

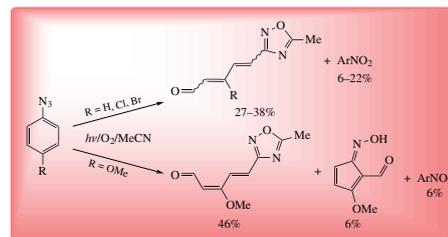
## Formation of 1,2,4-oxadiazoles in the course of photooxidation of aromatic azides in acetonitrile

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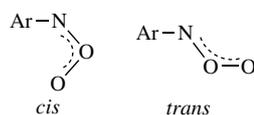
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Photolysis of aryl azides at room temperature in acetonitrile in the presence of oxygen proceeds as arene ring opening and acetonitrile trapping to afford 5-methyl-3-(5-oxopenta-1,3-dien-1-yl)-1,2,4-oxadiazoles. In the case of 4-methoxyphenyl azide, a product depriving of acetonitrile reactant, 1-hydroxyimino-3-methylcyclopentadiene-2-carbaldehyde, is also formed.



**Keywords:** photooxidation, aryl azides, aryl nitroso oxides, nitrile oxides, 1,2,4-oxadiazoles.

Aryl nitroso oxides (ArNOO) are labile species which are formed *via* the reaction of triplet nitrenes with molecular oxygen.<sup>1–6</sup> Nitroso oxides have a singlet ground state,<sup>7</sup> and their electronic structure may be described by superposition of the several resonances.<sup>4,8</sup> Owing to the partial double bond N–O in the NOO moiety, they exist as *cis* and *trans* isomers.<sup>4,9</sup> The isomeric forms differ in their spectral properties and reactivity in various reactions.<sup>4,10,11</sup>



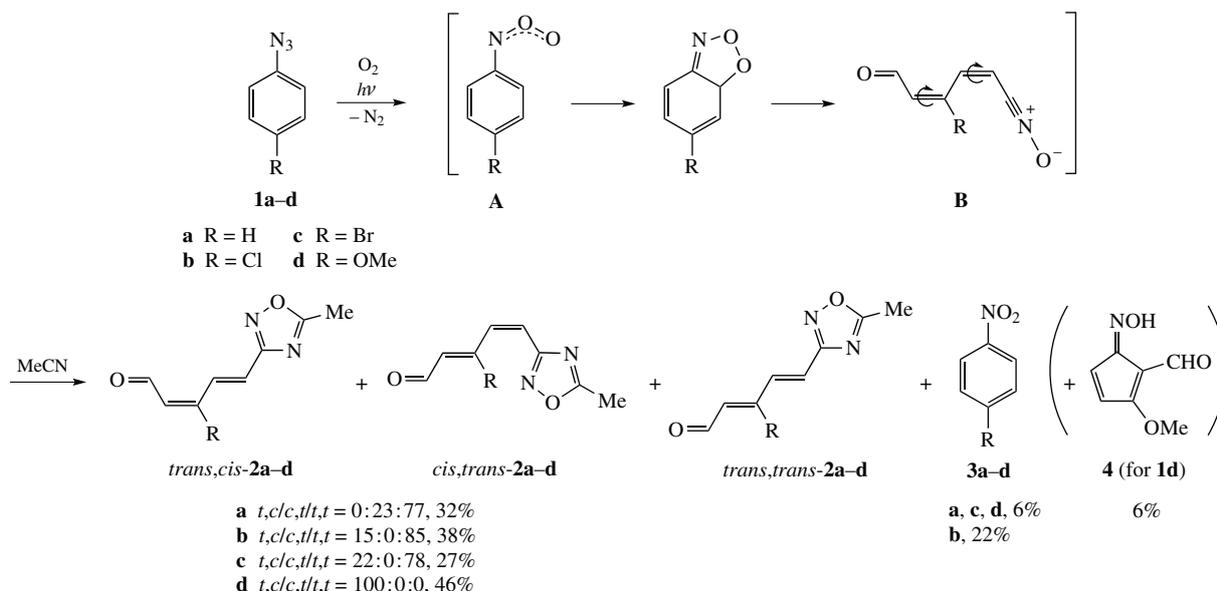
For a long time the corresponding nitroso- and nitrobenzenes were believed to be the main products of the photolysis of aromatic azides in the presence of oxygen.<sup>10,12,14</sup> Their formation was explained by recombination of the intermediate nitroso oxides.<sup>10</sup> Based on numerous examples it was supposed that the photoinduced isomerization of ArNOO also might lead to the corresponding nitroarenes.<sup>4,15</sup> Recently, it has been reported that there was the unimolecular channel for the consumption of nitroso oxides, namely, redox isomerization of the *cis* form with opening of the aromatic ring and the formation of a nitrile oxide.<sup>4,11</sup> The *trans* form was consumed *via* the transformation to the *cis* form. Nitrile oxides formed upon the photooxidation of 4-methoxy<sup>11</sup> and 2,4-dimethoxyphenyl<sup>16</sup> azides were isolated and identified.

Under thermal conditions, nitrile oxides would dimerize to give furoxans<sup>17</sup> and cyclize intramolecularly if they contain a suitable reactive center.<sup>18,19</sup> Transformations of aromatic azides to carbo<sup>20</sup> and heterocyclic<sup>4,16,21–23</sup> compounds are documented. Nitrile oxides formed upon the photooxidation of these azides contain either a double bond with which [3+2]-cycloaddition of the nitrile oxide group occurs,<sup>4,20,22</sup> or a nucleophilic center capable of reacting with the nitrile oxide carbon atom.<sup>4,20,21,23</sup> The ratio between the uni- and bimolecular channels of the consumption of nitroso oxides, which can be judged by the yields of the corresponding products, depends on various

reaction conditions, such as solvent polarity, temperature, concentration of the starting azide and/or irradiation intensity.<sup>20</sup>

The present study was undertaken to show the universality of the mechanism for the unimolecular consumption of *para*-substituted aryl nitroso oxides. For this, the products of the photooxidative decomposition of unsubstituted phenyl azide **1a** as well as its *para*-substituted analogues with electron-donating (**1d**) and electron-withdrawing (**1b,c**) groups in acetonitrile at room temperature have been studied (Scheme 1). It is assumed that upon the photooxidation of azides **1a–c** as in the case of previously studied azide **1d**, nitrile oxides which do not contain reactive centers suitable for intramolecular stabilization of the CNO group are formed from the corresponding nitroso oxides. It was established in this work that the end products of the photooxidation of aromatic azides were 1,2,4-oxadiazoles **2a–d**, which were formed *via* the [3+2]-cycloaddition of nitrile oxides with acetonitrile. Products of dimerization of the nitrile oxide have not been found. For the isolation and identification of the products, see Online Supplementary Materials.

Nitrile oxides, in turn, are the products of the aromatic ring opening of the *cis* form of the nitroso oxides **A** (see Scheme 1). Thus, intermediate compounds detected during the photooxidation of azides **1a–d** were nitrile oxides **B**, which were consumed by the reaction with acetonitrile to give 1,2,4-oxadiazoles **2a–d**. The 1,3-dipolar cycloaddition of nitrile oxides with nitriles, which proceeds *via* concerted formation of the C–O and N–O bonds, is one of the typical syntheses of 1,2,4-oxadiazoles.<sup>24–26</sup> Products **2** were obtained as mixtures of stereoisomers in the diene moiety. The activation energy of the *cis–trans* isomerization of conjugated dienes is ~12.0–14.5 kJ mol<sup>–1</sup>.<sup>27,28</sup> Therefore, in our case a rotation around the C=C bonds took place upon irradiation. Nitrile oxides **B** and oxadiazoles **2** absorb in the wavelength range of 240–350 nm with maxima at ~300 and 280 nm, respectively. The photolysis of azides was performed by light with a wavelength of >300 nm that corresponded to energy of <95 kcal mol<sup>–1</sup>. Therefore, the energy of this light is enough to activate *cis–trans* isomerization of the buta-1,3-diene chain. Presumably, both nitrile oxides **B** and oxadiazoles **2** may



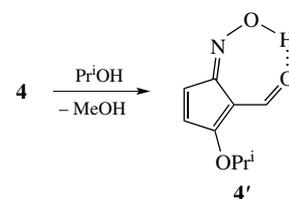
**Scheme 1** Reagents and conditions: O<sub>2</sub> (air), MeCN, room temperature, *hν* (300 nm), 3 days (for **1a,d**) or 4 days (for **1b,c**).

undergo this isomerization. Recently, the analogous product was found among the products of the photooxidation of 2-methyl-5-azido-1*H*-indole.<sup>23</sup>

Upon the photooxidation of azide **1d**, oxadiazole dienal **2d** was isolated as individual *trans,cis*-isomer. In this case, the formation of cyclopentadiene **4** (~6%) was also recorded (see Scheme 1).<sup>20</sup> Previously, an analogous cyclopentadiene was obtained as the main product upon the photooxidation of 4-*N,N*-dimethylaminophenyl azide in hexane at room temperature and in acetonitrile at 70 °C.<sup>20</sup> The mechanism for the formation of cyclopentadiene was studied by theoretical methods; MeO and Me<sub>2</sub>N were considered as substituents.<sup>20</sup> The reaction proceeds via a sequence of unimolecular transformations. In the case of nitrile oxide **B** with R = Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, the Gibbs activation energy for the intramolecular cyclization is 88.4 kJ mol<sup>-1</sup>, whereas the analogous transformation of nitrile oxide **B** with R = MeOC<sub>6</sub>H<sub>4</sub> requires more (121.4 kJ mol<sup>-1</sup>) energy. That is, the presence of the Me<sub>2</sub>N group greatly facilitates the reaction, since the strong mesomeric effect of this substituent promotes increasing nucleophilicity of the reaction center in the transition state. Upon the photooxidation of 4-*N,N*-dimethylaminophenyl azide in acetonitrile, the adduct of the corresponding nitrile oxide **B** with acetonitrile was not found<sup>20</sup> because that reaction could not compete with the intramolecular cyclization of the nitrile oxide into cyclopentadiene. In the present work it was found that the main products of the photooxidation of aromatic azides **1a-d** were 1,2,4-oxadiazole dienals **2** and only in the case of 4-methoxyphenyl azide **1d** the product of the intramolecular cyclization of the nitrile oxide, cyclopentadiene **4**, was obtained in a very small amount. Thus, for the efficient formation of cyclopentadiene **4** the presence of a strong electron-donating substituent in the *para*-position of the starting aryl azide is necessary.

During the isolation, methoxy cyclopentadiene **4d** underwent trans-etherification and the isolated product was isopropoxy derivative **4'** (Scheme 2). This transformation is presumably facilitated by column silica gel. The <sup>1</sup>H NMR spectrum of compound **4'** contains a very downfield signal (13.63 ppm), which indicates the presence of an intramolecular hydrogen bond between the oxime hydroxyl and the carbonyl oxygen atom, which is additional evidence for the structure of the obtained compound.

To conclude, using the example of unsubstituted phenyl azide as well as phenyl azides with electron-donating (MeO) and



**Scheme 2** Reagents and conditions: PrOH, SiO<sub>2</sub>, room temperature.

electron-withdrawing (Cl, Br) substituents at the *para*-position, we have shown that the photolysis of aryl azides in acetonitrile in the presence of oxygen leads to the formation of nitrile oxides, the products of the unimolecular transformations of the reaction intermediates nitroso oxides. The studied nitrile oxides formed from azides **1a-c** are stabilized by the reaction with acetonitrile to afford 1,2,4-oxadiazole dienals. In the case of azide **1d**, intramolecular addition of the carbon atom of the nitrile oxide group resulting in formation of cyclopentadiene with oxime substituent **4** also occurs to a small extent.

The study was performed within the framework of the State assignment on the themes of scientific research work of the Ufa Institute of Chemistry, UfRS RAS AAAAA-A17-117011910034-8. The HPLC investigations were performed and the NMR and mass spectra recorded on equipment at the Center for Collective Use 'Chemistry' of the Ufa Institute of Chemistry, UfRS RAS.

#### Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.03.029.

#### References

- K. Ishiguro and Y. Sawaki, *Bull. Chem. Soc. Jpn.*, 2000, **73**, 535.
- N. P. Gritsan, *Russ. Chem. Rev.*, 2007, **76**, 1139 (*Usp. Khim.*, 2007, **76**, 1218).
- N. Sawwan and A. Greer, *Chem. Rev.*, 2007, **107**, 3247.
- E. M. Chainikova, S. L. Khursan and R. L. Safiullin, in *The Chemistry of Peroxides*, eds. A. Greer and J. F. Liebman, John Wiley & Sons, Chichester, UK, 2014, vol. 3, pp. 357–420.
- G. Dequirez, V. Pons and P. Dauban, *Angew. Chem.*, 2012, **124**, 7498.
- C. Wentrup, *Angew. Chem.*, 2018, **130**, 11680.
- N. P. Gritsan and E. A. Pritchina, *J. Inf. Rec. Mater.*, 1989, **17**, 391.
- P. C. Hiberty and G. Ohanessian, *J. Am. Chem. Soc.*, 1982, **104**, 66.
- E. A. Pritchina, N. P. Gritsan and T. Bally, *Phys. Chem. Chem. Phys.*, 2006, **8**, 719.

- 10 E. A. Pritchina and N. P. Gritsan, *J. Photochem. Photobiol.*, A, 1988, **43**, 165.
- 11 E. M. Chainikova, R. L. Safiullin, L. V. Spirikhin and M. F. Abdullin, *J. Phys. Chem. A*, 2012, **116**, 8142.
- 12 R. A. Abramovitch and S. R. Challand, *J. Chem. Soc., Chem. Commun.*, 1972, 964.
- 13 C. L. Go and W. H. Waddel, *J. Org. Chem.*, 1983, **48**, 2897.
- 14 R. L. Safiullin, S. L. Khursan, E. M. Chainikova and V. T. Danilov, *Kinet. Catal.*, 2004, **45**, 640 (*Kinet. Katal.*, 2004, **45**, 680).
- 15 T. Harder, P. Wessig, J. Bendig and R. Stösser, *J. Am. Chem. Soc.*, 1999, **121**, 6580.
- 16 E. M. Chainikova, A. R. Yusupova, S. L. Khursan, A. N. Teregulova, A. N. Lobov, M. F. Abdullin, L. V. Enikeeva, I. M. Gubaydullin and R. L. Safiullin, *J. Org. Chem.*, 2017, **82**, 7750.
- 17 V. Jager and P. A. Colinas, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, eds. A. Padwa and W. H. Pearson, John Wiley & Sons, New York, 2002, vol. 59, pp. 361–472.
- 18 R. Annunziata, M. Cinquini, F. Cozzi, C. Gennari and L. Raimondi, *J. Org. Chem.*, 1987, **52**, 4674.
- 19 A. Hassner, A. S. Amarasekara, A. Padwa and W. H. Bullock, *Tetrahedron Lett.*, 1988, **29**, 715.
- 20 E. Chainikova, S. Khursan, A. Lobov, A. Erastov, L. Khalilov, E. Mescheryakova and R. Safiullin, *Tetrahedron Lett.*, 2015, **56**, 4661.
- 21 A. Albin, G. Bettinetti and G. J. Minoli, *Org. Chem.*, 1987, **52**, 1245.
- 22 E. Chainikova, A. Teregulova, A. Lobov, A. Erastov and R. Safiullin, *Tetrahedron Lett.*, 2015, **56**, 1332.
- 23 E. Chainikova, S. Khursan, A. Yusupova, A. Lobov, M. Abdullin and R. Safiullin, *Tetrahedron Lett.*, 2018, **59**, 3267.
- 24 K. Hemming, *Sci. Synth.*, 2004, **13**, 127.
- 25 M. L. Kuznetsov, V. Yu. Kukushkin and A. J. L. Pombeiro, *Dalton Trans.*, 2008, 1312.
- 26 A. R. Yarullin, M. Yu. Ovchinnikov, S. L. Khursan, E. M. Chainikova and R. L. Safiullin, *J. Mol. Graph. Model.*, 2020, **95**, 107491.
- 27 L. M. Stephenson, R. V. Gemmer and J. I. Brauman, *J. Am. Chem. Soc.*, 1972, **94**, 8620.
- 28 W. M. Marley and P. M. Jeffers, *J. Phys. Chem.*, 1975, **79**, 2085.

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