

**M.Sc. Semester-IV  
Core Course-9 (CC-9)  
Synthetic Organic Chemistry**



**III. Photochemistry**

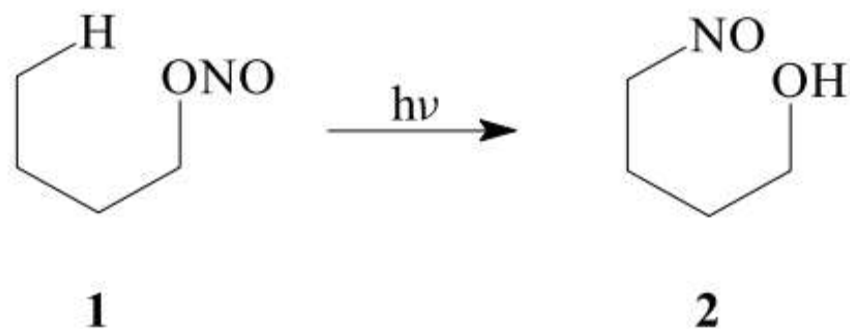
**21. The Barton Reaction : Mechanism and Examples**



**Dr. Rajeev Ranjan  
University Department of Chemistry  
Dr. Shyama Prasad Mukherjee University, Ranchi**

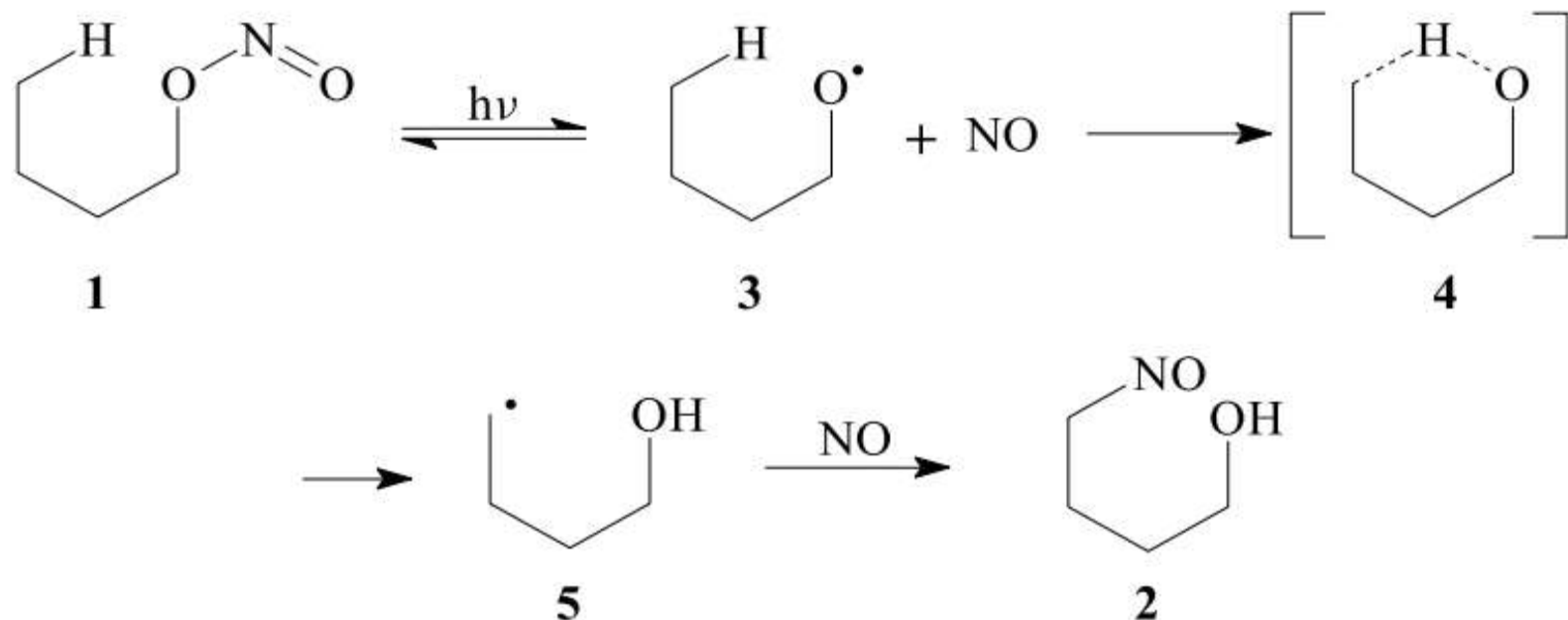
## Barton Reaction

Photolysis of nitrite esters



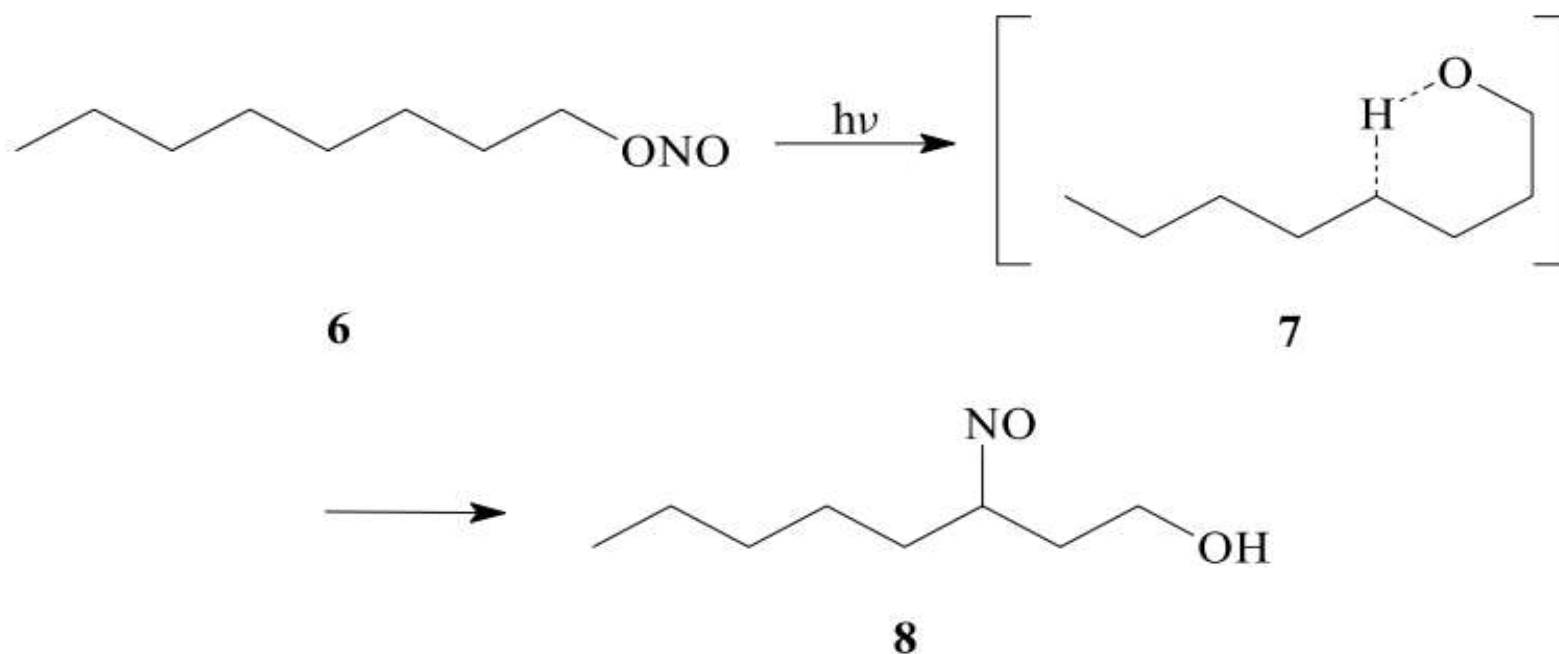
Nitrous acid esters **1** can be converted to  $\delta$ -nitroso alcohols **2** by irradiation with ultraviolet light. This conversion is called the *Barton reaction*.<sup>1-3</sup>

Upon the irradiation the nitrous acid ester **1** decomposes to give nitrous oxide (NO) and an alkoxy radical species **3**. The latter further reacts by an intramolecular hydrogen abstraction via a cyclic, six-membered transition state **4** to give an intermediate carbon radical species **5**, which then reacts with the nitrous oxide to yield the  $\delta$ -nitroso alcohol **2**:



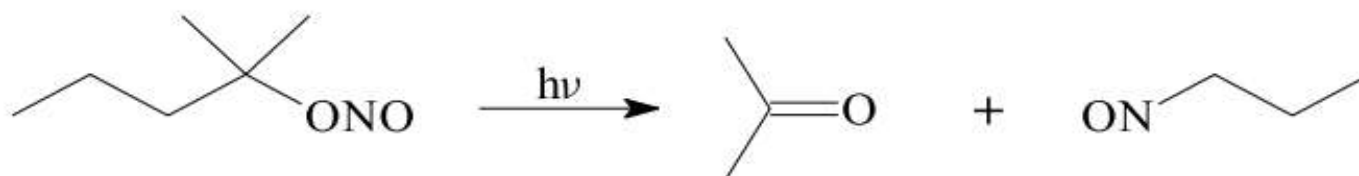
There is quite some evidence for a mechanism as formulated above,<sup>2,3</sup> especially for the six-membered transition state—the Barton reaction is observed only with starting materials of appropriate structure and geometry, while the photolysis of nitrite esters in general seldom leads to useful products formed by fragmentation, disproportionation or unselective intermolecular hydrogen abstraction.

The photolysis of 1-octyl nitrite **6** yields 4-nitroso-1-octanol **8** in 45% yield, via cyclic transition state **7**—the formation of regioisomeric nitroso alcohols is not observed:

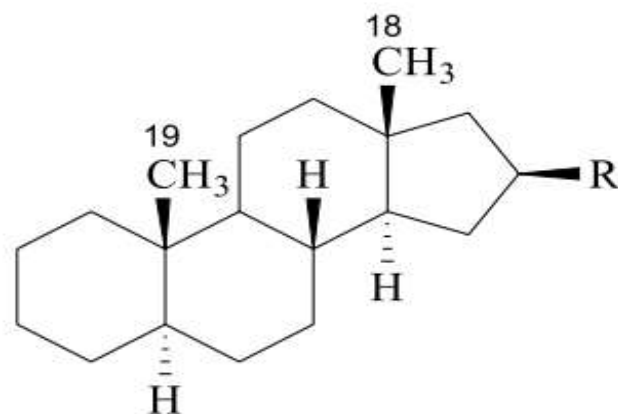


With a radical-scavenging compound present in the reaction mixture, an alkyl radical species like **5** can be trapped, thus suggesting a fast conversion of the alkoxy radical **3** by intramolecular hydrogen abstraction, followed by a slow intermolecular reaction with nitrous oxide.

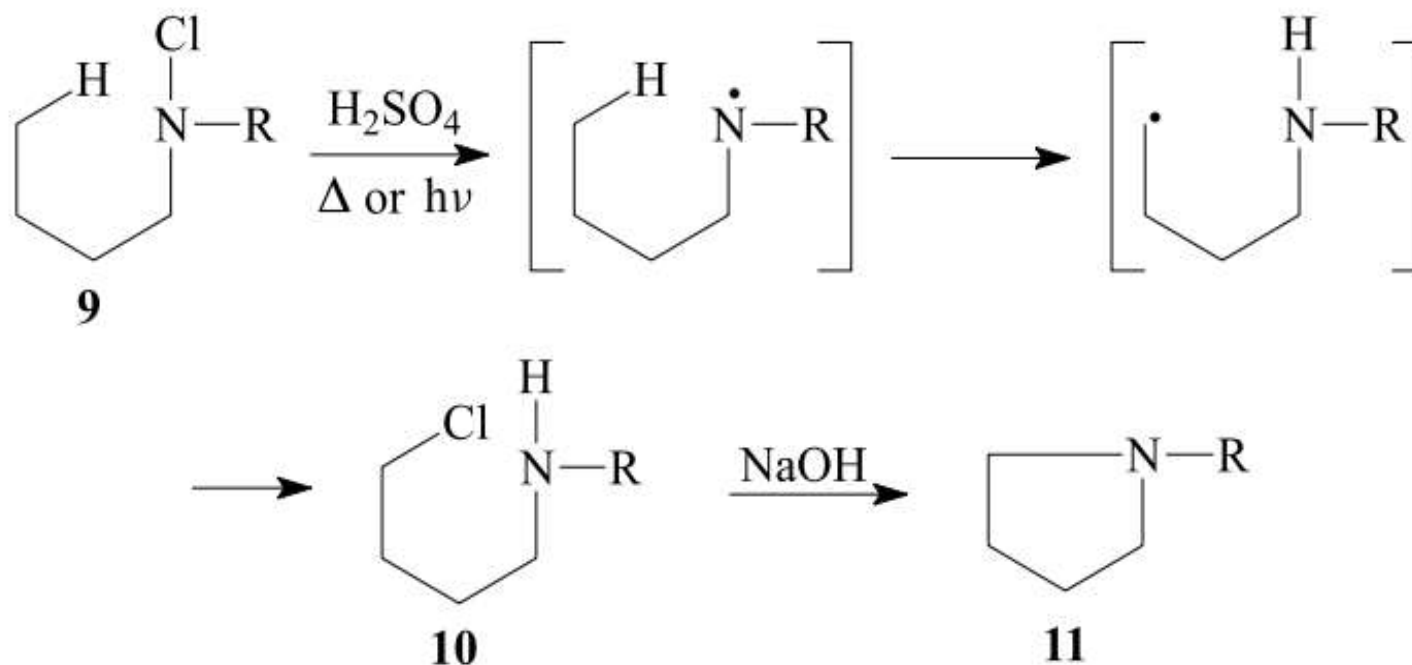
The Barton reaction is usually carried out by irradiation of a nitrite ester **1** dissolved in a hydroxyl-free solvent under nitrogen atmosphere. Possible side-reactions can be decomposition reactions and intermolecular reactions; sometimes the disproportionation may even predominate:



The required nitrite esters **1** can easily be obtained by reaction of an appropriate alcohol with nitrosyl chloride ( $\text{NOCl}$ ). The  $\delta$ -nitroso alcohols **2** formed by the Barton reaction are useful intermediates for further synthetic transformations, and might for example be converted into carbonyl compounds or amines. The most important application for the Barton reaction is its use for the transformation of a non-activated C–H group into a functional group. This has for example been applied for the functionalisation of the non-activated methyl groups C-18 and C-19 in the synthesis of certain steroids.<sup>2</sup>



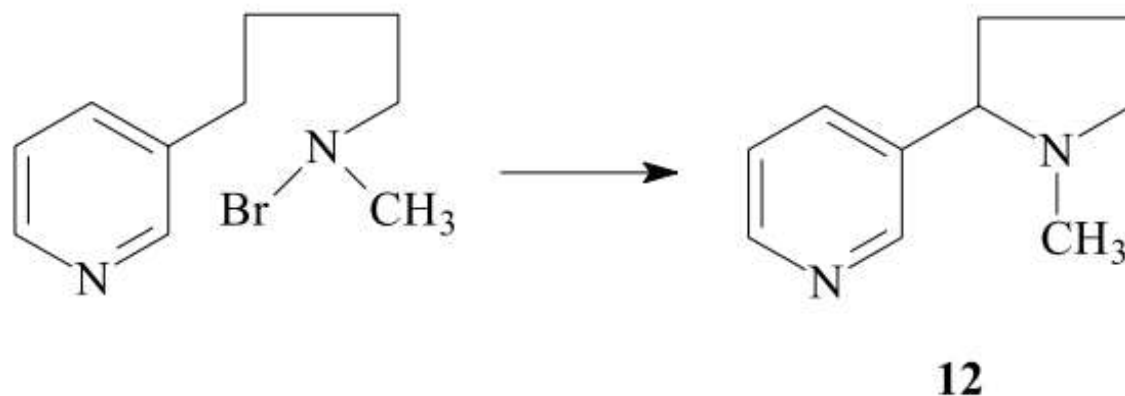
The so-called *Hofmann–Loeffler–Freitag* reaction<sup>4–8</sup> of *N*-chloroamines **9** proceeds by a similar mechanism, and is for example used for the synthesis of pyrrolidines **11**:



Upon heating or irradiation with uv-light of a solution of an *N*-chloroamine **9** in strong acid (concentrated sulfuric acid or trifluoroacetic acid) a δ-chloroamine **10** is formed, which however is usually not isolated, but rather reacts during workup with aqueous sodium hydroxide to yield a pyrrolidine **11**. A radical mechanism is presumed, since the transformation of the *N*-chloroamine does not take place in the dark and not at room temperature, but rather requires light, heat or the presence of Fe-(II) ions, while on the other hand the presence of oxygen inhibits the reaction. The highly specific hydrogen abstraction from the δ-carbon further suggests an intramolecular reaction via a cyclic, six-membered transition state. A mechanism as formulated above is supported by the fact, that in certain cases the intermediate δ-chloroamines **10** can be isolated.

The required *N*-chloroamines **9** can be prepared from the corresponding amine by treatment with sodium hypochlorite or *N*-chlorosuccinimide.

The *Hofmann–Loeffler–Freitag* reaction has been described with *N*-chloro- as well as *N*-bromoamines—the former however usually give better yields. *N*-chlorinated primary amines react well in the presence of Fe-(II) ions. Just like the Barton reaction, the Hofmann–Loeffler–Freitag reaction has been applied mainly in steroid chemistry. An interesting example from alkaloid chemistry is the synthesis of nicotine **12** by Loeffler:<sup>6</sup>



Many synthetically useful reactions are based on the presence of double or triple bonds, a good leaving group or a C–H bond that is activated by an adjacent functional group; radical reactions often are unselective and give products from side-reactions. In contrast the Barton reaction as well as the Hofmann–Loeffler–Freitag reaction and related intramolecular radical reactions are well suited for the introduction of a functional group by reaction with a specific, non-activated carbon–hydrogen bond.

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University Department of Chemistry  
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