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REVIEW ARTICLE

SOME CHEMICAL AND PHYSIOLOGICAL PROPERTIES OF NITRIC OXIDE: A MINI REVIEW

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ABSTRACT

Nitric oxide (NO) is a simple odd-electron molecule that is a primary pollutant. It transmits signals between neurons; playing a role in blood flow and sexual arousal. In this mini review we try to make accessible the properties and functions of this lipophilic molecule to non-specialists.

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INTRODUCTION

Some Chemistry of NO: Nitric oxide is a colorless, paramagnetic gas that is moderately soluble in water. It is produced in the body to help the millions of cells communicate with one another by transmitting signals throughout the entire body system (Clark, 2017). Nitric oxide is a radical that does not dimerize unless cooled to very low temperature at high pressure (Housecroft & Sharpe, 2012; Weller et al., 2010). Nitric oxide is a stable molecule with an odd number of electrons (11 valence electrons), $\bullet\text{N}=\text{O}$; with an unpaired electron in one of the pi (π) antibonding orbital, which means that the molecule is paramagnetic. The bonding between nitrogen and oxygen is intermediate between a double bond and triple bond. The molecular electron configuration for NO is:

$[\text{Core electrons}](\sigma_{2s})^2(\sigma_{2s}^*)^2(\pi_{2p})^4(\sigma_{2p})^2(\pi_{2p}^*)^1$. The net bond order is 2.5 and the oxidation state of nitrogen is +2. The molecular orbital description of the bonding in NO is shown below (Figure 1).

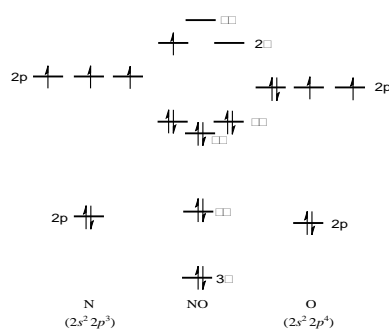


Figure 1. Molecular orbital energy level diagram for NO (Burrow et al., 2013)

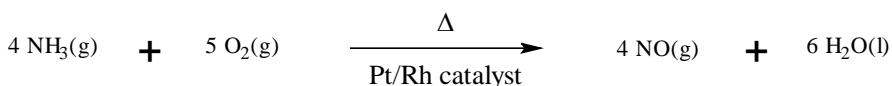
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Some physical properties of NO are presented in Table 1 below, where it can be seen that its solubility in water is low and heavier than water.

Table 1. Some physical properties of nitric oxide

Chemical formula	NO
Density	1.3402 g dm ⁻³
Boiling point	-152 °C
Melting point	-164 °C
Appearance	Colorless gas
Molar mass	30.01 g·mol ⁻¹
Solubility in water	0.0098 g/100 mL (0 °C) 0.0056 g/100 mL (20 °C)
Molecular shape	Linear

Nitric oxide is prepared industrially by the oxidation of ammonia; catalyzed by Pt/Rh catalyst at between 820°C to 950°C and at pressures between 1 atm and 12 atm.



It can be prepared by the reduction of nitrite ions with iodide ions:



The formation of NO from its elements is unfavorable, that is, its enthalpy of formation, ΔH_f is positive, $\Delta H_f = +90.2$ kJ/mol (Housecroft & Sharpe, 2012; Weller et al., 2010).

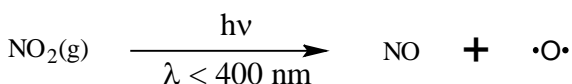
Nitric oxide, NO, is a primary pollutant, produced in the high temperature combustion cylinders of cars and jet engines.



In the atmosphere, it is oxidized to nitrogen dioxide, a brown gas, which is a major contributor to smog.



The NO₂ absorbs ultraviolet light dissociating into NO molecules and O atoms.

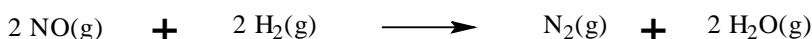


Nitric oxide undergoes a series of reactions to produce other chemical compounds and some of the reactions include:

Its reaction with oxygen to give nitrogen dioxide, NO₂, which when added to water gives nitric acid.



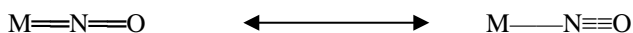
It reacts with hydrogen gas to form nitrogen and water



NO reacts with the halogens to form nitrosyl halides, of general formula XNO. For example, nitrosyl chloride, NOCl, this is a very toxic gas (Jones & Atkins, 1999; Kotz & Treichel Jr, 1999).

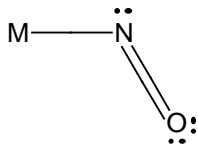


When nitric oxide reacts with transition metals, metal nitrosyls are formed. The metal nitrosyls are highly colored, deep reds, browns, purples or even black. The NO molecule binds to a low oxidation state metal atom. The most common bonding mode of NO is the terminal linear type (M—NO). The angle of the M—N—O varies from 160° to 180°. Here NO is behaving as a 3-electron donor.

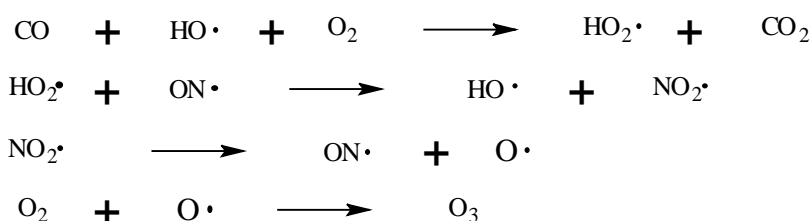


Classic examples of this type of bonding are found in the qualitative test for nitrates, “brown-ring” complex $[\text{Fe}(\text{H}_2\text{O})_5\text{NO}]^{2+}$; Roussin’s red and black salts $\text{K}_2[\text{Fe}_2(\text{NO})_4\text{S}_2]$ and $\text{K}[\text{Fe}_4(\text{NO})_7\text{S}_3]$ obtained by the action of NO on Fe^{II} ion the presence of S^{2-} ; and sodium nitroprusside, $\text{Na}_2[\text{Fe}(\text{CN})_5\text{NO}]\cdot\text{H}_2\text{O}$.

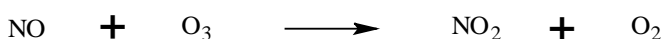
In the bent $\text{M}-\text{N}-\text{O}$ conformation the NO group behaves as a one electron donor. The bond angle is in the range $120 - 140^\circ$ (Greenwood & Earnshaw, 1989).



NO causes a wide range of health and environmental effects as a result of the various compounds and derivatives of the family of nitrogen oxides. In a series of reactions that occurs in the troposphere as shown in the reaction equations below, NO increases the concentration of $\text{HO}\cdot$ and O_3 . Ozone is formed when NO and volatile organic compounds (VOCs) react in the presence of heat and sunlight. Nitric oxide reacts with stratospheric ozone to form O_2 and nitrogen dioxide (Jones & Atkins, 1999).



NO acts as catalyst for the conversion of O_3 to O_2 and is therefore considered as a contributor to the depletion of the ozone layer.



Some Physiological Properties of NO

In 1998 Furchgott, Ignarro and Murad won the Nobel Prize for medicine and Physiology for their earlier discovery in 1986 that NO acted as a signaling agent in biological systems. The molecule penetrates membranes and regulates the functions of the cell (Furchgott, 1999; Ignarro, 1999; Murad, 1999). The ability of NO to act as a neurotransmitter arises from its small molecular size and high lipophilicity which allows it to pass through cell walls. It plays a role in a wide range of biological processes such as blood flow and sexual arousal, blood clotting, blood pressure control by dilating arteries; assisting in gastric motility and the immune system’s ability to kill tumor cells and intracellular parasites when it is produced in the macrophage, acting as a toxin (C&EN, 1993). NO has been implicated in the mechanism by which nitroglycerin, which has been used in the treatment of angina. It works by dilating the blood vessels, thereby decreasing the pressure and increasing blood flow. The brain has been found to be a rich source of nitric oxide synthase (NOS) and so it has been postulated that NO may be involved in long-term memory.

NO is synthesized *in vivo* from the amino acid L-arginine, which is catalysed by the haem-containing NO synthase (NOS) enzymes. There are three forms of NO synthases: neuronal NOS (nNOS), inducible NOS (iNOS) and endothelial NOS (eNOS). Inducible NOS (iNOS) is a high-output enzyme and its activity does not depend on the presence of Ca^{2+} ions whereas the isoforms nNOS and eNOS depend on Ca^{2+} for their activity. It has been shown that eNOS and nNOS synthesize NO in response to intracellular Ca^{2+} levels and the effectiveness of NOS isoforms depends on their binding with calmodulin (Omer et al., 2012). L-arginine is converted to L-citrulline and NO, in a two-step reaction, involving a 5-electron oxidation process, which requires oxygen in addition to the cofactor NADPH.

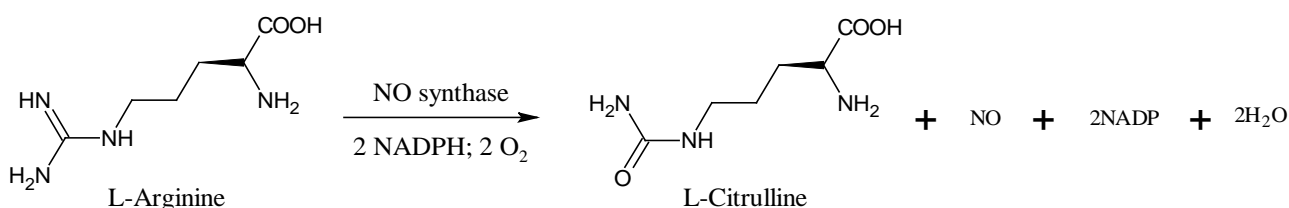


Figure 2. Synthesis of NO through the conversion of L-arginine to L-citrulline

NO has been linked with some non-human activities, for example, when the blood-sucking insect *Rhodnius prolixus* attacks a victim. Once its saliva is injected into its victim NO causes the blood vessels to expand and inhibiting blood clotting, making the victim an effective blood donor. The victim now releases histamine to aid healing of the wound but this favors the attacking insect (Burrow et al., 2013; Anderson, 2010). NO activities have been implicated in plant physiological and biochemical processes, which has led to its classification as a phytohormone (Pagnussat et al., 2002; Lamattina et al., 2003; Stohr & Stremlau, 2006; Leshem, 2000). NO in plants is thought to be generated through enzymatic and non-enzymatic pathways. The enzymatic pathway seems to be catalysed by cytosolic nitrate reductase (cNR), NOS or NOS-like enzymes and nitrite:NO reductase (N:NOR). Non-enzymatic pathway is nitrite dismutation to NO and nitrate at acidic pH values (Stohr & Ullrich, 2002; Neill et al., 2003; Graziano & Lamattina, 2005; Hayat et al., 2010; Besson-Bard et al., 2008). Even though NOS-like activity has been detected in plants, animal-type NOS has not been found. NO has been found to have significant effect on seed dormancy, growth, senescence, nitrate reductase activity, respiration, stomatal movement, chlorophyll content, photosynthesis and antioxidant system (Hayat et al., 2010). NO is also related to the function of the well-known anti-impotence drug Viagra® (*sildenafil*), which works by affecting the concentration of cyclic guanosine monophosphate (cGMP) in the body. On sexual stimulation, NO is released in the body and this leads to the production of cGMP. cGMP triggers relaxation of smooth muscle and an increase in blood flow in the penis, which causes an erection. However an enzyme cGMP phosphodiesterase type 5 (PDE5) destroys cGMP and this causes loss of erection. Viagra® inhibits PDE5, thereby maintaining the concentration of cGMP in the body and duration of erection.

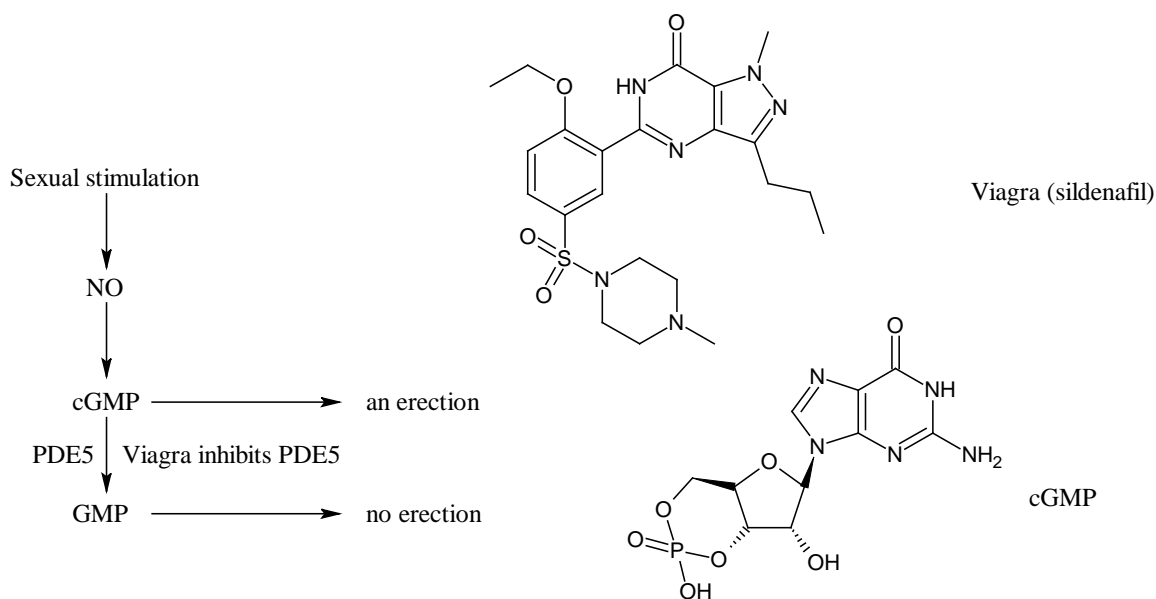


Figure 3. Role of Viagra® in erectile dysfunction; note that both Viagra and cGMP have similar heterocyclic rings ^[4]

Conclusion

Nitric oxide has been shown to play a remarkable role in living systems, as it is involved in blood pressure regulation and blood clotting, neurotransmission. With its involvement in this biochemical and physiological processes in both humans and plants, NO, a small inorganic substance deserves the attention it received which led to the award of the Nobel Prize and the attention it continues to receive. However, the mechanism of its action in plants still requires attention as NO-like protein has not been identified.

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