Tetrahedron Letters 59 (2018) 3267–3271

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

On the mechanism for the photooxidation of aromatic azides containing a secondary N–H bond: A sequence of intramolecular transformations with the formation of heterocyclic oximes

Ekaterina Chainikova *, Sergey Khursan, Alfia Yusupova, Alexander Lobov, Marat Abdullin, Rustam Safiullin

Ufa Institute of Chemistry of the Russian Academy of Sciences, Ufa Federal Scientific Center, 71 prosp. Oktyabrya, 450054 Ufa, Russian Federation

A R T I C L E I N F O

Article history:
Received 25 May 2018
Revised 4 July 2018
Accepted 12 July 2018
Available online 19 July 2018

Keywords:
Photooxidation of aryl azides
Reaction mechanism
Arylnitroso oxides
Nitrile oxides
Heterocyclic oximes

A B S T R A C T

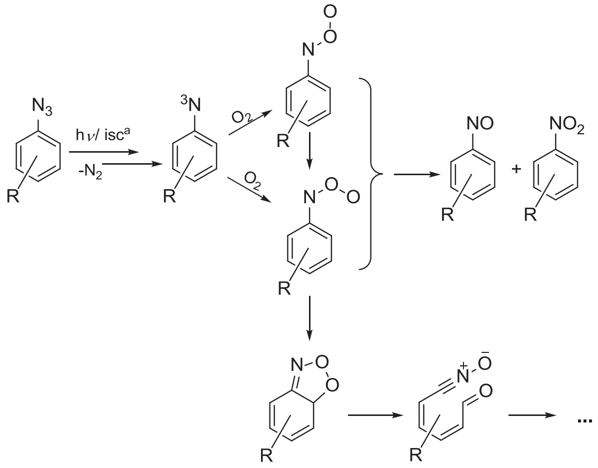
During the photooxidation of aromatic azides containing a secondary N–H bond at the *para*-position, a sequence of intramolecular transformations of nitroso oxides led to the formation of heterocyclic oximes along with the corresponding nitroso and nitro compounds.

Triplet nitrenes formed upon the photolysis of aromatic azides in the presence of molecular oxygen give nitroso oxides (ArNOO) which are labile species capable of transformation with opening of the aromatic ring to form nitrile oxides [1]. This nontrivial reaction is characteristic of the *cis* form of nitroso oxides, whereas the *trans* form is isomerized to the *cis* form or consumed in bimolecular reactions, the products of which are the corresponding nitroso and nitro compounds (Scheme 1). The nitro compound can also be formed *via* photochemical isomerization of the nitroso oxide [2].

A heterocyclic compound [2b,3] or a cyclopentadiene with an oxime substituent [4] are the final products of the sequence of transformations given in Scheme 1, provided that the nitrile oxide contains a reactive center suitable for further intramolecular reactions of the CNO group. Experimental conditions (solvent polarity, temperature, concentration of the starting azide and/or irradiation intensity) influence the ratio of uni- and bimolecular reaction products [4].

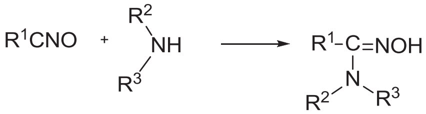
A characteristic reaction of nitrile oxides is the addition to different *N*-nucleophiles such as primary and secondary amines, amides, and *N*-heterocycles, containing a N–H bond. Amidoximes are formed as a result of this reaction [5] (Scheme 2).

A search of the literature did not indicate the possibility of a similar intramolecular reaction when the nitrile oxide group reacts



^{a} Intersystem crossing

Scheme 1. Mechanism of the photooxidation of aromatic azides.



Scheme 2. Reaction of nitrile oxides with *N*-nucleophiles.

---

* Corresponding author.
E-mail address: kinetic@anrb.ru (E. Chainikova).

https://doi.org/10.1016/j.tetlet.2018.07.034

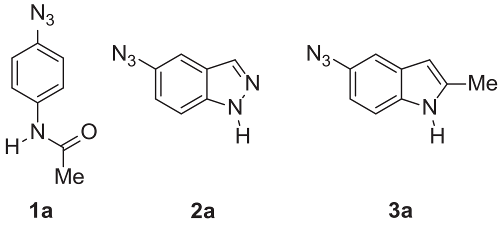


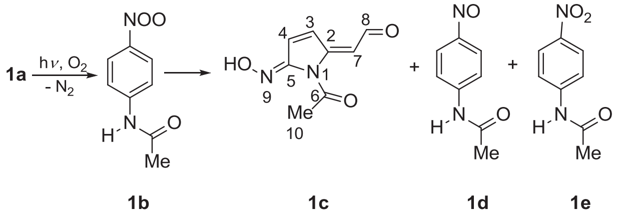
Fig. 1. Starting azides.

with the *N*-nucleophilic center to form a heterocycle. In the present work the mechanism of the photooxidation of aromatic azides containing a substituent with a N—H bond at the *para*-position (4-azidoacetanilide (**1a**), 6-azido-1*H*-indazole (**2a**), and 2-methyl-5-azido-1*H*-indole (**3a**), Fig. 1) in acetonitrile as the solvent was investigated. Products of the reaction were studied and quantum-chemical modeling of its elementary stages was performed. It was found that the nitrile oxides formed from the corresponding nitroso oxides undergo further intramolecular transformations similar to that shown in Scheme 2.

Results and discussion

The photolysis of azide **1a** was carried out in oxygen-saturated acetonitrile using light of the wavelength range 270–380 nm. The main products of the reaction were (2*E*)-[(5*E*)-1-acetyl-5-(hydroxyimino)-1,5-dihydro-2*H*-pyrrol-2-ylidene]ethanal (**1c**) which was present as two isomers, as well as 4-nitroso-(**1d**) and 4-nitroacetanilide (**1e**) (Scheme 3, see ESI).

Table 1 shows that the yields for the photooxidation of azide **1a** depend on the temperature. Increasing the temperature resulted in a decrease in the total yield of nitroso compound **1d** and nitro compound **1e** and an increase in the yield of oxime **1c**. Previously, similar results were observed for the photooxidation of 4-*N*,*N*-dimethylaminophenyl azide [4] and were explained by the fact that the oxime was formed as a result of unimolecular transformations of nitroso oxides, while the nitroso and nitro compounds were formed *via* recombination reactions involving these species. The recombination proceeds with a low activation energy, therefore, at higher temperature a more energy-consuming process consisting of a sequence of intramolecular transformations of ArNOO predominates (Scheme 1).



Scheme 3. Nitroso oxide **1b** and stable products resulting from the photooxidation of azide **1a**.

To clarify the mechanism for the formation of oxime **1c**, a theoretical modeling of possible transformations of nitroso oxide **1b** was performed using the M06L/6-311+G(d,p) + IEFPCM approximation (MeCN as the solvent, see ESI). Previously, it had been shown [3c,6] that this level of theory adequately describes the geometric characteristics of aromatic nitroso oxides as well as the activation parameters of their conformational and irreversible transformations. The results of the detailed DFT modeling for the transformations of nitroso oxide **1b** such as *cis*/*trans* and *syn*/*anti* isomerization of this species, *ortho*-cyclization of its *cis* isomer to form the nitrile oxide intermediate, and subsequent electrophilic addition of the carbon atom of the CNO group to the nitrogen atom of the acetamide moiety are provided in the ESI. The energy diagram in terms of the Gibbs free energy describing the most important transformations taking place in the system under study is given in Fig. 2. The *trans* isomer of **1b** is isomerized to the *cis* isomer or involved in a recombination process giving nitroso and nitro compounds **1d** and **1e**. The *cis* isomer undergoes intramolecular cyclization, the mechanism of which had been established previously [7], to form nitrile oxide **1f_1**, which is further transformed to the pre-reaction flat state **1f_3** (Fig. 2). Simultaneously the intramolecular ONC···H–N contact hindering formation of the ONC–N bond is formed. It was shown that the most likely mechanism for intramolecular addition of the nitrile oxide group to the nitrogen atom is amide-oxiimine tautomerization to structure **1g** and subsequent cyclization, in the transition state of which the synchronous formation of the C–N and O–H bonds completes the process of oxime **1c** formation (Fig. 2, ESI).

We also calculated the Gibbs energy of eight conformers of oxime **1c**, the formation of which is possible as a result of free rotation around single bonds as well as the *cis*/*trans* isomerism of the oxime moiety (see ESI). It was established that only two isomers with a total population of 99.5% can exist under our experimental conditions, which agrees with the results of the HPLC and NMR data (see ESI). These isomers are shown in Fig. 2.

The photooxidation of azide **2a** led to the formation of 6-(hydroxyimino)-6*H*-pyrrolo[1,2-*b*]pyrazole-3-carbaldehyde (**2c**) as a mixture of *cis* and *trans* isomers (ratio 2.5:1), 6-nitroso-1*H*-indazole (**2d**), and 6-nitro-1*H*-indazole (**2e**) (Scheme 4, see ESI).

Table 1
Effect of temperature on the product yields for the photooxidation of azides **1a–3a**.

a	[**a**]$_0$ × 10^5 [a] (M)	T (°C)	Δ[**a**] × 10^5 [b] (M)	[Product] × 10^5 [c] (M)		
				c	d	e
1a	10.80	20	8.77 (81)	2.25 (26)	0.73 (8)	3.23 (37)
	9.29	45	8.90 (92)	4.12 (46)	0.49 (6)	1.24 (14)
	9.35	60	9.20 (98)	5.15 (56)	0.32 (3)	0.50 (5)
	9.53	75	9.28 (97)	6.18 (66)	0.18 (2)	0.15 (2)
2a	40.30	20	20.60 (51)	17.30 (84)	0.95 (4)	1.19 (6)
	44.30	60	21.80 (49)	20.8 (95)	0.52 (2)	0.40 (2)
3a	17.90	8	15.60 (87)	0.54 (3)	6.25 (40)	2.95 (19)
	18.30	20	15.40 (84)	0.68 (4)	5.08 (33)	2.95 (19)
	18.80	75	18.60 (99)	7.45 (40)[d]	3.22 (17)[d]	2.75 (15)[d]

[a] Initial concentration of the starting azide.

[b] Concentration of the consumed azide, conversions in % are given in parentheses.

[c] Yields in % based on the consumed azide were measured by HPLC using calibration graphs and are given in parentheses.

[d] Along with these products, the yield of oxadiazol **3h** had been measured – 3.81 × 10^{-5} M (20%).