Pergamon

Tetrahedron, Vol. 53, No. 18, pp. 6401-6410, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00299-8

The Photolysis of Cycloalkyl Nitrites Esters: The Radical Intermediates as Studied by E.P.R..

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Abstract : The radical intermediates involved in the photolysis of alicyclic nitrites have been identified by EPR spectroscopy. In particular, cyclobutyl nitrite allows detection of the 2-pyrrolidinone-1-oxyl whose formation involves a 1,5-*exo* ring closure process which the 4-nitroso-1-acyl radical intermediate can undergo. Furthermore, experimental evidence supports for the formation of the alkyl alkoxy nitroxides a different reaction mechanism which involves an alkyl radical and an unreacted nitrite. © 1997 Elsevier Science Ltd.

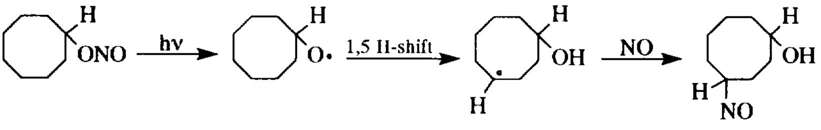
Introduction

The photolysis of alicyclic nitrites was previously investigated[1,2] to determine whether they do fail or not to undergo the Barton reaction;[3] products due to this type of rearrangement were obtained only with the cyclooctyl nitrite (**1**) and cycloheptyl nitrite (**2**). For such alicyclic nitrites as cyclopentyl nitrite (**4**) and cyclobutyl nitrite (**5**), the ring fission products were prevalent whilst for the cyclohexyl nitrite (**3**), cyclohexanol was the main product. However, previous results obtained in this laboratory photolysing directly in the EPR spectrometer cavity cyclopentyl nitrite[1] showed the possibility to detect the δ-valerolactam-1-oxyl radical formed *via* a five member ring expansion process; in the light of this unexpected result the behaviour to the photolysis of the nitrites (**1**)-(**5**) was studied to identify the radical intermediates, Table, and the most reliable reaction mechanisms involved.

Results and Discussion

When experiments were conducted on a deoxygenated acetonitrile solution of cyclooctyl nitrite, at different temperatures, continuously flowed in the EPR cavity and directly photolysed, two radical species were detected: the di-4-hydroxycyclooctyl nitroxide (**9**) and the 4-hydroxycyclooctyl cyclooctyloxyl nitroxide (**10**).

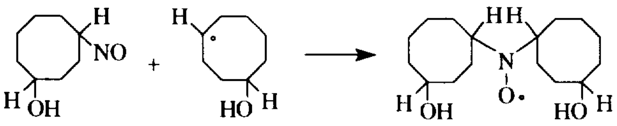
The formation of (**9**) could be accounted for *via* trapping of the 4-hydroxycyclooctyl radical (**7**) by the 4-hydroxy-1-nitrosocyclooctane, and (**10**) *via* trapping of the cyclooctyloxyl radical by the 4-hydroxy-1-nitrosooctane, as shown respectively in eq.2 and eq.3.



(1)

(**6**) (**7**) (**8**)

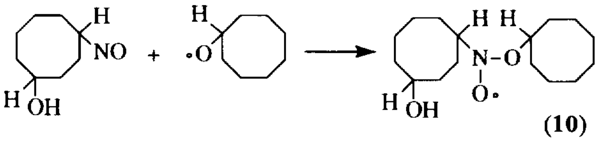
Radical (**7**) is likely formed through an intramolecular 1,5 H-shift which the cyclooctyloxyl (**6**) can undergo, eq. 1, and to verify if this process were really involved experiments at selected wavelengths could be useful.



(2)

(**9**)

In fact, the photolysis with light suitable only to induce the nitrite O-NO bond cleavage, $320 \leq \lambda \leq 420$ nm, should allow the formation of (**7**) exclusively through an intramolecular process; actually an experiment in these conditions allowed the detection of the radical (**9**), which upholds the formation of (**7**) as intermediate in the reaction mechanism shown in eq.1. An alternative source of (**7**) could be the cleavage[4] of the C-NO bond of the corresponding nitroso compound (**8**), induced by both red ($\lambda \approx 680$ nm) and U.V. ($\lambda \approx 280$ nm) light,[5] but experiments conducted with these wavelengths did not lead to unambiguous results being (**8**) formed *via* radical (**7**). As stated before, the experiment at $320 \leq \lambda \leq 420$ nm allowed even the radical (**10**) to be detected; the reaction mechanism usually reported for its formation[6] is that shown in eq. 3, although a different reaction mechanism involving a direct interaction of the intermediate alkyl radical (**7**) with unreacted nitrite ester could be hypothesized (see later in the text).



(3)

(**10**)

When the cycloheptyl nitrite (**2**) was investigated analogous results were obtained; thus the same reaction mechanism invoked for the formation of (**9**) and (**10**) might account for the detection of the di-4-

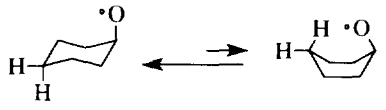
hydroxycycloheptyl nitroxide **(11)** and the cycloheptyloxyl 4-hydroxycycloheptyl nitroxide **(12)**. Actually, the radical species detected in the experiments with the nitrites **(1)** and **(2)** support the involvement of the Barton reaction in their formation, confirming that these transannular free radical rearrangements behave like their straight chain counterparts and do not seem to be influenced by ring size. Furthermore, these radicals, *via* coupling with nitric oxide, can be considered the precursors of the reaction products reported by Kabasakalian,[7] i. e. the nitroso alkane dimers or the corresponding oximes.

Table. Hyperfine Coupling Constants (Gauss) of the Detected Nitroxides.

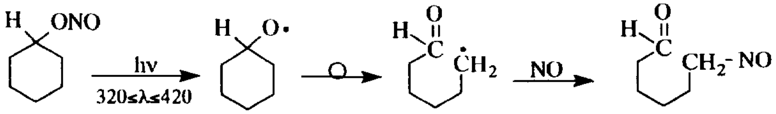
entry	**(9)**	**(10)**	**(11)**	**(12)**	**(16)**	**(17)**	**(18)**	**(20)**	**(21)**	**(22)**	**(23)**	**(24)**
a_N	15.00	25.70	15.12_5	25.70	15.00	27.87_5	7.50	15.00	7.25	14.75	7.50	6.68
a β-H	4.25 (2H)	4.00 (1H)	4.25 (2H)	4.00 (1H)	10.00 (4H)	8.12_5 (2H)	6.12_5 (2H)	10.00 (4H)	11.60 (2H)	10.25 (4H)	6.25 (2H)	15.25 (2H)
a γ-H									1.75 ($2H_3$)			3.68 ($2H_3$)
g-val*	2.0052	2.0053	2.0052	2.0053	2.0058	2.0053	2.0065	2.0054	2.0065	2.0054	2.0065	2.0065

* The g-factors have been calculated in comparison with the g-value (2.0037) of the DPPH.

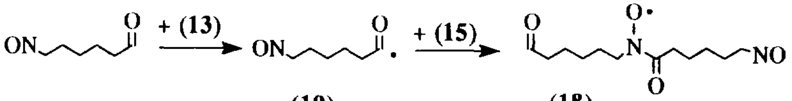
To verify if cyclic nitrite esters with a smaller carbon ring had a similar behaviour when photolysed, the cyclohexyl nitrite **(3)** was investigated,[8] a nitrite which is known to yield mainly cyclohexanol and a small quantity of 6-nitrosohexanal dimer. The photolysis of **(3)** led to the detection of different radical species: the di-hexanal-6-yl nitroxide **(16)**, the hexanal-6-yl cyclohexyloxyl nitroxide **(17)** and the 6-nitrosohexan-1-acyl hexanal-5-yl nitroxide **(18)**. From the analysis of the structure of these radicals it is evident that there is no need to invoke the involvement of an intramolecular 1,5 H-shift process, which could only take place if the intermediate cyclohexyloxyl radical were in the disfavoured boat form,



but the involvement of the β-cleavage of the intermediate alkoxyl radical can be confirmed. However, to obtain more information on the reaction mechanisms, experiments with selected wavelength light were required. When **(3)** was photolysed with light at 320 ≤λ≤ 420 nm, unexpectedly radical **(18)** was the only detectable species, Fig.1. To account for it, the cyclohexyloxyl radical acting as hydrogen abstractor from the aldehydic group of the 6-nitrosohexanal and leading to the acyl radical (**19**) could be invoked;[9] this can be trapped by the 6-nitrosohexanal and yield the radical (**18**), eq.s 4 and 5.



(**13**) (**14**) (**15**) (4)



(**19**) (**18**) (5)

This result is supported by Beckwith's[10] data on the rate ratio of the two competing processes, the hydrogen abstraction and the β-scission , *circa* 50 to 1, that cyclohexyloxyl radical can give;

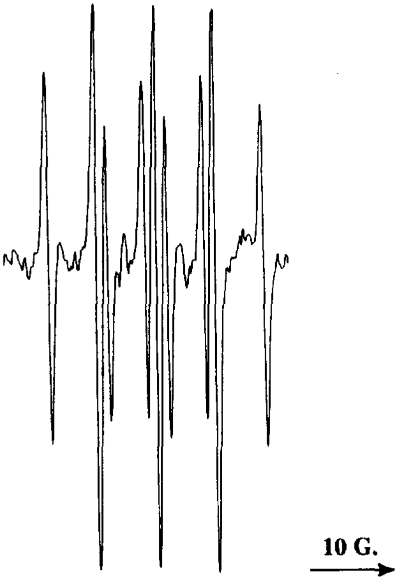
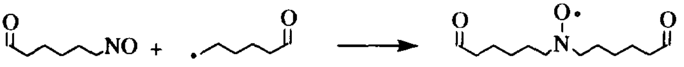


Fig.1. EPR spectrum, at -20°C in CH_3CN, of radical (**18**).

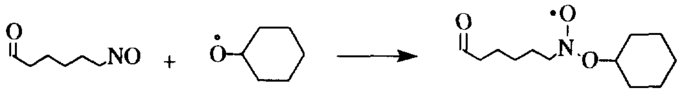
data that can also account for the non-detection of (**16**). In fact, in these experimental conditions the concentration of free hexanal-5-yl radical (**14**) is most probably too low to produce a spectroscopically detectable amount of **(16)**, eq. 6, and that because is poorly produced *via* β-scission of **(13)** and in the meantime efficiently trapped by NO to give the 6-nitrosohexanal, eq. 4;



(6)

(14) **(16)**

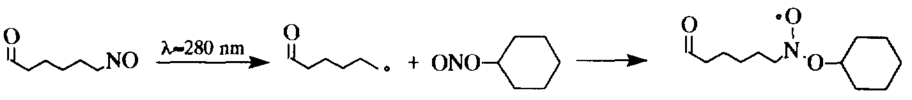
however, the non-detection of radical **(17)** seems to be still not defensible, eq. (7).



(7)

(17)

To prove which reaction pathway was mainly involved in the formation of **(16)** and **(17)**, further experiments at different selected wavelengths were then accomplished. The possible alternative source of radical **(14)** could be the cleavage of the C-NO bond of the 6-nitroso hexanal **(16)** induced by both U.V. and red light. Thus an experiment with light at λ≥320 nm, i.e. with the red light component able to induce the formation of radical **(14)** and then **(16)**, was at first conducted: only the radical **(18)** was detectable. This result, and that obtained in the previous experiment conducted at 320 ≤λ≤ 420 nm, indirectly supported the hypothesis that the possibility to obtain a spectroscopically detectable amount of **(16)** depends on the amount of radical **(14)** formed through the C-NO bond cleavage of **(15)** induced by U.V. light, and not by red light or *via* the β-cleavage of the radical intermediate **(13)**. To prove this the solution was then photolysed at λ≤ 420 nm: the nitroxide **(16)**, besides **(17)** and **(18)**, was detectable and that definitely strengthened the role of the U.V. light in the formation of its precursor the radical **(14)**. Nevertheless, nothing could still be said about the reaction mechanism involved in the formation of **(17)**. In fact, it should be detectable also in the experiment at 320 ≤λ≤ 420 nm being hypothesizable, in these conditions, a higher steady concentration of both the 6-nitrosohexanal and cyclohexyloxyl radical;[11] therefore, a different reaction mechanism could be suggested for the formation of **(17)** as, for example, the interaction of radical **(14)** with unreacted nitrite **(3)**, eq. 8.



(8)

(17)

Actually, this mechanism is supported by the fact that the detection of radical **(17)** is allowed only in those experiments where the steady concentration of **(14)** seems to be sufficiently high, and that can be perceived only when the photolysis is conducted with light at λ≤420 nm which efficiently can induce the C-NO bond cleavage of (**6**) by λ~280 nm. Such a mechanism could also account for the formation of the nitroxides (**10**) and (**12**), detected in the experiments with the nitrites having seven and eight membered rings, although they were detectable also when the photolysis was performed with light just able to induce the cleavage of the O-NO nitrite bond. In fact, with the substrates (**1**) and (**2**), the steady concentration of the intermediate alkyl radicals, formed *via* a fast and efficient 1,5 H-shift process which the parent alkoxyl radicals undergo at the expenses of competing processes such as hydrogen abstraction or disproportionation, could be reasonably high. That leads to a consideration of the reaction of the alkyl radical[12] with starting nitrite, instead of the reaction between the alkoxyl radical and the nitroso compound, a more conceivable reaction pathway also to account for the formation of (**10**) and (**12**).

Cyclopentyl nitrite, as reported in a previous paper,[1] led to the formation of radical species due to the β-scission of the intermediate cyclopentyloxyl radical: the di-pentanal-5-yl nitroxide (**20**), and the unpredicted δ-valerolactam-1-oxyl radical (**21**). This radical has been proved to be formed *via* a 1,6 *exo* ring closure process that the intermediate 5-nitroso-1-acyl-pentanal radical can undergo, a mechanism supported by the results obtained with several cyclopentyl-type nitrites which under photolysis allowed the detection of the corresponding δ-valerolactam-1-oxyl type radical.

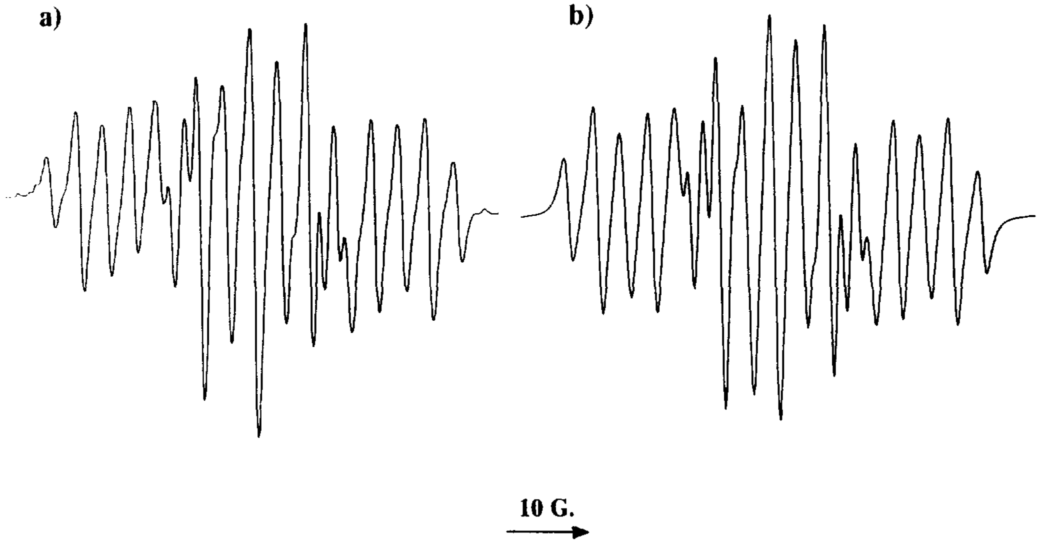
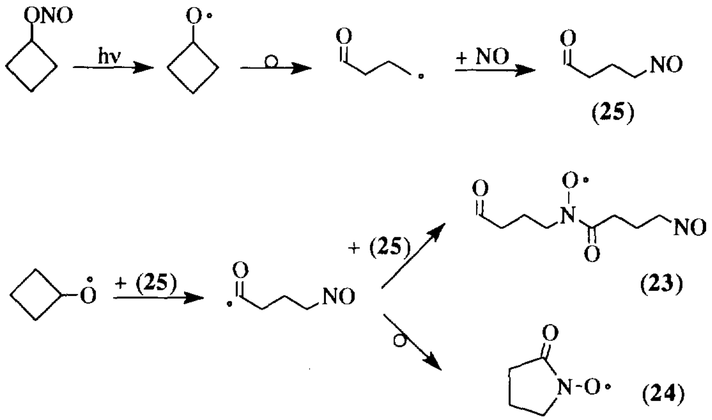


Fig.2. (**a**) EPR spectrum, at -17 °C in CH_3CN, of radical (**24**). (**b**) Computer simulation.

Finally, the cyclobutyl nitrite was studied. The direct photolysis of an acetonitrile solution of **(5)** led to the detection of the di-butanal-4-yl nitroxide **(22)**, in agreement with the detection of the 4-nitrosobutanal dimer among the reaction products.[2] A second radical species was also present, and it was identified as the 4-nitrosobutan-1-acyl butanal-4-yl nitroxide **(23)**, deriving from the photoreaction involving the 4-nitrosobutanal and the cyclobutyloxyl radical, like the mechanism proposed for the formation of radical **(18)**, see eq.5. However, in following experiments with more dilute[13] solutions of **(5)**, beside radicals **(22)** and **(23)** a third radical species became detectable, Fig.2. Its spectroscopic parameters were characteristic of a cycloalkyl acyl nitroxide and, in the light of the result obtained with **(4)**, the only hypothesizable structure accounting for this was the 2-pyrrolidinone-1-oxyl radical **(24)**. Actually its structure was confirmed by comparison with the spectroscopic parameters of an authentic radical sample obtained by photolysis of the parent N-Nitroso-2-pyrrolidinone in the presence of oxygen. Also with this nitrite to verify the most reliable reaction mechanism, it was necessary to conduct experiments with selected wavelengths. In particular, when the photolysis was conducted with light at $320 \leq \lambda \leq 420$ nm it was possible to detect both the radical species **(23)** and **(24)**. Following the reaction scheme proposed for the formation of the δ-valerolactam-1-oxyl radical obtained from the photolysis of the cyclopentyl nitrite,[1] it could also be hypothesized here that the involvement of the cyclobutyloxyl radical acting as hydrogen abstractor on the 4-nitrosobutanal and the possibility for the resulting 4-nitroso-1-acyl-butanal radical to undergo two different reaction pathways are as shown in the Scheme.

SCHEME.



As stated by Baldwin & Beckwith[14] rules for ring closure processes, the formation of **(24)** can be inferred to be a kinetically favoured 1,5-*exo* cyclization, as well as the 1,6-*exo* ring closure mechanism which is involved in the ring expansion process of the cyclopentyl-type nitrites.[1]

Conclusions

The radical species detected by E.P.R. during the photolysis of alicyclic nitrites seem to confirm that the reaction products identified by Kabasakalian[2] come mainly from the β-scission and 1,5 H-shift processes which the intermediate cycloalkyloxyl radical can undergo and subsequent trapping of the resulting alkyl radical by NO. The alkyl alkoxy nitroxides, on the contrary of that usually reported, seem most likely produced by interaction of an alkyl radical with unreacted nitrite and in particular, preliminary results on alkyl nitrites have shown the possibility to use them as spin traps of alkyl radicals. Finally, another result worthy of note concerns the process of ring expansion which cyclobutyl nitrite undergoes, confirmed by the detection of the 2-pyrrolidinone-1-oxyl radical. This process occurs through a 1,5-*exo* cyclization and in principle it should lead to the corresponding hydroxamic acid as reported for the norbornyl-type nitrite[15] or for the steroidal 17-nitrites;[16] however, in the light of this result and those previously reported[1] for the cyclopentyl-type nitrites it seems reasonable to exclude a protolytic intramolecular substitution which the nitroso aldehyde can undergo as responsible for the formation of the corresponding hydroxamic acid.

Experimental

Material. All the alicyclic nitrites were prepared according to the general method by esterification of the corresponding alcohols with nitrous acid at 0°C and were vacuum distilled before use. Each of the light-yellow distilled oils was identified, and the purity controlled, by GC-Mass Spectroscopy. The N-Nitroso-2-pyrrolidinone was prepared in accordance with the method reported by Huisgen and Reinertshofer.[17] The acetonitrile (99.9+%, HPLC grade) and the alcohols, except cyclobutanol which was synthesized as reported in the literature,[18] were obtained from Aldrich.

Photolysis apparatus.- Irradiation were performed with an OSRAM HBO 500W/2 high pressure mercury lamp, provided with Corning glass coloured filters. The Corning glass filter number 0160(0-54) was used for the experiments at $\lambda \geq 320$ nm and the filter number 9863(7-54) for those at $\lambda \leq 420$ nm; a combination of the two was used for the experiments at $320 \leq \lambda \leq 420$ nm.

Spectroscopic measurements.- The U.V.-visible absorption spectrum of nitrites in acetonitrile were recorded using a Perkin-Elmer spectrometer. GC-MS analysis were carried out with a Carlo Erba QMD 1000 instrument. E.P.R. spectra were recorded on Varian E-104 X-band spectrometer with a 100 KHz modulation and the dynamic E.P.R. experiments were performed using a 50 ml gastight SGE syringe driven by a INFORS Precidor.

E.P.R. Experiments.- The solutions of cycloalkyl nitrites in acetonitrile, which concentration was in the range of 10^{-3} M., were photolysed within the cavity of the E.P.R. spectrometer, equipped with a variable temperature control system; the solution was flowed in cavity through a flat cell arrangement (0.3 mm. cell width) and the flow was ranging between 0.1 and 0.6 ml/min. The solutions were deareated prior to use by purging with N_2-gas for 50-60 min. The light was focused onto the sample by an elliptical mirror and two quartz lenses. The g-value for the radical species were determined by comparison with the g-value (2.0037) of DPPH.

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7. However, with the cycloheptyl nitrite no direct evidence of radical species deriving from the ring fission product, i.e. the 7-nitrosoheptanal dimer, have been obtained, although reported[2] to be formed (5%).
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11. In particular the concentration of the cyclohexyloxyl radical should be quite high being the reaction product of the primary photochemical process characterized by an high quantum yield, and the rate of the β-scission process low.[10]
12. The 4-hydroxycyclooctyl radical and the 4-hydroxycycloheptyl radical can react with the corresponding nitroso and nitrite compounds; the 4-hydroxycyclooctyl leads to the formation of radicals **(9)** and **(10)** in ratio 97:3, the 4-hydroxycycloheptyl to the formation of radicals **(11)** and **(12)** in ratio 90:10, as shown by the EPR spectra.

13. The concentration in these cases was in the range of 10^{-4} M..
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(*Received in UK* 9 *January* 1997; *revised* 17 *March* 1997; *accepted 20 March* 1997)