Title

(1) Title: Gas-phase oxidation and disproportionation of nitric oxide

(2) Running title: Gas-phase oxidation and disproportionation of NO

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**Introduction**

Nitrogen and oxygen together comprise over 98% of the air we breathe. Nitric oxide (NO) is a simple molecule, consisting of a single nitrogen bonded to one oxygen atom, which makes its chemistry accessible to study in great detail.\(^1,2\) However, it is only recently that mammalian cells were discovered to produce NO as a short-lived intercellular messenger.\(^3,4\) NO participates in blood pressure control, neurotransmission and inflammation. Moreover, NO is the biologically active species released from a variety of cardiovascular drugs such as nitroglycerin and isosorbide dinitrate.\(^5\) One important function of NO is in the macrophage-dependent killing of invaders, and possibly cancer cells, indicating the potential of this free radical to mediate cytotoxic and pathological effects.\(^6\)

When inhaled, NO acts as a selective pulmonary vasodilator. There is intense clinical interest in inhalation of low doses of NO (less than 1 to 80 ppm) in the treatment of diseases characterized by pulmonary hypertension and hypoxemia (Table I).\(^7,8\) The inhaled NO therapy is fairly inexpensive, but it seems that it is not indicated for everybody with regards to the paradigm of its efficiency and potential toxicity. NO reacts with O\(_2\) in the gas phase to form nitrogen dioxide (NO\(_2\)):\(^1,2,9,10\)

\[
2\text{NO (g)} + \text{O}_2 \text{(g)} = 2\text{NO}_2 \text{(g)} \quad (1)
\]

In this therapy, the inhaled NO\(_2\) level must be kept as low as possible.
because of its toxic pulmonary effects.\textsuperscript{7,8}

Commercial NO, which is stored under compression, invariably contains impurities. Formation of the two main contaminants, NO\textsubscript{2} and nitrous oxide (N\textsubscript{2}O), is due to a disproportionation reaction, whose rate is immaterially slow at 1 atm and below but becomes alarmingly high at elevated pressures:\textsuperscript{2}

\begin{equation}
3\text{NO (g)} = \text{N}_2\text{O (g)} + \text{NO}_2\text{(g) (2)}
\end{equation}

Potential adverse effects of N\textsubscript{2}O are also a cause of concern in NO inhalation. N\textsubscript{2}O, known as laughing gas, works both as an anesthetic and as an analgesic. Under most conditions N\textsubscript{2}O appears to be inert, but prolonged exposure may produce myelotoxic, neurotoxic and reproductive adverse effects.\textsuperscript{11} Therefore, a proper assessment of the chemical kinetics, i.e., rate law and the relevant rate constants, of Reactions (1) and (2) is indeed necessary in the medical community.

Reaction (2) must also be borne in mind when compressed NO in commercial cylinders is employed in high precision experiments. The presence of NO\textsubscript{2} in the compressed NO clearly creates difficulties in experimental studies of NO reactions and can pose explosion hazard when the gas is brought into contact with hydrocarbons.\textsuperscript{2}

Our goal here is to provide an introduction to the reaction kinetics of gas-phase oxidation and disproportionation of NO, while emphasizing the prediction of NO\textsubscript{2} formation from Reactions (1) and (2).
Gas-phase oxidation of NO

Chemical kinetics of the reaction of NO with O₂

In the oxygenated gaseous environments the reaction of NO with O₂:

\[ 2\text{NO} + \text{O}_2 = 2\text{NO}_2 \]  

proceeds as a third-order reaction:\(^1,2,9,10\)

\[-d[\text{NO}] / dt = +d[\text{NO}_2] / dt = 2k[\text{NO}]^2[\text{O}_2] \]  

Since the first chemical kinetic study of this reaction by Bodenstein and Wackenheim\(^12,13\) 80 years ago, a majority of published experimental results supports the differential rate law (3) and the view that Reaction (1) is a homogeneous gas-phase reaction and does not require a participation of solid surfaces.\(^9,10\) These results include the older data obtained with the NO pressures ranging from few torrs to a few hundred torrs and the more recent ones involving low NO concentrations down to the ppm level. In this section, we will briefly review the reaction mechanisms that have been proposed to explain the rate law (3).

Three mechanisms have been proposed.\(^10\)

(i) Termolecular reaction: According to this view, two molecules of NO and one O₂ molecule simultaneously collide and form a transient complex, which thus takes a single step to form two molecules of NO₂. Although this reaction has long served as a classical example of termolecular reaction in chemistry textbooks, a majority of researchers in
recent years prefer the two-step mechanisms, as described below.

(ii) Pre-equilibrium mechanism with dimer of NO as an intermediate:

\[ \text{NO} + \text{NO} \rightleftharpoons (\text{NO})_2 \quad \text{[fast]} \quad (4a) \]

\[ (\text{NO})_2 + \text{O}_2 \rightarrow 2\text{NO}_2 \quad \text{[slow and rate determining]} \quad (4b) \]

\[-d[\text{NO}]/dt = k_1 \cdot k_2 \cdot [\text{NO}]^2 \cdot [\text{O}_2] / (k_{-1} + k_2 \cdot [\text{O}_2]) \quad (4c)\]

Equation (4c) results from the assumption that the rate constants \( k_1 \) and \( k_{-1} \) for the forward and reverse reactions of (4a) are significantly greater than that \( k_2 \) of the second step, (4b). Since \([\text{O}_2]\) is only 0.041 mol·L\(^{-1}\) even in pure \( \text{O}_2 \) gas at 1 atm and 298 K, the relation \( k_{-1} \gg k_2 \cdot [\text{O}_2] \) is assumed valid, thus making Equation (4c) take the form of Equation (3).

(iii) Pre-equilibrium mechanism with \( \text{NO}_3 \) as an intermediate:

\[ \text{NO} + \text{O}_2 \rightleftharpoons \text{NO}_3 \quad \text{[fast]} \quad (5a) \]

\[ \text{NO}_3 + \text{NO} \rightarrow 2\text{NO}_2 \quad \text{[slow and rate determining]} \quad (5b) \]

\[-d[\text{NO}]/dt = k_3 \cdot k_4 \cdot [\text{NO}]^2 \cdot [\text{O}_2] / (k_{-3} + k_4 \cdot [\text{NO}]) \quad (5c)\]

In Equation (5c), \( k_3 \) and \( k_{-3} \) are, respectively, the rate constants of the forward and reverse directions of (5a) and \( k_4 \) the constant for Reaction (5b). The molar concentration of NO is low even with the NO pressures at a few hundred torrs, and the expression (5c) converges to the form of Equation (3). \( \text{NO}_3 \) is a well-known intermediate in the decomposition of dinitrogen pentoxide to \( \text{NO}_2 \) and \( \text{O}_2 \). Two structures for \( \text{NO}_3 \) are in the literature: (a) nitrogen trioxide, a nitrate-like planar trigonal structure, in which the N atom is surrounded by three equivalent O atoms; and (b)
peroxynitrite radical, a bent-chain structure with an atomic sequence O-O-N-O.\(^{1,16}\) Although peroxynitrite radical is more persuasive than nitrogen trioxide as an intermediate of Mechanism (iii), there is insufficient evidence to definitely favor one over the other. The formal oxidation state of the N atom in NO\(_3\) is +6. At 298K the standard reduction potential \(E^\circ\) for \(\text{ONOO}^- + e^- \rightarrow \text{ONOO}^\cdot\) is 0.4 V;\(^{17}\) that is, peroxynitrite radical is more oxidative than peroxynitrite anion (ONOO\(^-\)), which itself is a strong oxidant: \(E^\circ\) for \(\text{ONOO}^- + 2\text{H}^+ + e^- \rightarrow \text{NO}_2 + \text{H}_2\text{O}\) is 1.4 V at pH 7.\(^{17}\) For nitrogen trioxide, various estimates for \(E^\circ\) of \(\text{NO}_3^- + e^- \rightarrow \text{NO}_3^-\) fall within a limit of 2.5 ± 0.2 V,\(^{18}\) again indicating a highly oxidative nature of the intermediate of Mechanism (iii). Thus, the intermediate of the pathway (iii) could be biologically at least as damaging as ONOO\(^-\) and more damaging than NO\(_2\). However, reactivity and toxicity studies of NO\(_3\) have largely escaped biologists’ attention.

Bodenstein considered both Mechanisms (ii) and (iii) as possible explanations of his experimental results.\(^{12,13}\) More recent investigations compared the two mechanisms and concluded that both have equal merits.\(^{9,19,20}\)

*Rate constant for oxidation of NO to NO\(_2\)*

Equation (3) defines the rate constant \(k\) for Reaction (1), which will be used in this section. Experimental results from 22 investigations on the rate constant \(k\) for the oxidation of NO have recently been
summarized.\textsuperscript{10} In these investigations, the concentration of NO ranged over five orders of magnitude from $8.2 \times 10^{-8}$ to $1.8 \times 10^{-2}$ mol·L$^{-1}$ and the temperature from 225 to 843 K. In many recent studies N$_2$ gas was used as a diluent. Most of the kinetic studies agree that the rate constant k is independent of variations in the total pressure (from less than 20 torr to atmospheric pressure) and the absolute NO concentration or the NO:O$_2$ ratio (up to a thousandfold variation) and that the logarithm of the rate constant is inversely proportional to the absolute temperature. The addition of N$_2$, CO$_2$, methane and olefins, or moisture (up to 90% relative humidity) has no apparent effect on the order and rate constant for the reaction of NO and O$_2$. Since water reacts with NO$_2$ but not with NO in the absence of dissolved O$_2$, it is expected that the presence of water in the NO/O$_2$ reaction systems will shift the final equilibrium toward the products, including oxyacids of nitrogen and their anions, but it will not change the rate with which NO is oxidized.

The best accepted temperature-dependence of k in T = 273 to 600 K is represented by an Arrhenius-type equation:\textsuperscript{9,10}

$$k \text{ (L}^2\text{·mol}^{-2}\text{·s}^{-1}) = 1.2 \times 10^3 e^{530/T} = 1.2 \times 10^3 \times 10^{230/T}$$ (6)

where T is the absolute temperature. It is noted that the rate constant of Reaction (1) has a negative temperature coefficient. In summary, k = $7.0 \times 10^3$ L$^2$·mol$^{-2}$·s$^{-1}$ near the ambient temperature ($\sim$ 298 K) and decreases by only $0.04 \times 10^3$ L$^2$·mol$^{-2}$·s$^{-1}$ per degree of rise in the
temperature. Thus, the rate constant is rather insensitive to changes of temperature over a wide range.

**Prediction of NO\textsubscript{2} formation using the rate constant k**

In the setting of NO inhalation environment as well as of ambient atmospheres, NO is present in much lower concentrations than O\textsubscript{2}, and it can be assumed that [O\textsubscript{2}] remains unchanged. Therefore, a pseudo-second-order kinetics can be applied to Reaction (1). Integration of Equation (3) yields:

\[
\frac{1}{[\text{NO}]_t} - \frac{1}{[\text{NO}]_0} = 2k\cdot[\text{O}_2]\cdot t \quad (7a)
\]

where [NO\textsubscript{t}] represents the molar concentration of NO after a residence time \( t \) and [NO\textsubscript{0}] is the initial NO concentration. Since the difference between [NO\textsubscript{0}] and [NO\textsubscript{t}] is [NO\textsubscript{2}],

\[
t = \frac{1}{2k\cdot[O_2]\cdot[NO\textsubscript{0}]\cdot[NO\textsubscript{2}]/([NO\textsubscript{0}] - [NO\textsubscript{2}])} \quad (7b)
\]

\[
t = \frac{1}{2k\cdot[O_2]\cdot[NO\textsubscript{0}]\cdot f/(1-f)} \quad (7c)
\]

where \( f \) is the fraction of NO that has become NO\textsubscript{2} in time \( t \) (i.e., \( f = [NO\textsubscript{2}]/[NO\textsubscript{0}] \)) and \( k = 7.0 \times 10^3 \text{ L}^2\cdot\text{mol}^{-2}\cdot\text{s}^{-1} \) near the ambient temperature. It is evident from Equation (7c) that the time required for the conversion of a certain fraction of NO to NO\textsubscript{2} is inversely proportional to the initial NO concentration and the rate constant \( k \). Equation (7c) can be used to calculate the time to reach a certain concentration of NO\textsubscript{2} for any concentrations of initial NO in O\textsubscript{2} (Table II).

The initial rate of production of NO\textsubscript{2} is proportional to the square of
the initial concentration of NO. Thus, gas-phase oxidation of NO is slow at very low concentrations of NO in ambient atmospheres. For example, about 6 h is required for 50% oxidation of 10 ppm NO. Conversely, with high-inspired O$_2$, a small error in the initial timing of NO inhalation could lead to a larger error in the exposure to the undesirable NO$_2$. Under a condition of inspired O$_2$ fraction = 1.0, the concentration of NO$_2$ reaches 52, 8.8, 2.3, 0.57 and 0.023 ppm in the first 10 sec of inhalation of 500, 200, 100, 50 and 10 ppm NO, respectively. At high NO concentrations, even a 1-sec error in the timing could cause serious consequences.

**Gas-phase disproportionation of NO**

*Chemical kinetics and rate constant of the disproportionation of NO*

NO is thermodynamically unstable, as indicated by its large positive Gibbs energy of formation (\(\Delta G^0_{298} = 86.32 \text{ kJ} \cdot \text{mol}^{-1}\)).\(^1,^2\) Despite the thermodynamic instability of NO, its decomposition and disproportionation are kinetically hindered near the ambient temperature. The following reaction does not occur to any appreciable extent near the ambient temperature and near 1 atm pressure:\(^2,^21\)

\[
3\text{NO (g)} = \text{N}_2\text{O (g)} + \text{NO}_2 \text{ (g)} \quad (2)
\]

However, the rate of this reaction can be increased by the use of catalysts\(^22\) and elevated pressures.\(^23\) Melia\(^23\) reported that after having
been stored in a cylinder under pressures between 50 and 100 atm and near the ambient temperature, freshly purified NO showed an increase of NO\(_2\) and N\(_2\)O contents at a rate of 2-3 % per month. Although the above observations are the only quantitative experimental data available until now, and the experiments were performed at temperatures above the ambient and under relatively high pressures, the data of Melia\(^{23}\) have been generally referred to in the contemporary review papers on the chemistry of NO gas.\(^{2,10,21}\)

It has been proposed that under elevated pressures, NO undergoes disproportionation proceeding by the following pre-equilibrium mechanism:\(^{2,21,23}\)

\[
2\text{NO} \rightleftharpoons (\text{NO})_2 \quad [\text{fast}] \quad (8a)
\]

\[
\text{NO} + (\text{NO})_2 \rightarrow \text{NO}_2 + \text{N}_2\text{O} \quad [\text{slow and rate determining}] \quad (8b)
\]

and the overall rate law:

\[-\frac{d[\text{NO}]}{dt} = k'[\text{NO}][(\text{NO})_2] = Kk'[\text{NO}]^3 \quad (8c)\]

where K is the equilibrium constant for Reaction (8a), and k’ the rate constant of Reaction (8b). Melia\(^{23}\) concluded that in the temperature range, 303 to 323 K, and at pressures up to 400 atm, the overall reaction for the disproportionation of NO obeys the third-order kinetics. Melia gave the overall rate constant Kk’ = 2.6 \times 10^{-5} \text{ L}^2\cdot\text{mol}^{-2}\cdot\text{hr}^{-1} at T = 303 \text{ K} and Kk’ = 2.7 \times 10^{-5} \text{ L}^2\cdot\text{mol}^{-2}\cdot\text{hr}^{-1} at T = 323 \text{ K}, with an initial pressure P_0 = 200 \text{ atm}. According to Melia the insensitivity of Kk’ to changes of
temperature in this range appears to result from the increase in the rate constant k’ being offset by the decrease in concentration of \((NO)_2\) brought about by its thermal decomposition.

*Buildup of NO\(_2\) and N\(_2\)O in pressurized NO gas*

At very low pressures, the behavior of a real gas approaches the ideality. At higher pressures, however, the physical properties of a real gas may deviate substantially from the ideality. In Melia’s equations (8a-c), [NO] is the molar concentration of NO as a real gas (NO\(_{\text{real}}\)) and not an ideal gas (NO\(_{\text{ideal}}\)). Keeping in mind that the non-ideality of NO plays a central role in the evaluation of quantitative implication of Melia’s experimental results on Reaction (2), we calculated the compressibility factor, defined as \(z = [NO_{\text{ideal}}]/[NO_{\text{real}}]\), of NO at 298 K and at 12 values of pressure (from 1 to 200 atm) using the ideal gas law and van der Waals equation, and then least-squares fitted these z to a cubic function of pressure:

\[
z(P) = 0.998 - 0.001438P - 0.000008488P^2 + 0.0000003735P^3
\]

where P is the pressure (in atm).

Since \([NO] = (1/RT)(P/z)\) in which R is the gas constant (0.08206 L·atm·mol\(^{-1}\)·K\(^{-1}\)), T the absolute temperature and (P/z) a function of P, Equation (8c) becomes:

\[
-\frac{1}{(P/z)^3}d(P/z) = \frac{Kk'/(RT)^2}{dt}
\]

Integration of this equation between \(t = 0\) and \(t = t\) yields:
\[(1/2)\{(z_f/P_f)^2 - (z_0/P_0)^2\} = \{Kk'/(RT)^2\} \cdot t \quad (9)\]

where the subscripts, “0” and “f”, refer to the initial and final states, respectively. For a given \(P_0\), \(T\) and \(t\), Equation (9) can be solved by finding the value of \(P_f\) (and the corresponding \(z_f\)) that satisfy Equation (9). Between \(t = 0\) and \(t = t\), the number of moles of NO decreases from \(n_0 = \{V/(RT)\} \cdot (P_0/z_0)\) to \(n_f = \{V/(RT)\} \cdot (P_f/z_f)\), where \(V\) is the internal volume of a container that has been assumed unchanged. Then, from the stoichiometry of Reaction (2), the number of moles of \(NO_2\) and \(N_2O\) at residence time \(t\) is \(1/3 \cdot (V/RT) \cdot (P_0/z_0 - P_f/z_f)\) and the total number of moles of \(NO\), \(NO_2\) and \(N_2O\) is \(1/3 \cdot (V/RT) \cdot \{2(P_0/z_0) + (P_f/z_f)\}\).

Consequently, the mole fractions, \(x\), of the three gases at time \(t\) are:

\[x_{NO} = 3 \cdot (P_f/z_f) / \{2(P_0/z_0) + (P_f/z_f)\} \quad (10a)\]

\[x_{NO_2} = x_{N_2O} = ((P_0/z_0 - P_f/z_f)) / \{2(P_0/z_0) + (P_f/z_f)\} \quad (10b)\]

These computations have been carried out at \(T = 298\) K for 8 initial NO pressures (from 1 to 200 atm) and for 8 reaction periods (from 1 to 8,760 hours). The results on the final mole fractions of \(NO_2\) and \(N_2O\) based on Melia’s data, \(Kk' = 2.6 \times 10^{-5}\) L²·mol⁻²·hr⁻¹, are summarized in Table III. This value of \(Kk'\) is for \(T = 303\) K, but \(Kk'\) is very insensitive to the changes in temperature. A similar calculation done at \(T = 303\) K has yielded a practically same result.

It can be seen from Table III that formation of \(NO_2\) and \(N_2O\) due to the disproportionation of \(NO\) is generally negligible at low initial
pressures, but becomes higher at elevated pressures. After 10 days of storage, the mole fractions of these contaminants are 0.01 % or lower under an initial pressure 5 atm or below, while they can become as high as 12 % in the same period when \( P_0 = 200 \text{ atm} \). Even when pure NO is stored under an initial pressure = 50 atm, the mole fractions of NO\(_2\) and N\(_2\)O can reach as high as 17 % after 1 year.

**Threshold for the exposure to NO\(_2\)**

The USA Occupational Safety and Health Administration has set the permissible limits for NO not to exceed 25 ppm for an 8-hr time-weighted average period and NO\(_2\) not to exceed 5 ppm during any part of the working day.\(^7\)\(^,\)\(^8\) On the other hand, the USA National Institute for Occupational Safety and Health has set the recommended exposure limit for NO\(_2\) not to exceed 1 ppm for a 15-min exposure and a maximum inhaled NO\(_2\) level of 5 ppm. Public Safety agencies from other countries have adopted similar or lower levels. However, these recommendations are intended for healthy workers and not for patients (especially neonates) with serious diseases, although some guidelines regarding the use of NO in patients have been based on these recommendations.\(^24\)\(^,\)\(^25\) In addition, inhaled NO therapy must frequently be continued for prolonged periods ranging from several hours to several weeks.
The national ambient air quality standard for the annual NO\textsubscript{2} level in USA is 0.05 ppm.\textsuperscript{26} A “safe” level of NO\textsubscript{2} is difficult to determine. NO\textsubscript{2} levels of less than 0.5 ppm may enhance human airway hyperreactivity. Toxic pulmonary effects of breathing NO\textsubscript{2} at or below 5 ppm have been reported.\textsuperscript{7,26} These include altered surfactant chemistry and metabolism, epithelial hyperplasia of terminal bronchioles and increased cellularity of alveoli in rats, as well as diffuse inflammation and hyperreactivity. At higher inhaled doses, pulmonary edema and death have been reported.

**Preparation, storage and application of ultrahigh-purity NO**

Disproportionation of NO under pressure must be born in mind when compressed NO in commercial cylinders is employed, as described above. For this reason, purification of commercial NO, most particularly for removal of NO\textsubscript{2}, is essential to its use in either research or clinically.\textsuperscript{2}

The normal (1 atm) melting and boiling temperatures are 109 K and 121 K for NO, 262 K and 294 K for NO\textsubscript{2}, and 182 K and 185 K for N\textsubscript{2}O, respectively.\textsuperscript{1} In our laboratory, NO is purified by a repeated bulb-to-bulb distillation at the cryogenic temperatures as follows. The all-borosilicate glass purification system has been designed to provide the bulb-to-bulb distillation in a most effective manner (Figure 1). When the gas mixture is evaporated from Trap 1 to Trap 2, the NO\textsubscript{x} impurities, which are all higher-boiling than NO, tend to condense on the walls of
Trap 2 near the entrance to the trap, while NO tends to condense on the walls deeper down the trap. When the condensates are evaporated from Trap 2 back to the (degassed) Trap 1, the pathway between the two traps are built in such a way that NO leaves Trap 2 while the majority of NO\textsubscript{x} impurities remain trapped in Trap 2. If the impurities ever leave Trap 2 for Trap 1, they must be the last ones to leave Trap 2. This procedure can be repeated to remove completely the impurities and to obtain ultrahigh-purity NO. The final ultrahigh-purity NO can be transported through the high vacuum system from Trap 2 to the storage tank (Type-316 stainless steel), which is put in a liquid N\textsubscript{2} trap during the transfer. Once purified, NO can be safely stored in the storage tank at low pressures (e.g., 5 atm or below).

NO gas is colorless, and the solid and liquid forms exhibit very faint blue, which can be taken as being colorless. The condensates of dinitrogen trioxide (N\textsubscript{2}O\textsubscript{3}) is bright blue, so that some regards the faint blue color of condensed NO as evidence of NO\textsubscript{2} since NO and NO\textsubscript{2} readily react to form N\textsubscript{2}O\textsubscript{3} at the cryogenic temperatures.\textsuperscript{1} The melting and boiling temperatures of N\textsubscript{2}O\textsubscript{3} are 162 K and 275 K, respectively. When more NO\textsubscript{2} is present, the condensates’ color becomes greenish.

In the study of aqueous NO systems it is important that the solvent be thoroughly deoxygenated. NO readily reacts with O\textsubscript{2} to form NO\textsubscript{2} and, further, N\textsubscript{2}O\textsubscript{3} and dinitrogen tetroxide (N\textsubscript{2}O\textsubscript{4}). NO\textsubscript{2}, N\textsubscript{2}O\textsubscript{3} and N\textsubscript{2}O\textsubscript{4} will
form the nitroxy anions on interaction with water causing side reactions, some of them catalytic. Inert gas-bubble-purging is one of the most effective deoxygenation methods, as long as the gas is sufficiently pure. In our laboratory, N$_2$ is purified by passage through activated charcoal and silica gel and then through copper metal-turnings heated red-hot in a silica tube furnace to remove NO$_x$ (e.g., $2\text{NO} + 2\text{Cu} \rightarrow \text{N}_2 + 2\text{CuO}$) and O$_2$ (i.e., $\text{O}_2 + 2\text{Cu} \rightarrow 2\text{CuO}$). Preparation of ultra-pure water involves a two-step purification process. The first step yields the water, which we may call acid-permanganate distillation water, which is free of all impurities with an exception of O$_2$ (Figure 2). The second step is removal of dissolved O$_2$ by purging with the ultra-pure N$_2$ in a specially built all-borosilicate glass apparatus. This water is used throughout our investigation in aqueous solutions.
References


<table>
<thead>
<tr>
<th>Table I.  Potential clinical uses for inhaled NO.</th>
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<tbody>
<tr>
<td>Persistent pulmonary hypertension of the newborn</td>
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<tr>
<td>Primary pulmonary hypertension</td>
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<td>Acute respiratory distress syndrome</td>
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<td>Pulmonary hypertension following cardiac surgery</td>
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<td>Cardiac transplantation</td>
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<tr>
<td>Lung transplantation</td>
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<td>Congenital diaphragmatic hernia</td>
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<td>Chronic obstructive pulmonary disease</td>
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<td>Bronchospasm</td>
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Table II.  Time (min) to yield 5 ppm NO\textsubscript{2} from Reaction: 2NO + O\textsubscript{2} = 2NO\textsubscript{2} at T = 298 K under a constant total volume.

<table>
<thead>
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<th>O\textsubscript{2} (%)</th>
<th>NO (ppm)</th>
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<th>20</th>
<th>40</th>
<th>80</th>
<th>200</th>
<th>400</th>
<th>800</th>
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<td>0.114</td>
<td>0.028</td>
<td>0.007</td>
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<tr>
<td>90</td>
<td>79.10</td>
<td>13.18</td>
<td>2.83</td>
<td>0.66</td>
<td>0.101</td>
<td>0.025</td>
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<tr>
<td>100</td>
<td>71.17</td>
<td>11.86</td>
<td>2.54</td>
<td>0.59</td>
<td>0.091</td>
<td>0.023</td>
<td>0.006</td>
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</table>

Threshold values of NO\textsubscript{2} have been set at 5 ppm or lower for permissible exposure limit for workers\textsuperscript{7,8}. Therefore, we have calculated the time to reach 5 ppm NO\textsubscript{2} from NO concentrations of 10 to 800 ppm in O\textsubscript{2} concentrations of 20 to 100 %.
**Table III.** Mole fractions of NO$_2$ and N$_2$O formation from Reaction:

\[ 3\text{NO} = \text{N}_2\text{O} + \text{NO}_2 \text{ at } T = 298 \text{ K under a constant total volume.} \]

<table>
<thead>
<tr>
<th>Initial pressure (atm)</th>
<th>Time (hr)</th>
<th>200</th>
<th>100</th>
<th>50</th>
<th>20</th>
<th>10</th>
<th>5</th>
<th>2</th>
<th>1</th>
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<td>1</td>
<td>0.0008</td>
<td>0.0002</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>3</td>
<td>0.0024</td>
<td>0.0005</td>
<td>0.0001</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>6</td>
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<td>0.0011</td>
<td>0.0002</td>
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<td>0.0484</td>
<td>0.0123</td>
<td>0.0029</td>
<td>0.0004</td>
<td>0.0001</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>240</td>
<td>0.1192</td>
<td>0.0373</td>
<td>0.0094</td>
<td>0.0014</td>
<td>0.0004</td>
<td>0.0001</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
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<td>0.0903</td>
<td>0.0264</td>
<td>0.0043</td>
<td>0.0011</td>
<td>0.0003</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(30 days)</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>8,760</td>
<td>0.3941</td>
<td>0.2984</td>
<td>0.1689</td>
<td>0.0449</td>
<td>0.0124</td>
<td>0.0032</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>(1 year)</td>
<td></td>
<td></td>
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</table>
**Figure 1.** Procedure for bulb-to-bulb distillation of pure NO.

<table>
<thead>
<tr>
<th>Step</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>J</th>
<th>Trap 1</th>
<th>Trap 2</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>--</td>
<td>--</td>
<td>Evacuate.</td>
</tr>
<tr>
<td>2</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>LN₂</td>
<td>--</td>
<td>NO to Trap 1.</td>
</tr>
<tr>
<td>3</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>S</td>
<td>LN₂</td>
<td>NO to Trap 2.</td>
</tr>
<tr>
<td>4</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>HWᵇ</td>
<td>LN₂</td>
<td>NOₓ from Trap 1 to Waste</td>
</tr>
<tr>
<td>5</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>--</td>
<td>LN₂</td>
<td>Degas Trap 1.</td>
</tr>
<tr>
<td>6</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>LN₂</td>
<td>S</td>
<td>NO to Trap 1.</td>
</tr>
<tr>
<td>7</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>LN₂</td>
<td>HW</td>
<td>NOₓ from Trap 2 to Waste</td>
</tr>
<tr>
<td>8</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>LN₂</td>
<td>--</td>
<td>Degas Trap 2.</td>
</tr>
<tr>
<td>9</td>
<td>C</td>
<td>C</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>S</td>
<td>LN₂</td>
<td>NO to Trap 2.</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(Go back to Step 4, if necessary)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: O, open; C, closed; LN₂, liquid nitrogen. *Slurry of organic solid in its own liquid. Choose a preferably non-flammable compound whose melting temperature is above the boiling temperature of NO but below the melting temperatures of other NOₓ. †Hot water (~ 50°C), which will evaporate all NOₓ. *Traps 3 and 4 are always kept in LN₂ during the procedure.
Figure 2. Water distillation apparatus.

Water is distilled from $10^{-3}$ M permanganate solution in $10^{-2}$ M H$_2$SO$_4$ at a rate of 150 mL/hr for at least 24 hr, during which the distillate is continuously fed back to the still by gravity. This is then followed by a period of withdrawal of product water at a rate of 150 mL/hr. The still is a 5-L round-bottom flask with three tapered ground points. Water vapor from the still passes through two liquid traps, which catch spatters of permanganate solution. The system is continuously purged by a stream of specially purified N$_2$ (cf. Section, “Preparation, storage and application of ultrahigh-purity NO,” of this article) to carry the gaseous impurities out of the apparatus through a “vent,” a poly(perfluoroethylene) check valve.