcal mol^{-1} for pathway B. Moreover, both LMs are exclusively enthalpic in character, since the entropic factor ($T\Delta S$) excludes the possibility of their existence at room temperature in the form of stable intermediates ($\Delta G > 0$). Within both LMs the distances between the reaction centres are much longer than the lengths of typical σ-bonds formed in the transition complexes. The structures of LM_A and LM_B have no features of orientation complexes (OCs).[12,21] Moreover, they are not charge transfer complexes due to the lack of charge transfer between the substructures (t = 0.00 e).

Any further approach of the reaction centres leads to a transition state. As the critical point on the energy profile is reached, the system enthalpy ($\Delta H^{\neq}$) increases by 12.1 kcal mol^{-1} in pathway A and by 11.9 kcal mol^{-1} in pathway B. The formation of TS_A and TS_B complexes coincides with the system entropy ($\Delta S^{\neq}$), which is reduced by 46.6 and 45.0 cal mol^{-1} K^{-1}, respectively. This is typical of concerted [2+3] cycloadditions proceeding *via* highly rigid transition complexes.[12] Note that, in the light of B3LYP/6-31g(d) simulations, both stereoisomeric pathways are allowed from the kinetic point of view ($\Delta G^{\neq}$ = 26.0 and 25.3 kcal mol^{-1} K^{-1} for pathways A and B, respectively); this is consistent with the experimental data. However, the values of $\Delta G^{\neq}$ in the competitive regioisomeric paths are more than 2 kcal mol^{-1} higher than those of the most favoured path B ($\Delta G^{\neq}$ = 28.1 and 27.4 kcal mol^{-1} K^{-1} lead to 3,5-*cis*- and 3,5-*trans*-2,3-diphenyl-5-nitroisoxazolidines, respectively). Unfortunately, the predicted stereoisomer ratio is different from that specified for crude post-reaction mixture.

In both TSs, new σ-bonds form simultaneously. Their degree of advancement (l), however, is different. The C(5)–O(1) bond is more advanced. Its length is 1.789 Å ($l_{C(5)–O(1)}$ = 0.757) for TS_A and 1.782 Å ($l_{C(5)–O(1)}$ = 0.760) for TS_B. The other σ-bonds [C(3)–C(4)], formed in the TS_A and TS_B complexes, have the lengths of 2.491 ($l_{C(3)–C(4)}$ = 0.431) and 2.418 Å ($l_{C(3)–C(4)}$ = 0.452), respectively. Both complexes are polar, as confirmed by their dipole moments (μ_D > 5.5 D) and the degree of charge transfer between the substructures (t = 0.15–0.16 e). However, the polarity of the structures is insufficient for inducing a zwitterionic reaction mechanism.

The energy profile of the reactions **1** + **3** → **6** is somewhat different. In this case, only one critical point corresponding to TS occurs between the substrate and product minima. When the transition state is achieved, the system enthalpy increases by 14.1 kcal mol^{-1}, which is accompanied by an entropy reduction of 48.7 cal mol^{-1} K^{-1}. Similarly as in the case of the **1** + **2** reactions, the value of $\Delta S^{\neq}$ is typical of concerted cycloadditions, while $\Delta G^{\neq}$ is 28 kcal mol^{-1}.

In the analysis of the TS complex geometry, it is noticeable that the C(5)–O(1) bond is formed more rapidly ($r_{C(5)–O(1)}$ = = 1.645 Å, $l_{C(5)–O(1)}$ = 0.857) than the C(3)–C(4) bond ($r_{C(3)–C(4)}$ = = 2.584 Å, $l_{C(3)–C(4)}$ = 0.365). The asymmetry of the TS (Δl = 0.49) is higher than those of the reactions **1** + **2** → **4** and **1** + **2** → **5**. The polarity is also higher (μ_D = 8.51 D, t = 0.20 e). However, neither the degree of asymmetry of the σ-bonds being formed in TS nor the TS polarities are sufficiently high to induce a zwitterionic reaction mechanism. This was confirmed by IRC calculations, which proved that the localised TS was the only transition state involved in the conversion of addents into products.

In conclusion, the π-deficiency of nitroethene is not sufficient to induce an ionic course of its [2+3] cycloaddition to aryl-nitrones. It seems necessary to introduce electron-accepting group to 1-position of nitroalkene to force a zwitterionic reaction character. Hence, the use of 1-halo-1-nitroethenes as the dipolarophiles may induce an ionic reaction course. Kinetic studies of these reactions are planned to be performed.

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References

1 R. Jasiński, M. Kwiatkowska and A. Barański, *J. Phys. Org. Chem.*, 2011, **24**, 843.

2 R. Jasiński and A. Barański, *Pol. J. Chem.*, 2006, **80**, 1493.

3 R. Jasiński, *Czech. Coll. Chem. Commun.*, 2009, **74**, 1341.

4 R. Jasiński, *Khim. Geterotsikl. Soedin.*, 2009, 932 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 2009, **45**, 748].

5 M. Kwiatkowska, R. Jasiński, M. Mikulska and A. Barański, *Monatsh. Chem.*, 2010, **141**, 545.

6 R. Jasiński, P. Michorczyk, E. Jasińska, O. I. Koifman and A. Barański, *Izv. Vuzov Khim. Khim. Tekhnol.*, 2011, **54** (5), 89 (in Russian).

7 R. Jasiński, K. Wąsik, M. Mikulska and A. Barański, *J. Phys. Org. Chem.*, 2009, **22**, 717.

8 R. Jasiński and A. Barański, *J. Mol. Struct. (TheoChem)*, 2010, **949**, 8.

9 R. Jasiński and A. Barański, *Pol. J. Chem.*, 2007, **81**, 1441.

10 L. R. Domingo and J. A. Saéz, *Org. Biomol. Chem.*, 2009, **7**, 3576.

11 L. Pasa-Tolić, L. Klasinc and S. P. McGlynn, *Chem. Phys. Lett.*, 1990, **170**, 113.

12 R. Huisgen, in *1,3-Dipolar Cycloaddition Chemistry*, ed. A. Padwa, Wiley-Interscience, New York, 1984.

13 R. Huisgen and G. Mloston, in *Modern Problems of Organic Chemistry*, eds. A. A. Potekhin, R. R. Kostikov and M. Baird, St. Petersburg University, St. Petersburg, 2004.

14 R. Jasiński, M. Kwiatkowska and A. Barański, *Wiad. Chem.*, 2007, **61**, 485.

15 P. Perez, L. R. Domingo, A. Aizman and R. Contreras, in *Theoretical and Computational Chemistry*, ed. A. Toro-Labbé, Elsevier, 2007, vol. 19.

16 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 and J. A. Pople, *Gaussian 03, Revision B.04*, Gaussian, Inc., Pittsburgh PA, 2003.

17 M. Barone, M. Cossi and J. Tomasi, *J. Comput. Chem.*, 1998, **19**, 404.

18 G. Leroy, M. Sana, L. A. Burke and M. T. Nguyen, *Quantum Theory Chem. React.*, 1980, **1**, 91.

19 R. Herrera, J. A. Mendoza, M. A. Morales, F. Méndez, H. A. Jiménez-Vázquez, F. Delgado and J. Tamariz, *Eur, J. Org. Chem.*, 2007, 2352.

20 L. R. Domingo, W. Benchouk and S. M. Mekelleche, *Tetrahedron*, 2007, **63**, 4464.

21 A. I. Konovalov, in *Stroenie i reaktsionnaya sposobnost organicheskikh soedinenii* (*Structure and Reactivity of Organic Compounds*), Nauka, Moscow, 1978 (in Russian).

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