### **ARTICLE IN PRESS**

#### Tetrahedron Letters xxx (2015) xxx-xxx

Contents lists available at ScienceDirect

## **Tetrahedron Letters**

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



# A simple one-pot preparation of 3,3a-dihydro-5*H*-pyrano [3,3a-c]isoxazol-5-ylideneethanal from 4-vinyloxyphenyl azide: an example of aromatic azide photooxidation for the synthesis of nitrogen-containing heterocyclic compounds

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#### ARTICLE INFO

Article history: Received 24 November 2014 Revised 19 January 2015 Accepted 4 February 2015 Available online xxxx

Keywords: Aromatic azides Arylnitroso oxides Nitrile oxides Nitrogen-containing heterocycles

#### ABSTRACT

Photolysis of 4-vinyloxyphenyl azide in the presence of oxygen in acetonitrile leads to the formation of a fused heterocyclic compound due to the ability of the intermediates of this reaction to undergo a unique domino reaction sequence. The rate constants and activation parameters of some elementary stages of the process are measured by flash photolysis.

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The reaction of triplet aromatic nitrenes with molecular oxygen leads to labile species—nitroso oxides (ArNOO)—which play a key role in the photooxidation of aromatic azides.<sup>1</sup> The bond order of the N–O bond in the NOO group is ~1.5,<sup>2</sup> therefore nitroso oxides exist as geometric (*cis* and *trans*) isomers.

Under thermal conditions in the absence of oxidizable compounds, nitroso oxides undergo a sequence of rather specific transformations: the *trans* isomer is converted into the *cis* isomer and rearrangement of the *cis* isomer via cleavage of the aromatic ring leads to the formation of a conjugated diene with nitrile oxide and carbonyl end groups.<sup>3</sup>

http://dx.doi.org/10.1016/j.tetlet.2015.02.014 0040-4039/© 2015 Elsevier Ltd. All rights reserved.



If the nitrile oxide possesses a reaction center which is able to interact with the nitrile oxide group, then another step is added to the above sequence of transformations and a heterocycle is the end product. Thus, a heterocyclic compound of the benzisoxazole type was the product of the photooxidation of phenyl azide with an allyl substituent at the para position<sup>3b,4</sup> and photolysis of 6-azidoquinoline in the presence of oxygen led to formation of a substituted indolizine.<sup>4</sup> Hence, photooxidation of aromatic azides of a particular structure can be used as a simple one-pot method for the synthesis of nitrogen-containing heterocyclic compounds. A nitrile oxide with a double bond at a distance of six atoms from the nitrile oxide group is expected to be formed as an intermediate during photooxidation of a phenyl azide with a vinyloxy substituent at the para position. Such a structure is favorable for the intramolecular [3+2]-cycloaddition of nitrile oxide to the double bond and allows another oxygen atom to enter into a fused heterocyclic compound. In the present work the products of the photolysis of

Please cite this article in press as: Chainikova, E.; et al. Tetrahedron Lett. (2015), http://dx.doi.org/10.1016/j.tetlet.2015.02.014

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4-vinyloxyphenyl azide (**1**) in acetonitrile in the presence of oxygen at 293 K were investigated. In addition, the electronic spectra, kinetics, and activation parameters of the consumption of the *cis* and *trans* isomers of nitroso oxides **2** have been studied using flash photolysis.



A solution of azide **1**  $(1 \times 10^{-3} \text{ M})$  in oxygen-saturated acetonitrile was irradiated with light of wavelength range of 270–380 nm at 293 K. The progress of the reaction was monitored by reversephase HPLC.<sup>5</sup> The main reaction product was 3,3a-dihydro-5*H*-pyrano[3,3a-c]isoxazol-5-ylideneethanal (**4**) (93% per consumed azide), the formation of which can be explained by the recently discovered mechanism of aromatic azide photooxidation<sup>3</sup> (Scheme 1).

Pyranoisoxazole **4** was separated as a mixture of two isomers, **4a** (60%) and **4b**  $(40\%)^6$  (Fig. 1). The fact that the isomers differ in the location of the aldehyde group with respect to the double bond C(5)=C(8) plane (the atom numbering is shown in Scheme 1) was confirmed from the NOESY spectra (see Supplementary data). An NOE interaction was observed for the endocyclic double bond proton at C(6) with the aldehyde proton in the case of **4a** and with the double bond proton at C(8) in the case of **4b**. The formation of the *cis* isomer **4b** occurs apparently via a photochemical reaction. The *trans-cis* isomerization can occur both in the nitrile oxide **3** and in the final product **4**.



<sup>a</sup> Intersystem crossing.

Scheme 1. Mechanism of the formation of pyranoisoxazole 4



Figure 1. The isomers of pyranoisoxazole 4.

4-Vinyloxynitrobenzene, which is formed as a result of the photochemical isomerization of nitroso oxide  $2^{4,7}$  was the minor reaction product (<5% per consumed azide).<sup>8</sup>

Using flash photolysis as described previously,<sup>3</sup> the optical spectra of the isomeric forms of nitroso oxide 2 and the kinetics of their decay in acetonitrile have been studied. The absorption maxima of the cis and trans isomers are 420 and 460 nm, respectively. Both species are consumed by first-order kinetics with rate constants at 295 K of:  $k_{trans} = 0.30 \pm 0.02 \text{ s}^{-1}$  [transformation of *trans*-**2** into *cis*-**2** (Scheme 1)] and  $k_{cis} = 5.9 \pm 0.5 \text{ s}^{-1}$  [reaction of the nitroso oxide group of the cis form at the ortho-position of the aromatic ring (Scheme 1)]. The dependence of the rate constants on the temperature in the range of 278-348 K is described by the following equations:  $\log k_{trans} = (12.1 \pm 0.1) - (70 \pm 1)/$ 2.303RT and log  $k_{cis} = (11.9 \pm 0.2) - (64.3 \pm 0.5)/2.303$ RT [k (s<sup>-1</sup>);  $E_{a}$  (k[ mol<sup>-1</sup>)]. The high yield of pyranoisoxazole **4** indicates that it is the end product of the transformations of both isomeric forms of nitroso oxide 2 and once again confirms the proposed mechanism for the photooxidation of aromatic azides (Scheme 1).

Thus, we have reported yet another example of the use of the photooxidation of aromatic azides as a simple one-pot method for the synthesis of nitrogen-containing heterocyclic compounds. The conversion of the aromatic ring of the azide in the fused heterocyclic system is due to the ability of the intermediates of this reaction, nitroso oxides, to undergo a sequence of unique domino transformations.

#### Acknowledgments

This work was supported by the Russian Academy of Sciences (Department of Chemistry and Material Sciences program 'Theoretical and experimental study of the nature of the chemical bond and the most important mechanisms of chemical reactions and processes') and by the Russian Foundation for Basic Research, project no. 13-03-00201.

#### Supplementary data

Supplementary data (experimental details, characterization data of compounds and copies of <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra and the HPLC chromatogram) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet. 2015.02.014.

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- 5. Photooxidation of 4-vinyloxyphenyl azide (1): azide 1 (8.7 mg, 0.054 mmol) was dissolved in MeCN (50 mL) and placed in a thermostatically controlled (293 K) quartz reactor. The mixture was saturated with oxygen by bubbling O<sub>2</sub> through it for 5 min. The resulting solution was further purged with oxygen and irradiated with a xenon lamp through a UFS-2 filter (270–380 nm) until the starting material had disappeared. The mixture was concentrated to about 0.5 mL and separated by HPLC [ReprosilPur C18-AQ 5  $\mu$ m 8  $\times$  250 mm column (Dr. Maisch GmbH), eluent: acetonitrile].
- 6. Pyranoizoxazole **4** was obtained in amount of 8.0 mg (93% per consumed azide). Spectral data for the isomers of (3,3a-dihydro-5H-pyrano[3,3a-c]isoxazol-5-ylideneethanal (**4**): **4a** <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>CN):  $\delta$  (ppm) = 4.12 (dd, <sup>2</sup>J = 9.5 Hz, <sup>3</sup>J<sub>A3-3a</sub> = 10.7 Hz, 1H, Ha(3)), 4.81 (t, <sup>2</sup>J = 9.5 Hz, <sup>3</sup>J<sub>B3-3a</sub> = 9.5 Hz, 1H, Ha(3)), 5.60 (dd, <sup>3</sup>J<sub>3a-A3</sub> = 10.7 Hz, <sup>3</sup>J<sub>3a-B3</sub> = 9.5 Hz, 1H, H(3a)), 5.66 (dd, <sup>3</sup>J<sub>8-9</sub> = 7.6 Hz,

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 $\begin{array}{l} ({\rm C}(7)),\,131.58\;({\rm C}(6)),\,151.75\;({\rm C}(7a)),\,163.32\;({\rm C}(5)),\,190.38\;({\rm C}(9)).\,MS\;(EI,\,70\;eV),\\ m/z\;(\%):\,165\;[M]^{+}\;(88),\,149\;[M-O]^{+}\;(8),\,136\;[M-CHO]^{+}\;(81),\,135\;[M-NO]^{+}\;(26),\\ 123\;[M-CHCHO]^{+}\;(4),\,108\;[M-CHCH_2NO]^{+}\;(100),\,69\;[M-CHCHC(O)CHCHO]^{+}\;(55).\,HR-MS\;(EI)\;calcd\;for\;C_8H_7NO_3\;[M]^{+}:\,165.0420.\;Found:\;165.0398.\;UV-Vis\;(CH_3CN):\;\lambda_{max}=320\;nm\;(\epsilon=1.98\times10^4\;M^{-1}\;cm^{-1}). \end{array}$ 

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- 4-Vinyloxynitrobenzene was identified by mass spectrometry: MS (EI, 70 eV), m/z (%): 165 [M]<sup>+</sup> (100), 149 [M–O]<sup>+</sup> (15), 119 [M–NO<sub>2</sub>]<sup>+</sup> (8).