

**The Chemistry of Solvated Nitric Oxide:
As the Free Radical and as Super-saturated Dinitrogen
Trioxide Solutions**

By

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Abstract

The unusual behaviour of the mid-oxidation state nitrogen oxides, nitric oxide (NO) and dinitrogen trioxide (N_2O_3), are explored in solution.

Nitric oxide is shown to catalyze the *cis-trans* isomerizations of diazo species in aqueous and organic solutions, and a model is presented by which this proceeds by spin catalysis, making use of the unpaired electron of NO to permit access to triplet pathways. Five diazo compounds are tested and compared to stilbene, which is not found to isomerize under these conditions.

Dinitrogen trioxide is found to form easily in organic solvents, which stabilize the molecule even above room temperature. Solutions can be formed at chemically useful concentrations and levels of purity, and this result is compared with the sparse literature concerning this phenomenon. The chemistry of these solutions at 0°C is surveyed extensively, with 23 distinct organic reactions and 15 inorganic reactions being described. The first reported room temperature adduct of dinitrogen trioxide is presented, as well as novel syntheses for nitrosyl chloride and nitrosylsulfuric acid. X-ray structures are also given for a previously reported benzoquinone-phenol adduct, as well as a new mixed valent-mercury nitride salt of the form $\text{Hg}_4\text{N}_4\text{O}_9$.

Résumé

Le comportement inhabituel des oxydes d'azote aux états d'oxydations moyens, comme l'oxyde nitrique (NO) et le trioxyde dinitrique (N_2O_3), est exploré en solution.

L'oxyde nitrique s'avère à catalyser les isomerizations *cis-trans* des espèces diazoïques dans les solutions aqueuses et organiques. Un modèle est présenté dans lequel le procédé est accomplie via catalyse de spin, par l'entremise d'un électron non-apparié de l'oxyde nitrique qui donne accès aux états triplets. Cinq composés diazoïques sont testés et comparés avec le stilbene, qui ne s'isomérise pas dans ces conditions.

Le trioxyde dinitrique s'avère à se former facilement dans les solvants organiques, qui stabilisent la molécule même au-dessus de la température ambiante. Les solutions peuvent être synthétisées à concentrations chimiquement utile et suffisamment pures, et ce résultat est comparé avec le nombre faible des littératures concernant ce phénomène. La chimie de ces solutions au 0°C est explorée en profondeur, décrivant 23 réactions organiques distinctes et 15 réactions inorganiques décrites. La première synthèse reportée d'un adduit du trioxyde dinitrique qui demeure stable à température ambiante est présentée, en plus de synthèses originales pour le chlorure de nitrosyl et de l'acide nitrosylsulfurique. Les structures en Rayons-X sont aussi présentées pour l'adduit bezoquinone-phenol antécédemment reporté, ainsi qu'un nouveau composé à valence mixte d'un sel de nitrure de mercure sous la forme $\text{Hg}_4\text{N}_4\text{O}_9$.

Dedicated to my parents, John and Kathy
who thought it was fine to let me keep
powdered charcoal,
sulfur,
and potassium nitrate
in my room, next to the stuffed animals and bones.

and to J.W. Mellor:
Right back at you, Sarge.

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Contribution Of Authors

This dissertation contains the work of a submitted manuscript, in Chapter 2:

Nitric Oxide Catalysis of Diazene *cis-trans* Isomerization.

D. Scott Bohle, Kristopher Rosadiuk, *Inorganic Chemistry*.

All DFT calculations were carried out by D. Scott Bohle.

All other work was carried out solely by the author under the supervision of Professor D. Scott Bohle.

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Prologue: The Domain of the Real

Not long after a budding chemist first learns about the simple rules of chemical bonds-- that carbon makes four bonds, nitrogen three, oxygen two, hydrogen one-- they draw their first absurd chemical structure by trying to follow those rules (Fig P.1). There is an entire subcategory of chemical species that exist only in the notebook margins of students (and we are all students, forever¹), because naturally these rules are not rules at all, but only roughly defined general observations.



Fig P.1: A true chemical (benzotriazole, left) and an imaginary one (right).

What makes these rules attractive to us-- their simplicity and apparent explanatory power-- is also what should make us suspicious of them. A great many factors determine chemical behaviour, as we might learn the first time a more experienced hand tells us that the structure we've drawn does not exist, even though it "follows the rules." In our eagerness to understand a phenomenon we amputate the feature that caught our eye-- a fine and useful scientific practice-- but whether it's out of a failure of humility or a hunger for mastery or mere carelessness, we tend to forget about the body we took it from. When we finally realize our mistake, we break off another piece and describe another rule. The amendment of rules with more rules is a process of slowly sketching an accurate

picture, like Newton estimating a curve with infinitely smaller rectangles, gradually growing closer to knowledge of the real. We err not in doing this, but in conflating these rectilinear ideas themselves with knowledge.

A recent paper by Christopher Reed² provides an excellent example of this: there is in chemistry something called the 'proton' (or as exacting first year tutors sometimes insist, the 'hydronium' ion, H_3O^+) that is found everywhere in chemistry textbooks, and almost nowhere else in chemistry. As much as the proton describes a real physical entity, it rarely occurs as such in the world of our experience. Reed presents instead the best current model for what is found in aqueous solutions, dubbed the Stoyanov ion (Fig P.2), $\text{H}_{13}\text{O}_6^+$, which looks like the chemical equivalent of a scofflaw.

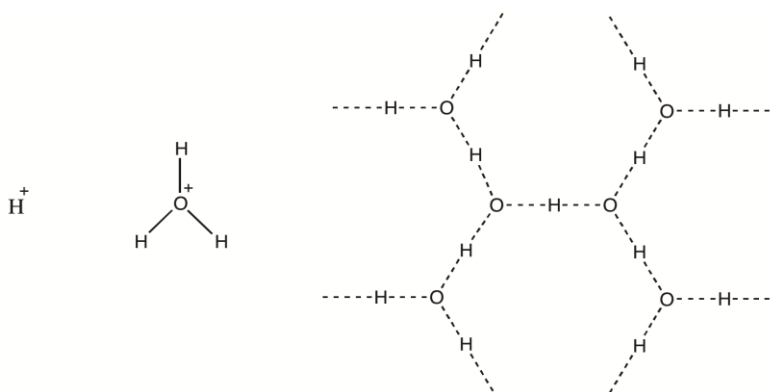


Fig P.2: Two mostly imaginary molecules and the Stoyanov ion, $\text{H}_{13}\text{O}_6^+$ (positive charge delocalized over the structure shown).

It's tempting to dismiss this as mere pedantry, simply pointing out what we know: that the proton is temporarily interacting with other molecules, but the 'real' species is the H^+ . But at this point one must question what our criteria for reality are: the spectroscopic data, with which we establish all other real chemical species, point to the Stoyanov ion as the true entity that exists. A proton may be a discrete thing in

physics, and in rarefied gas phase reactions, but as a chemical actor in condensed media (almost all chemistry) it is an idea, nothing more. A great deal of our chemical understanding is composed of mere ideas, in which we've considered molecules in isolation from the environment that makes them what they truly are.

The point is not that our education and shorthand is wrong but that it is incomplete, and shortcuts in thinking can grow into overconfidence. Thus a student who has learned that the second structure in Fig P.1 is 'ridiculous' (as opposed to 'not seen') will be inclined to see the last structure of Fig P.2 as 'just theory'. They may then reasonably look at those in Fig P.3 (below) and conclude that they are also mere fancy, the unicorn and hydra of chemical literature. When told that they do exist, one concludes that they must not be very stable, and indeed, in most literature nitric oxide and dinitrogen trioxide are discussed in terms of their great reactivity and their transience, more as reaction mechanisms than as chemical species.



Fig P.3: Two unlikely looking molecules, nitric oxide (NO) and dinitrogen trioxide (N_2O_3). Nitric oxide, at least, has some status due to its venerable history (it was discovered by Joseph Priestley³ in 1776), but it has often been discussed as though it were a fragment of a chemical, a radical 'on its way' to being something real. When research in the 1980s demonstrated that in fact it was made by the human body and had essential roles as a long-lasting signaling molecule⁴, the scientific community was taken aback, because it was a reactive gas⁵, and could not exist for long in a soft

living cell. Dinitrogen trioxide, meanwhile, is often left off the list of nitrogen oxides entirely. By virtue of being 'not stable'-- that is, prone to reaction under the conditions that we're habituated to or find convenient to work in-- these two compounds are subtly less real, more like accidents of chemistry than true parts of the world. Having banished the alchemists and their cardinal elements (earth, water, fire and air) to the dustbin of history, modern chemists mostly work with carbon, hydrogen, oxygen and nitrogen, of which carbon is often treated as the 'body' of the real and the others are the active components, the hinges upon which chemistry turns. Compounds made of only oxygen and nitrogen seem like a mechanism composed entirely of hinges, or a sentence made only of verbs, or-- to borrow from the old alchemical understanding-- a substance made only of fire and air. As anyone familiar with this class of compounds knows, there is some truth to these descriptions, but these are nevertheless important entities in the real world; they too have 'body'.

It is the focus of this work to discuss two poorly understood and widely unknown aspects of these intimately related species. Before beginning a discussion of my own work, in Chapter One I will provide a brief background of the voluminous body of literature surrounding nitrogen oxides in general, so as to better appreciate the potential reactivities of the middle-oxidation state species such as NO and N₂O₃. In Chapter Two, I will describe my research into nitric oxide's role as a spin catalyst, this being a species which catalyzes other reactions not by chemical bonds but by spin exchange; that is, into the mix of our perceptions of nitric oxide as either a short-lived, reactive species or a long-lived, unreactive one, nitric oxide can also--by

possessing a different kind of reactivity-- be both reactive and long-lived. In Chapters Three through Five, I will discuss the phenomenon of dinitrogen trioxide's remarkable stability in organic solutions: when considered together with its environment (solvent and atmosphere), this normally fragile molecule behaves as a stable, persistent, and selective reactant at room temperature.

On the common intuitive criterion that 'real' species are stable, these two rule-bending molecules are quite a lot more real than we usually give them credit for. My own response on encountering the dinitrogen trioxide solutions for the first time was, "Well, that can't be." It is my hope that this work, if nothing else, reminds the reader of how even the most well known realities can still prove to be both strange and colourful.

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Chapter 1: An Introduction to the Oxides of Nitrogen

Nitrogen, like carbon, commonly assumes up to eight different formal oxidation states, ranging from -3 to +5 (as opposed to carbon's +4 to -4)¹. When combined with oxygen to form one of the many oxides of nitrogen, it is found in the narrower range of +1 to +5. In Fig 1.1, we see the common menagerie of nitrogen oxides²; some stranger creations exist or have been reported, and of course some form functional groups of larger molecules (i.e. the hyponitrites (**J**) are diazenium diolates³ when bound to another group, which can be seen as $R^+ - N_2O_2$ or $R^- - (NO)_2$) but these are the ones made solely of N and O that are most commonly encountered by nitrogen chemists. Compounds **A**, **D**, **G**, **K**, **N** and **O** are all neutral molecules, **C** and **F** positively charged, the rest are negatively charged. Compounds **A**, **C**, **D**, **E**, **F**, **G**, **H**, **L**, **N**, and **O** are commercially available, **I**, **J**, **M** and **P** are usually only made in the lab, while **B** and **K** are treated as transient intermediates⁴.

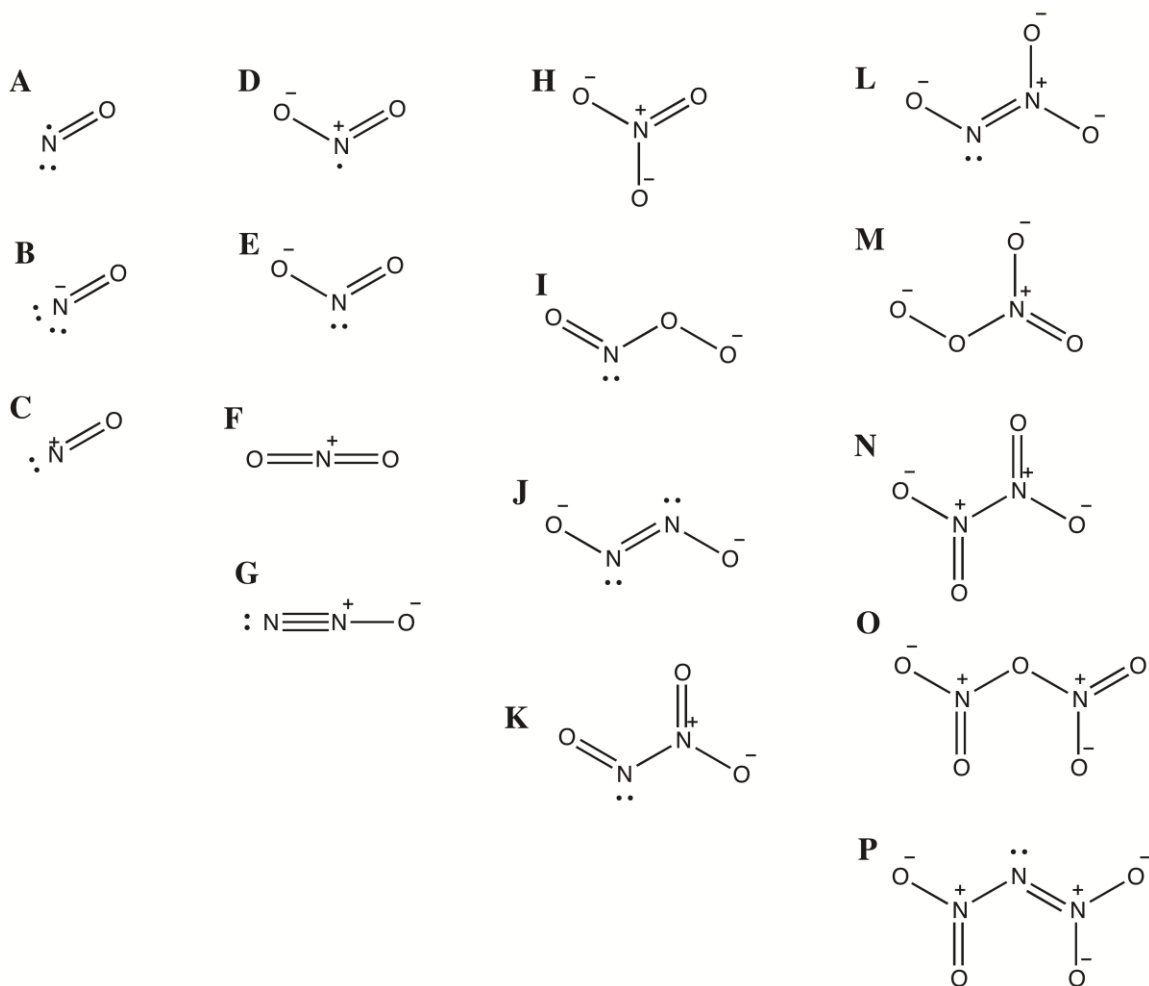


Fig 1.1: Lewis representations of some common oxides of nitrogen: A) Nitric oxide, B) Nitroxyl anion, C) Nitrosonium cation, D) Nitrogen dioxide, E) Nitrite anion, F) Nitronium cation, G) Nitrous oxide. H) Nitrate anion, I) Peroxynitrate anion, J) Hyponitrite dianion (trans, cis not shown), K) Dinitrogen trioxide, L) Trioxodinitrate dianion (Angeli's salt), M) Pernitrate anion, N) Dinitrogen tetroxide, O) Dinitrogen pentoxide, P) Dinitramide. anion.

The simplest oxide is **A**, nitric oxide (NO). It is a diatomic radical, yet is relatively unreactive, much like molecular oxygen⁵. It has 15 total electrons and 11 valence electrons in the configuration $(K^2K^{2-}(2s\sigma)^2(2s\sigma^*)^2(2p\pi)^4(2p\sigma)^2(2p\pi^*)^1$, Fig 1.2 below)⁶. The unpaired electron is in the anti-bonding π^* orbital, one of two

degenerate orbitals, giving this electron a delocalized character over the entire molecule; for Lewis structure purposes it may be considered to be 'on' the nitrogen, as this is where these orbitals are more strongly localized⁵. This gives the molecule a non-zero magnetic spin $S=1/2$, and so at room temperature the gas behaves paramagnetically.

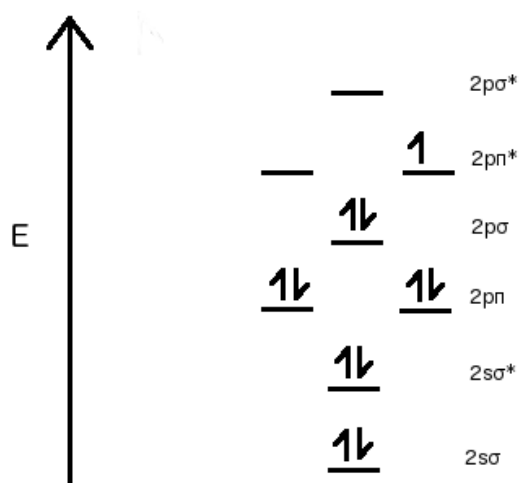


Fig 1.2: Molecular orbital energy diagram for the valence shell of NO.

Despite this, the molecule is all but invisible by EPR, which is normally very sensitive to $S=1/2$ radicals. The cylindrical symmetry of the molecule, and hence the symmetrical electrical fields created by electron occupation of these degenerate orbitals means that both the spin $1/2$ magnetic moment and the angular orbital momentum $L=1$ are aligned together along the internuclear axis, resulting in strong spin-orbit coupling⁶ (i.e. it is a type A molecule in Hund's classification)⁷. The magnetic spin and angular momentum can be antiparallel (giving the lower energy doublet state, designated $^2\Pi_{1/2}$) or parallel (the higher energy $^2\Pi_{3/2}$ state). Not only

does this greatly broaden the range of its magnetic susceptibilities (hence the EPR signal is correspondingly broadened out to the vanishing point) but in the true ground state ($^2\Pi_{1/2}$) the molecule ends by having no total magnetic moment⁶ (its spin magnetism and angular orbital magnetism effectively cancel), i.e. it is theoretically not paramagnetic in the ground state. In practice, since the parallel-coupled first excited state ($^2\Pi_{3/2}$) is paramagnetic, and at room temperature this state is about 70% occupied, it will behave paramagnetically. When the gas binds to another atom (i.e. a metal) the symmetry will be broken and it will thereafter behave as a normal paramagnet. Cooling the gas to put more molecules in the lower energy state only succeeds in provoking its dimerization, to diamagnetic N_2O_2 , which is how it exists in the liquid and solid states. This dimer has a special significance in NO chemistry, as abundant kinetic and theoretical studies have demonstrated that it is the active species in many NO reactions⁸; often, this radical gas needs to combine to form a non-radical before it can engage in chemistry.

This goes some distance to explaining how nitric oxide can simultaneously be a radical but also a stable gas. The perception that radicals are particularly reactive stems from studies of σ -based radicals (such as $\cdot\text{CH}_3$ or $\cdot\text{Ph}$), which are high energy molecules. A double degenerate π^* bound ground state radical is a different matter. In fact, nitric oxide is only reactive with specific species that meet its particular electronic criteria⁹. Its combination with its preferred partner, superoxide (O_2^{2-}), is diffusion controlled¹⁰; other potential partners, such as oxygen and nitrogen dioxide (Fig 1.3), combine more slowly:

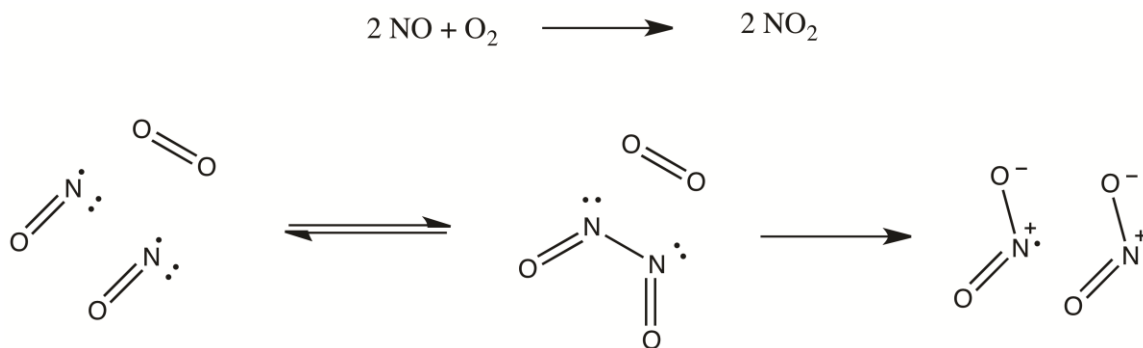


Fig 1.3: Formation of NO₂ from NO

This reaction with oxygen proceeds readily, although since the reaction mechanism depends on the dimerization of two NO, the rate law⁹ is thus:

$$d[\text{NO}_2]/dt = -4k_3[\text{O}_2][\text{NO}]^2$$

Eq 1.1: Rate law of nitrogen dioxide formation from nitric oxide.

where $k_3 = 2 \times 10^6 \text{ M}^{-2}\text{s}^{-1}$. This means that nitric oxide can be found even when oxygen is around, as its lifetime depends inversely on the square of its concentration, and at low levels this can mean quite an extended lifespan; the half life of 1 μM NO in an oxygenated buffer has been calculated to be 560 s.

The factor of 4 in Eq 1.1 corrects for another pathway that necessarily follows upon the first, due to nitric oxide being reactive with its own product (Fig 1.4).

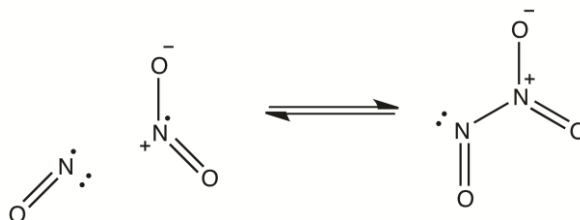
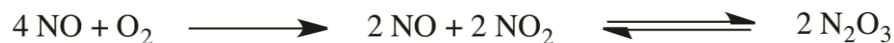


Fig 1.4: Gas phase equilibrium of NO and NO₂ to N₂O₃.

Thus it would be accurate to represent Eq. 1.1 as Eq. 1.2:



Eq 1.2: Formation of the $\text{N}_2\text{O}_3/\text{NO}_2$ equilibrium from NO and oxygen.

By Le Chatelier's principle, the addition of this equilibrium depletes the products of the initial irreversible reaction and drives it forward. With the appearance of this new species, dinitrogen trioxide (N_2O_3) (**K**), one can see that attempting to discuss these species in isolation from one another is an idealization rather than fact (an idealization I will honour by returning to N_2O_3 later). For now, we note the ready transformation of NO into other oxides of nitrogen, a definitive feature of this chemistry.

Finally, nitric oxide can react with nitric oxide, and then with nitric oxide. That is, without oxygen around to oxidize the dimer to two nitrogen dioxide, this function can be performed by a third NO, leading to a disproportionation reaction¹¹ (Fig 1.5):

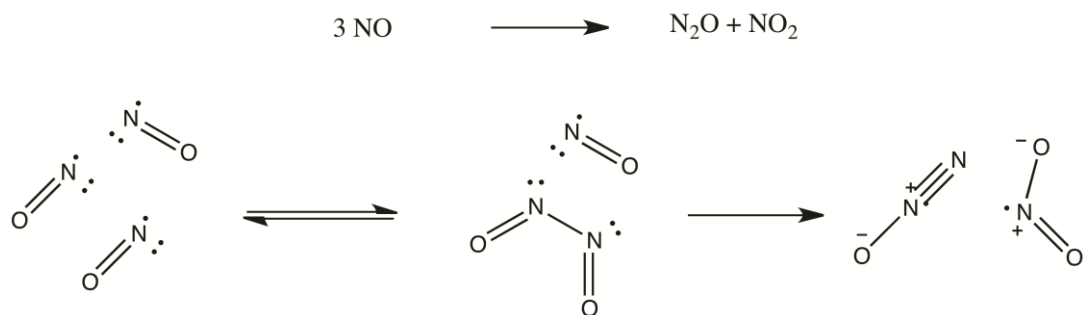


Fig 1.5: Disproportionation reaction of nitric oxide.

While this suggests that NO is never long for this world, this reaction is relatively slow and depends on higher pressures of the gas, though it can be accelerated by a heterogenous catalyst¹²; NO compressed gas cylinders usually have their interior

metal surface coated with polymer to prevent this reaction from occurring by surface catalysis, and as such will remain useful for years.

Curiously, nitric oxide is in a sense a 'reactive molecule' by dint of circumstance. Since oxygen is ubiquitous in terrestrial chemistry and the product of their union is also reactive, NO ends by seeming to be 'very reactive', much as paper would seem to be very reactive if one's office happens to be on fire. Kept isolated from a select list of potential, mostly radical partners, nitric oxide is seen to be only modestly reactive, or even passive in the presence of other supposedly reactive species. This is, in fact, the key point behind the surge of interest that nitric oxide has received in the past two decades (being dubbed 'Molecule of the Year' in 1992)¹³; NO is produced in the human body as a vasodilator and a signaling molecule, and far from being an obscure toxin (as it had been treated for the preceding century) it is a regular feature of biology.

From nitric oxide spring its two ions, (**B** and **C**): nitroxyl anion (NO^-) and nitrosonium (NO^+). The first ionization energy of NO is 9.25 eV, whereas its electron affinity is 0.015 ± 0.1 eV^{14 15}, making it reasonably easy to oxidize but a poor electron acceptor, despite being composed of two electronegative atoms (here one must consider that oxidation means the loss of an electron in an anti-bonding orbital, whereas reduction means a second anti-bonding electron and the lengthening of the N-O bond). Nitrosonium salts have become commonplace in chemistry, mostly as nitrosonium tetrafluoroborate (NO^+BF_4^-) and nitrosyl chloride (NOCl). Nitroxyl, on the other hand, is a short-lived intermediate. It has been proposed¹⁶ that nitric oxide can react with alkali metals to form metal nitroxyls (i.e.

LiNO), but characterization of such a species had to be carried out at 15°K in inert matrices¹⁷. The closest that the nitroxyl anion comes to being seen at room temperature is in the proposed nitroxyl, HNO¹⁸. This species has also been described in low temperature inert matrix experiments, and some work has been done to develop direct fluorescent detection methods that are specific to it¹⁹, but typically its formation is inferred by its breakdown products, in which HNO is a necessary remainder of a reaction and is expected to decay to nitrous oxide, by Eq 1.3:



Eq 1.3: Proposed dehydration of nitroxyl.

This is one way among many that the oxides of nitrogen can recombine to form nitrous oxide (**G**), which is characterized by its inertness to almost everything; unlike most nitrogen oxides, it does not easily interconvert with other forms, and represents an end point in a reaction chain.

When bound to other molecules, NO can be intermediate between the extremes of its ionic forms (when bound, it is often called a nitroso group, R-N=O). Its position on the spectrum between pure nitrosyl anion and pure nitrosonium can be gauged by IR spectroscopy²⁰: nitrosyl anion absorbs at 1353 cm⁻¹, nitric oxide itself is at 1876 cm⁻¹, and nitrosonium is found at 2345 cm⁻¹. This shift in vibration represents the changes to the antibonding 2pπ* orbitals: filling them weakens the N=O double bond, lowering the wavenumber of absorbance, where emptying them strengthens it and raises the wavenumber of absorbance. This also makes nitrosonium or nitrosyl anion effectively opened or closed, respectively, to subsequent π donation from their bound substituents (i.e. from the d-orbitals of a metal), which gives nitrosyl ligands a bent configuration, and nitrosonium a linear

form. In practice, the degree of π^* donation depends on the number of substituents on the metal which are engaged in such donation (i.e. if many substituents are engaged in π^* interactions, the degree that each is doing so decreases, as formalized by the Feltham and Enemark)²¹, but bent-nitroxyl and linear-nitrosonium is a useful rule of thumb.

Nitrogen dioxide (**D**, NO₂), the foul red-brown component of smog, is also a radical, but unlike nitric oxide its unpaired electron is localized on the nitrogen²², and displays very different reactivity. For example, NO₂ hydrolyses quickly into nitrous and nitric acid² (Eq 1.4); NO, meanwhile, is poorly soluble in water, and so long as it is deprived of oxygen undergoes no reaction. This is another reason that NO is able to have so many important biological functions, despite forming in a wet environment.



Eq 1.4: Hydrolysis of nitrogen dioxide.

Thus a small amount of deoxygenated water can be a handy way to remove excess nitrogen dioxide from NO.

The dimer of nitrogen dioxide is dinitrogen tetroxide²³, N₂O₄ (compound **N**), which forms as a clear liquid (bp: 21.69 °C, mp: -11.2 °C; compared to the dimer of NO, N₂O₂, which at its boiling point of -151.8 °C is only 0.5% associated²⁴). Where the NO dimer is a transient reaction intermediate, the NO₂ dimer is a major industrial chemical and a constituent of rocket fuel. N₂O₄ can also behave chemically as a nitrosonium donor²⁵, [NO⁺][NO₃⁻], and has been used extensively as a nitration agent; when anhydrous, it can form metal nitrates (in which the nitrate is formally

bound to the metal rather than forming a cation). Like NO, the chemistry of NO₂ cannot be fully separated from the chemistry of its dimer.

The ions of nitrogen dioxide are both used extensively: the cation (**F**), nitronium, is the active species of textbook nitration reactions using nitric acid and sulfuric acid (Fig 1.6)²⁶; nitronium is a powerful electrophile and is commonly used to attack aromatic rings. The anion, meanwhile, is common nitrite (**E**). The ionization energy and electron affinity of NO₂ are 11.23 and 2.3 eV¹⁴, respectively, which follows from its greater oxidation state than NO: it takes on electrons more readily to form nitrite and gives them up less easily.

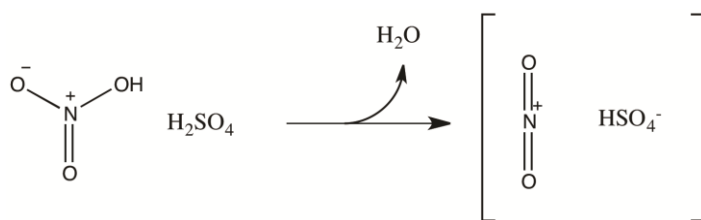


Fig 1.6: Nitronium intermediate formation for nitration reactions.

Nitrite is stable by itself, but can go through further transformations, most notably through reaction with any mineral acid, which produces pale blue solutions of nitrous acid. This protonated form of nitrite is part of the chemist's standard toolbox, typically for its ability to carry out nitrations and diazotizations²⁷. Though a weak acid (pKa: 3.4) nitrous acid performs dramatic oxidations, and like both NO and NO₂ the secret lies in its dual nature. Nitrous acid is seldom the active component in the reactions for which it is known: rather, it dimerizes and dehydrates into another nitrogen oxide: N₂O₃. The formation of N₂O₃ is a dehydration reaction, which is why dinitrogen trioxide is often known as nitrous anhydride (Fig 1.7).

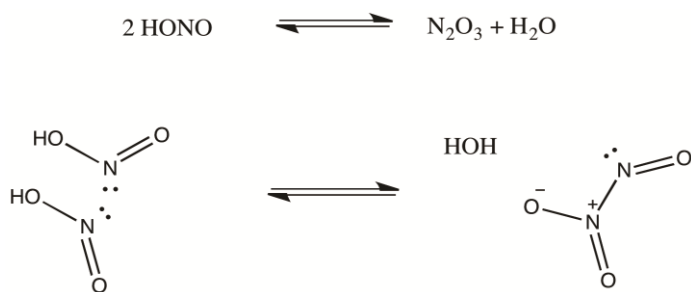


Fig 1.7: Equilibrium between nitrous acid and dinitrogen trioxide.

This molecule then performs the chemistry for which nitrous acid is known (Fig 1.8)²⁸.

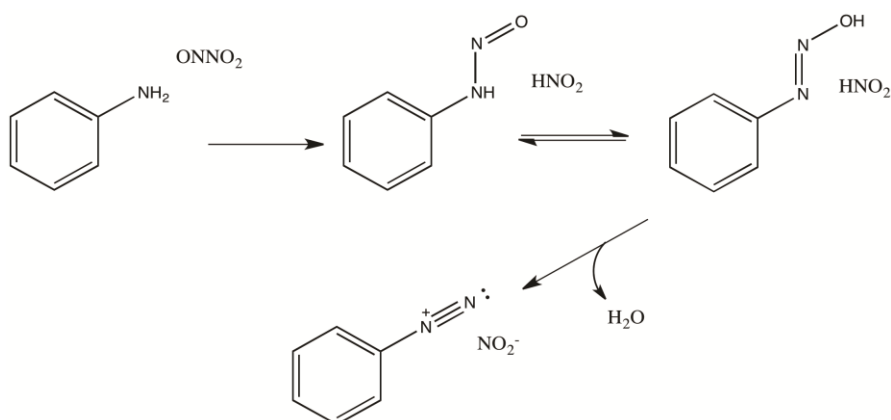


Fig 1.8: Diazotization of aniline by the anhydride of nitrous acid.

Dinitrogen trioxide, an intensely azure blue chemical, is thus the heart of nitrous acid reactivity, and is responsible for the characteristic pale blue cast of the acid solutions. In aqueous solutions it exists only at millimolar concentrations²⁹, but that is enough to perform its function as a nitronium donor. We have seen N_2O_3 before as the result of NO radical binding to NO_2 radical; comparing their relative redox potentials, it's easy to see that when so bound, NO_2 can oxidize NO to form NO^+ , becoming nitrite in the process; in solution the molecule can be thought of as

nitrosonium nitrite. Or, alternatively, the two could cleave homolytically and reform NO and NO₂ radicals, which is the preferred mode in the gas phase³⁰ (though concentrated nitrous acid will exude a small amount of NO and NO₂ gas from this mode of cleavage).

In fact, dinitrogen trioxide shows up frequently in the chemistry of nitrogen oxides as an unnoticed participant. We have already seen it play a role in the reaction between NO and O₂ (Eq 1.2). In a classical synthesis¹ of nitrosylsulfuric acid, nitric oxide is bubbled through sulfuric acid, but as researchers improved their techniques, some (Berzelius and Gay-Lussac) noticed that nitric oxide itself is not absorbed by the acid, but will be as a mixture with other oxides (presumably, this meant NO₂); Sanfourche specifically noted the similarity between this reaction and that which occurred with condensed dinitrogen trioxide, and N₂O₃ was proposed as the true intermediate. In another, somewhat less antique synthesis³¹, NOCl was prepared from NO₂ gas and KCl (Eq 1.5):



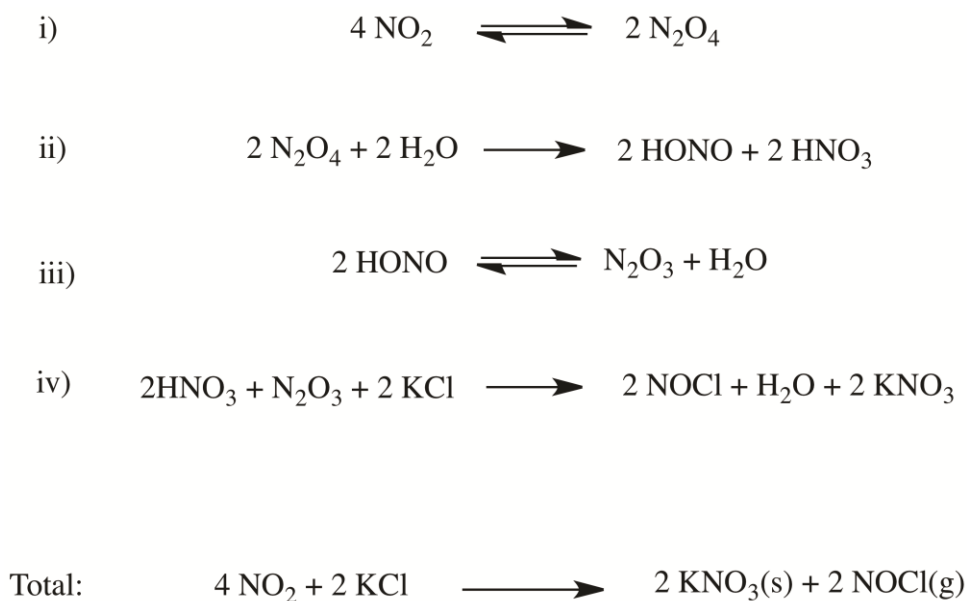
Eq 1.5: Nitrosyl chloride from "nitrogen dioxide".

But as the writers noted (page 42):

"The potassium chloride must contain a small amount of moisture (2.4%) the role of which is not clear. In practice the moistened KCl crystals are placed in long glass tubes, through which NO₂ is allowed to stream."

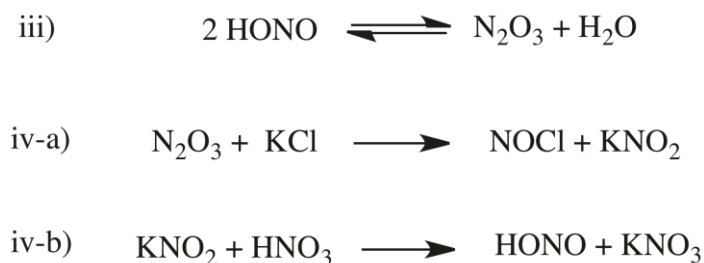
In theory, NO₂ could yield N₂O₄, which could ionize to give NO⁺ and NO₃⁻, accomplishing the reaction in one step. Yet if this were occurring then the reaction could proceed without moisture. One possible explanation is that the water is merely present to disrupt the lattice structure of the salt and allow the N₂O₄ to react.

However, another possibility is that the nitrogen dioxide mixes with the water as in Eq 1.4 to make nitrous acid and nitric acid. Neither of these are sufficient to deliver an NO^+ ion to pair with the chloride, but from nitrous acid one can produce dinitrogen trioxide, an intermediate which does have this ability. This modified reaction scheme can be seen in Eq. 1.6, and it can be appreciated that the overall stoichiometry is preserved, with water serving as a catalyst:



Eq 1.6: Modified NOCl production scheme with N_2O_3 as a hidden intermediate.

Step iv) in the above scheme may seem mysterious, but can be understood as the sum of a further cycle by which the reacting N_2O_3 can regenerate itself (Eq 1.7):



Eq 1.7: Regeneration of N_2O_3 by production of nitrous acid.

Step iv-b) of Eq 1.7 produces nitrous acid, which feeds back into step iii. Ultimately, this means that one N_2O_3 can deliver two equivalents of NO^+ (thus step iv, in which one N_2O_3 reacts with 2 KCl , represents two cycles of steps iv-a and iv-b). This all depends, of course, on whether step iv-a) does in fact proceed. I will return to this question in Chapter 5.

Despite N_2O_3 acting as an ionic species in aqueous solution, rigorous electrochemical studies³² have shown that it does not typically exist in an ionized state. The IR signature³³ of N_2O_3 gives the $\text{O}=\text{N}-$ stretch at 1860 cm^{-1} , putting it firmly in the region expected for formal nitric oxide, rather than NO^+ or NO^- . This is confirmed by the bond lengths of the molecule as compared to its constituent radicals (Fig 1.9, from Kishner et al.³⁴):

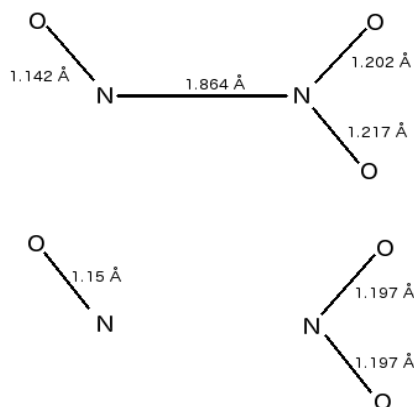


Fig 1.9: Bond lengths of N_2O_3 , NO , and NO_2 .

The dinitrogen trioxide molecule is thus a truly neutral molecule, but one held together by an uncommonly long N-N bond (1.864 Å). Kishner et al. attribute this distended bond to the lone pair of the oxygen on the $\text{N}=\text{O}$ (left hand) side, which donates into the anti-bonding orbital. It is also worth noting that this puts the $\text{N}=\text{O}$

substituent at a bond length similar to that of free nitric oxide (which has a formal bond order of 1.5 due to the unpaired electron in its $2p\pi^*$ orbital). The $-\text{NO}_2$ oxygens are also distended compared to NO_2 and slightly asymmetrical (placing the greater double bond character *cis* to the NO double bond). Nevertheless, this demonstrates that the two radical halves of N_2O_3 are altered but little by their association, explaining the lability of this bond in the gas phase, as dissociation may proceed with minimal rearrangement.

Analogous to the dehydration of nitrous acid (the conjugate acid of nitrite) to form dinitrogen trioxide, one may also dehydrate nitric acid (the conjugate acid of nitrate, **H**) to form dinitrogen pentoxide³⁵ (compound **O**) (Eq 1.8).



Eq 1.8: Dehydration of nitric acid to dinitrogen pentoxide.

Exposing the pentoxide to water will regenerate the nitric acid. Unlike dinitrogen trioxide, the pentoxide is stable in its pure form at room temperature, though the crystals sublime easily. Over time it will decay to NO_2 and O_2 . What is perhaps most noteworthy about this reaction (for the purposes of this writing) is how nitrate-- often treated as a stable, passive counter-ion-- can be returned to lower oxidation states by being put through harsh dehydrating conditions. This is seen in an even more common reaction: the standard nitration²⁶ of aryl rings, which employs nitric and sulfuric acid (Eq 1.9) to make nitronium as the active intermediate.



Eq. 1.9: Nitronium formation by nitric and sulfuric acid.

The nitronium is of course a potent oxidant, but having lost an oxygen it is open to being reduced to a nitro or nitrite species.

Nitramides, hyponitrites, and peroxyxynitrites, (compounds **P**, **J**, and **M** in Fig 1.1) are all further permutations of the chemistry described to this point, but do not bear specifically on this research, and are mentioned only to illustrate the breadth and flexibility of this chemistry. One salient detail is that while these complex oxides appear unstable, and are not frequently seen as pure substances, this does not mean they are mere laboratory curiosities; in the case of the bound form of hyponitrites (diazonium diolates), they can be naturally occurring, and are found as amino acid derivatives in a number of bacterial species. One such compound, called poecillanosine (Fig 1.10) is found in marine sponges³⁶.

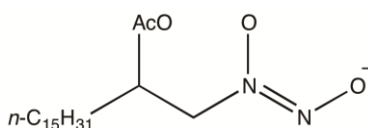


Fig 1.10: Poecillanosine, a naturally occurring diazenium diolate.

1.2 Summary

The chemistry of nitrogen oxides is characterized by its fluidity, as multiple oxides of different forms will co-exist during a single chemical procedure. In a sense this is the case with all chemistry, but what distinguishes nitrogen chemistry is that many of these intermediate products are stable species in their own right. A given nitrogen oxide is seen as tremendously reactive because it quickly becomes other nitrogen oxides, yet we know about this change because these other oxides are easily identifiable, and often isolable.

Of these, nitric oxide, nitrogen dioxide, and dinitrogen trioxide form an intimate system, and their chemistry does not disentangle easily. However, in the following chapters I will describe two systems in which the pure compounds may be isolated and allowed to act in the ways peculiar to them.

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General Experimental

The following describes the basic tools and techniques employed in this thesis, and experiments should be assumed to adhere to these protocols except where otherwise stated. Specialized techniques or those developed in the course of research will be discussed in their appropriate section.

Chemicals:

Most chemicals are purchased from Sigma-Aldrich, Fisher Scientific, or their partners and subsidiaries, and used as received. When it is specified that a reactant was purified, the procedures recommended by Perrin's "Purification of Laboratory Chemicals"¹ were employed.

Most solvents are used dry. Toluene is distilled in-house with a sodium/benzophenone-ketyl still and stored over activated molecular sieves. Other solvents are obtained from an automated solvent system and likewise stored. Xylene, mesitylene, and anisole were used as received.

Gases are provided from high purity gas cylinders. Oxygen was obtained from MEGS, while argon, nitrous oxide and nitric oxide are purchased from Praxair. Nitric oxide is purified before use by passing it through a packed column of sodium/potassium hydroxide and glass wool to remove the bulk of NO₂ (red-brown colour should not be visible in a small vessel filled with the gas). Where all trace of NO₂ must be removed and water is not a concern, the gas is passed into a vessel containing a small amount of water and shaken to remove the remaining NO₂. NO gas is delivered through a vacuum manifold system that may be evacuated or

flushed with argon gas, as needed. Small doses are delivered by SGE gas tight syringes through rubber septa. Rubber tubing, septa, or teflon stopcocks are exposed to the NO/NO₂ gas for the minimum time necessary to conduct the experiment, in order to prevent their destruction/ absorption of gas.

Spectroscopy/Analysis:

-UV-Vis: An HP 8453 Diode-Array UV-Vis spectrometer was used, with both a tungsten and deuterium lamp in operation.

-IR: An ABB Bomem MB Series IR spectrometer with a spectral resolution of 4 cm⁻¹ was used. Peaks are reported in wavenumbers per centimetre (cm⁻¹). Specified spectra were prepared in hexachlorobutadiene mulls, due to reactions with KBr; otherwise a KBr pellet should be assumed.

-NMR spectra were recorded on Varian Mercury 200, 400, or 500 MHz instruments. All chemical shifts are recorded in δ (ppm) relative to the residual solvent signals.

-X-Ray Crystallography: Crystals are mounted on a glass fiber with epoxy resin, or Mitegen mounts in a Paratone-N suspension from Hampton Research. Experiments were performed on a Bruker Apex-II CCD diffractometer using graphite monochromated MoK α radiation ($\lambda = 0.71073 \text{ \AA}$), and chilled with a Kryoflex system. SAINT is used for the integration of the intensity reflections and the scaling, and SADABS for the absorption correction. Direct methods were used to solve the structures. The location of non-hydrogen atoms is carried out using Fourier difference maps; refinements are made by full-matrix least-squares

methods on F² of all data using SHELXTL software. The positions of hydrogen atoms were calculated.

-Theoretical Methods: Gaussian03 was used for all calculations with B3LYP density functional theory and the triple zeta basis set 6-311++G**.

-Elemental Analysis was performed by the Laboratoire d'Analyse Elementaire de l'Université de Montreal.

-Mass spectroscopy was performed on a Bruker GC-MS Scion Single quadrupole instrument.

-Thermographic analysis was performed with a TGA-Q-500 machine from TA instruments.

- DSC measurements were performed with a DSC 2010 Differential Scanning Calorimeter from TA instruments.

Methods:

-Where dropwise addition is specified, this is performed with an addition funnel at a rate of approximately 1 drop per second with rapid stirring.

-Reactions performed at -78°C are immersed in an ethanol/dry ice slurry bath, those at 0°C are performed in an ice/water bath, and room temperature was ~25°C.

- Solvents are deoxygenated by one of two techniques: freeze-thaw-degassing or argon purging. Freeze-thaw-degassing is accomplished by freezing the sample in liquid nitrogen, evacuating the vessel with a high-pressure vacuum, then allowing it to warm while under an argon atmosphere. This is repeated three times. Argon

purging is accomplished by chilling the solution (to minimize losses due to evaporation) then vigorously bubbling argon through it for 5-10 minutes.

Preparation of Trioxide Solutions by Dynamic Absorption:

A sealed vessel equipped with a stir bar is evacuated under high vacuum, and is then flushed with nitric oxide gas. A chosen solvent is then injected. Alternatively, solvent can be added first, then freeze-thaw-degassed or sparged with argon, before finally flushing with NO. A measured amount of oxygen gas is then injected with a gas tight syringe. The mixture is allowed to stir gently for 5 minutes while under a weak positive pressure of NO gas (~ 0.7 kPa above atmospheric pressure).

A solution prepared in this way will slowly absorb NO until it reaches a saturation point. The oxygen should be introduced slowly in steps, followed by some NO exposure, or else pressure will accumulate; slow addition allows it to become tetroxide/trioxide and become solvated. Stepwise addition allows one to add liters of gas to only a few millilitres of solvent in a 50 mL vessel without developing any overpressure. The nitric oxide atmosphere should be left intact to protect the solution, or replaced if the vessel must be opened or otherwise disturbed.

Handling of Trioxide Solutions

In all reactions the reactant was added to the trioxide solution, usually into a stoppered vessel with appropriate venting, rather than the other way around. Transfer of the trioxide solutions into an atmosphere that is not already suffused with NO gas will cause some loss of trioxide, as the more volatile NO component is

driven out of solution. To maintain proper stoichiometric measurements and avoid complication, the reactions should be carried out in the same vessel in which the trioxide solutions were formed.

The addition of liquids to trioxide solutions is performed with a syringe through a septum while the reaction vessel is allowed to vent to a gas bubbler or a gas collection vessel. Reactant solutions are cooled in the appropriate medium before addition to a cooled trioxide solution (cold solutions must be added promptly as pipette tips/ syringe needles can condense atmospheric water during transfer; failure to chill prior to addition can cause some nitric oxide/nitrogen dioxide to boil out of solution). Solids are added quickly, and the vessel closed immediately afterwards.

Table G1: Glossary of Abbreviations

NMR Abbreviations		IR Abbreviations	
singlet	s	broad	br
doublet	d	weak	w
triplet	t	strong	s
quartet	q	very strong	vs
quintet	qn	shoulder	sh
sextet	sx	hexachloro butadiene mull	hex
septet	sp		
multiplet	m		

(1) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed.; Pergamon Press: Great Britain, 1988.

Chapter 2: Nitric Oxide Catalysis of Diazene E/Z Isomerization

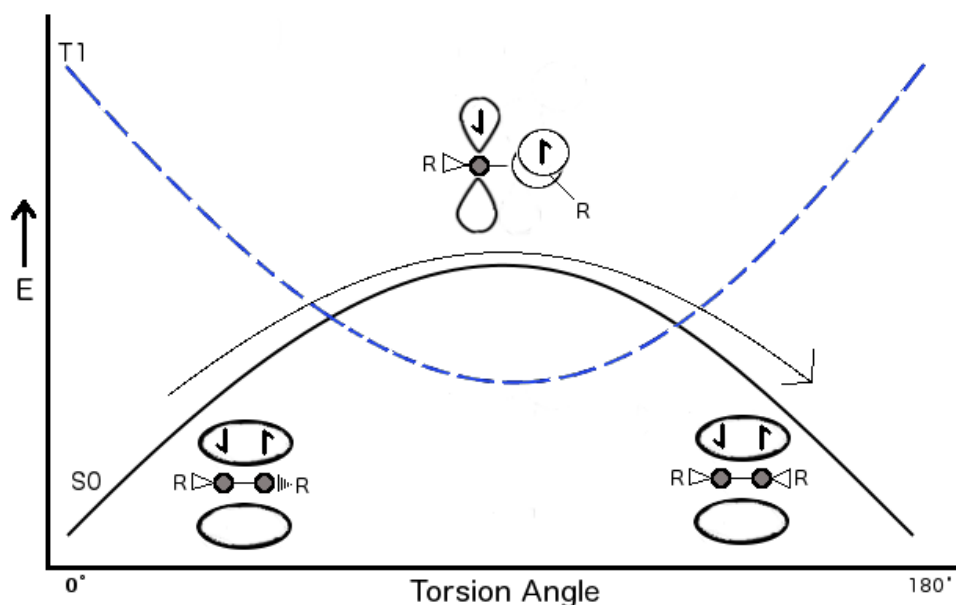
2.1 Introduction to Spin Catalysis

The isomerization of fatty acids by 'oxides of nitrogen' was first reported by J.J.E. Poutet in 1819,¹ and intermittent investigations since then have shown that nitric oxide,^{2,3} nitrogen dioxide,^{4,5} and even oxygen itself⁶ can catalyze the *cis/trans* isomerization of olefins, CTI. The adventitious oxygenation of NO to NO₂ has led to some confusion on which is the more active *cis-trans* catalyst, and it is noteworthy that for those working in carefully controlled, low concentration experiments, NO is reported as the catalyst for gas phase experiments, while researchers working in solution usually report NO₂ as the catalyst. De Maré *et al.* have found that photosensitized NO, in its ⁴Π excited state, will catalyze *cis-trans* isomerizations in 2-butene but that ground state NO on its own is not catalytically active.^{7,8}

As both NO and NO₂ are stable radicals, it is possible that they catalyze *cis-trans* isomerizations (CTI) by virtue of a spin exchange,^{9,10} which allows access to triplet pathways.^{11,12} What makes these pathways normally inaccessible, and hence the intersystem crossing significant, is the inability of electrons to spontaneously change spins. In most cases, intersystem crossing proceeds by spin orbital coupling, in which the interaction between the magnetic moment of an electron in a high energy molecular orbital and the magnetic spin of that electron is sufficiently strong to effect a change in spin; this occurs commonly in the d-orbitals in transition metals. This can be considered a form of 'spin catalysis'.⁹ Another form, less well

known, involves an open shell radical species associating with a system (such as a transition state) and exchanging its unpaired electron for an electron of opposite spin from this associated system, thus transforming a singlet to a triplet, or vice versa. Since a singlet to triplet transfer is usually energetically uphill, it only occurs in conformations where the triplet energy has dropped or is otherwise energetically available and the spin change remains as the sole barrier. Since the original radical is released unchanged, it qualifies as a catalyst.

Double bond isomerization in general is an excellent candidate for spin catalysis; as the double bond rotates out of plane, the potential energy surface of the T1 state drops below that of the ground state (at 90°, the π electrons cannot be in the same orbital, and this separation is more easily achieved for two electrons of the same spin, i.e. the triplet state). Thus any process which allows easy access to the triplet state can allow access to lower energy pathways (Fig 2.1).



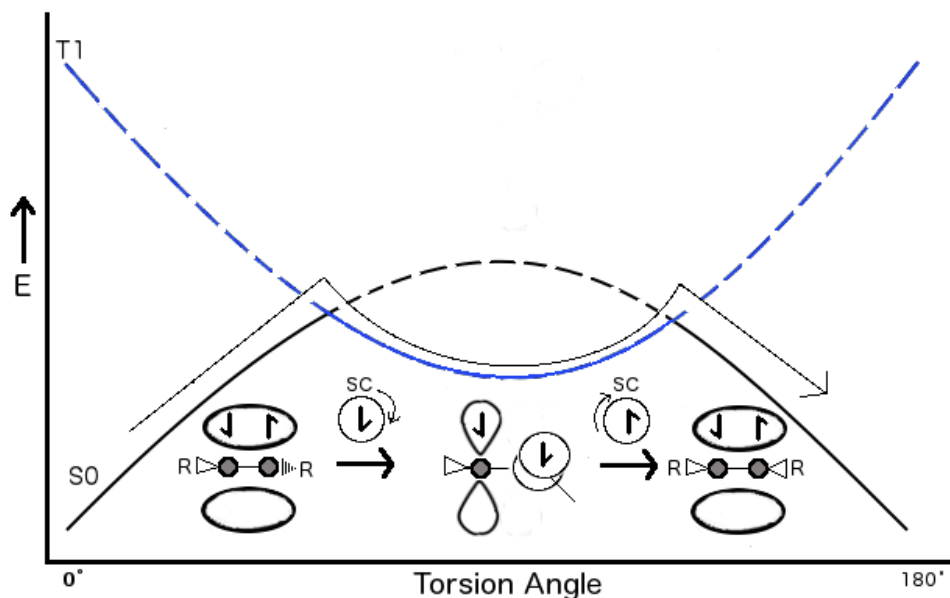


Fig. 2.1. Energy profile as a double bond is twisted from 0° to 180°. Top: the normal situation, in which the higher energy triplet state (T1) is inaccessible, and rotation proceeds only through the ground singlet state (S0); at 90°, the triplet state is effectively lower in energy, as the electrons with the same spin are out of plane. Bottom: when a spin catalyst (SC) is present, spin can change freely back and forth, and the lower energy pathway is available.

Nitric oxide is a pervasive biological messenger and cytotoxin, and since it is more persistent in solutions at low concentrations than its apparent reactivity would indicate, it is important to clarify whether or not it is a spin catalyst, and whether this could be part of its chemistry in solutions. As part of this investigation we have studied the interaction between nitric oxide and azo bonds (-N=N-) and compared them to the interactions with the olefin analog (stilbene) under tightly controlled conditions. Though very similar, there are key differences between the two systems: the energy of isomerization (azo bonds are more easily isomerizable), the presence of lone pairs on nitrogen in place of hydrogen (potentially allowing association through this lone pair), the mechanism of isomerization (azo bonds

isomerize either by rotation or by inversion, where olefinic bonds can only rotate), and the geometry of the *cis* conformer (*cis*-stilbene is planar and somewhat more sterically hindered, whereas *cis*-azobenzene twists into a 3-dimensional 'palm to palm' formation (Fig. 2.2)).¹³ Differences in how these two systems behave when exposed to NO can therefore help illuminate the mode of interaction.

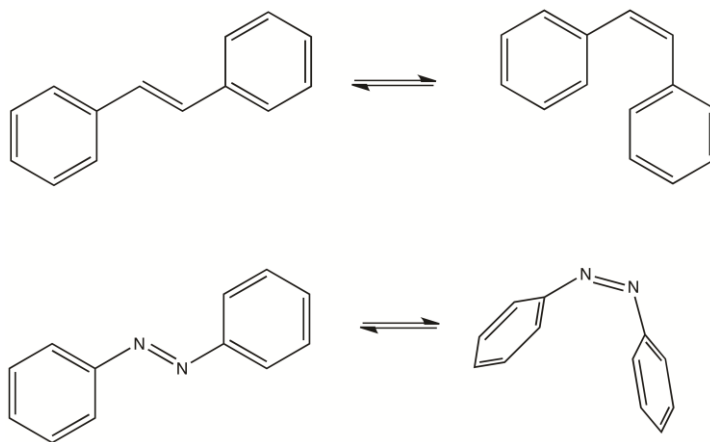


Fig. 2.2. Isomerization of *trans*-stilbene (top) and azobenzene (bottom).

The isomerization of diazo bonds in the presence of NO has not been previously described; NO was thus tested, in solution at room temperature and at low concentrations, on stilbene, azobenzene, and four derivatives of azobenzene, two soluble and two insoluble in water (Fig. 2.3). The results were then compared to DFT calculations to produce a tentative model of NO spin catalytic behaviour.

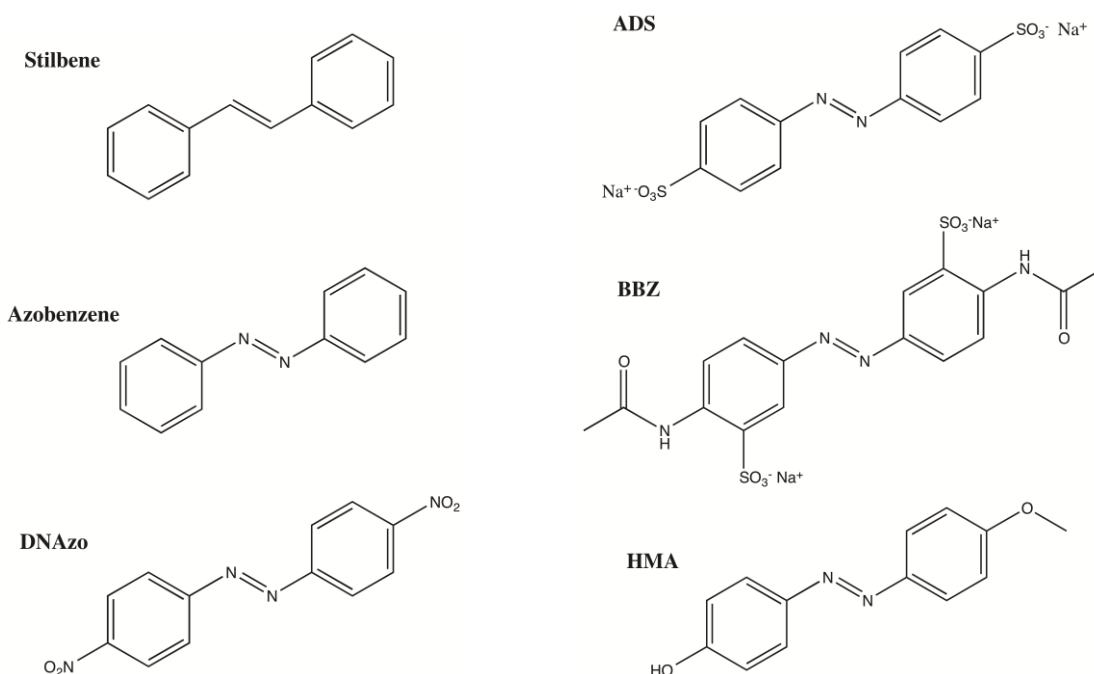


Fig. 2.3: The diazo derivatives used in the study. Left hand column, from top: stilbene, azobenzene, 4,4'-dinitroazobenzene. Right column, from top, 4,4'-azobenzenedisulfonate (ADS), 3,3'-bis-sulfonato-4',4'-bis-acetamidoazobenzene (BBZ), 4-hydroxy-4'-methoxyazobenzene (HMA).

2.2) Experimental:

The five diazo compounds are 1) prepared, and dissolved in appropriate solutions, 2) isomerized under UV light, 3) the test gases are prepared by two different methods, 4) the solutions are treated with these test gases, and then 5) the kinetics of the isomerization back to the original configuration are determined by UV-Vis spectroscopy.

1. Diazo Preparation: The five diazo compounds used (Fig. 3) were all prepared in house. *Cis/trans* stilbene and those reagents used to prepare the diazo substrates were purchased from Sigma-Aldrich.

Azobenzene: Method used by Hien et al was modified¹⁴. Aniline and two equivalents of sodium perborate are dissolved in acetic acid (2 g aniline to 50 mL acid) at 64°C. Solution quickly darkens to black. After 30 minutes, adding excess hexane extracts a red-orange product. Removing hexane and residual acid from product, then redissolving in hexane and recrystallizing gives a purified azobenzene (vivid orange, 35% yield). UV-Vis: (in hexane) 314 (major), 441 nm.

Azobenzenedisulfonate (ADS): Method used by Zhang et al. was modified¹⁵. Sulfanilic acid is dissolved in warm water with two equivalents of Na₂CO₃ (1 g sulfanilic acid to 12 mL of water works well). It is cooled in an ice-salt bath to below 0°C. A 15% NaOCl solution is added dropwise, about 1 every 3 seconds. An immediate colour change to deep orange should be seen. When addition is complete, the reaction vessel is left in a 4°C refrigerator for 12 hours, then filtered: the filtrate will be rich in the kinetic product (*cis*-ADS, which must be protected from ambient light if it is to be kept in this state) while the precipitate will be predominantly *trans*-ADS and side products. Dissolving in (or reducing to) the minimum water and adding ethanol or isopropanol will crash out the inorganic salt. Further two solvent recrystallization with water/THF or water/ethanol can separate the desired

dye from the more brightly coloured side product. A telltale test of purity is to leave a very dilute solution of the compound in a quartz vessel under 365 nm UV light for ~20 minutes: trace impurities in this reaction will begin to visibly fluoresce (if left under UV for >1 hour, photochemistry will also produce these fluorescent impurities). UV-Vis: 320 (major), 433 nm. NMR: ^1H : 7.883 (d), 7.826 (d).

3,3'-bis(sulfonato)-4,4'-bis(acetamido)azobenzene (BBZ):

Diaminobenzenesulfonic acid is dissolved in distilled acetic acid with one equivalent of acetic anhydride. Acetamido product precipitates, and is removed by filtration. Intermediate product is treated as in the procedure for ADS to create the rich orange azo-acetamido product. UV-Vis: 354 (major), 245, 445 nm.

4-hydroxy-4'-methoxyazobenzene (HMA): The method used by Amoros et al¹⁶ was modified. 4-anisidine is dissolved in 1 M HCl at 0°C (as well as possible), and equimolar NaNO_2 is added as an aqueous solution. This mixture is allowed to stir for 30 minutes. Meanwhile, equimolar phenol is dissolved in 1 M NaOH solution (phenol to NaOH molar ratio should be 1:2), and stirred. After 30 minutes, it is added dropwise to the first solution, and the two are stirred at 0°C for 1 hour. Solution is neutralized with 5% HCl, and product is filtered out (adding more water can help precipitate it). Desired

product can be separated with column chromatography, with a DCM eluent.

UV-Vis: 337, 355, 372 (major peak, vibronic coupling), 440 nm (shoulder).

4,4'-dinitroazobenzene: The dinitroazobenzene is synthesized by dissolving 4-nitroaniline in ethanol, cooling to 0°C, then adding 10% NaOCl solution dropwise and stirring for two hours. It is separated by column chromatography. UV-Vis: 336 (major), 446 nm.

2. Isomerization Protocol: All of the diazo species prepared undergo rapid isomerization from their thermodynamically favored *trans* form to the higher energy *cis*-form when exposed to low intensity UVA light. We found that 5-10 minutes of 365 nm light with a 7 nm half-width (emitted by a 18.4 W handheld UV lamp) was enough to achieve a steady state of approximately 70% *cis* (measured by NMR and confirmed by comparison to the UV spectrum of pure *cis*) for azobenzene, ADS, DNazo and BBZ, and close to 100% for HMA and stilbene. HMA, unlike the others, was found to have a profound solvent dependence; it isomerizes very slowly under 365 nm UV light in toluene, while in some polar solvents, such as ethanol, the *cis*-to-*trans* thermal return is on the millisecond scale. Ethyl acetate or THF were found to both allow easy isomerization while maintaining a slow, observable thermal return rate.

3. Nitric Oxide Preparation: Nitric oxide is delivered to the solution by either one of two sources.

Method A: A dipropylammonium salt of dipropylamine diazenium diolate (DPA-NONO, which breaks apart in neutral conditions into two equivalents of nitric oxide and two of dipropylamine), is prepared according to literature procedure.¹⁷ Stock solutions of 10 mmol/L DPA-NONO are prepared fresh in 0.01 mol/L NaOH solution on ice, and mixed as needed into a phosphate buffer (0.0029 mol/L K_2HPO_4 + 0.0073 mol/L KH_2PO_4 in water, ~ pH 6.8) 6 minutes prior to use. Aliquots of this solution are then injected via syringe, thus giving controlled and relatively high concentrations of NO in solution. Since the concentration of NO in solution depends on the partial pressure of NO in the headspace, the level of dissolved nitric oxide will slowly drop as the gas diffuses out of solution into the headspace. Thus measurements are made soon after injection, with a minimum of stirring or shaking.

Method B: A commercial sample of nitric oxide is injected with a gas tight syringe into a sealed and purged cuvette (filled with solvent) and agitated to dissolve the gas. NO_2 was purged from the gas stream by a packed column of potassium hydroxide; the gas was examined by IR spectroscopy for the presence of N_2O but this was determined to be present in only trace amounts. This method has the advantage of saturating the headspace with NO and thus maintaining the NO solution concentration over the long term, but the compressibility of gas allows for large differences when measuring small volumes, and reproducible results are more difficult to obtain; it was used for qualitative comparisons with experiments completed by Method A, and for the non-aqueous experiments (HMA and stilbene).

Control experiments for NO_2 and N_2O were also carried out:

Nitrous oxide: The gas was obtained from a Praxair cylinder. The solution to be tested was saturated with the gas.

Nitrogen Dioxide: To obtain NO₂ without significant NO, lead (II) nitrate is heated over a flame to produce the gas. Calculations are adjusted to account for the half equivalent of oxygen produced per 2 equivalents of NO₂.¹⁸

4. Solution Treatment: All solutions are purged of oxygen with vigorous bubbling under argon on ice (15 minutes for bulk (~10 mL solutions), 5 minutes for small cuvette samples (<2 mL); initial tests were performed by freeze-thaw-degassing the solutions, but this yielded the same results). Since acid is also known to catalyze *cis-trans* isomerizations, all aqueous solutions are adjusted to pH 6.8 with the phosphate buffer previously described; ADS and BBZ solutions are prepared in buffer only, while azobenzene is prepared in 50:50 acetone/buffer, HMA in ethyl acetate, DNAzo in 50:50 ethanol/buffer, and stilbene is dissolved in hexane. Dye solutions are placed in a gas tight quartz cuvette in a dark box and irradiated for 5 minutes with 365 nm light. DPA-NONO is mixed with a buffer and left to incubate for 6 minutes (just over 4.3 half-lives, until 95% has decayed), and the desired amount of this NO solution is injected into the dye cuvette once it has been transferred to the spectrometer. The cuvette is mixed, and the rate of isomerization is measured.

5. Measurement: The sample is placed into an HP 8453 Diode-Array UV-Vis spectrometer; it is protected from ambient light throughout the measurement time, and measurements are evenly spaced every 60 seconds at 0.5 second exposures over 30 minutes, to minimize the effects of the measurement on the rate of isomerization. The possibility of a back reaction due to photolysis during the UV detection was found to be insignificant (the difference in isomerization rate between a sample measured 30 times and one measured twice was found to be less than the calculated measurement error). All controls were subjected to the same measurement procedure. The changing absorption at the λ_{max} is plotted against time, and the rate constant is determined by a least-squares fit to a first order curve (catalyzed isomerization will be pseudo-first order). Error is reported as the standard deviation of a minimum of three repeated measurements, or as the error in slope derived from the variance between the data and the first order model, whichever error is larger.

NO₂ and N₂O control experiments were performed only in dry hexane solutions of azobenzene and stilbene, as well as ethyl acetate solutions of HMA. The gas is injected via syringe, and this is compared to equimolar injections of NO gas.

EPR measurements of the solutions after mixing were taken using a Bruker ElexSYS 580 X-band spectrometer, in an effort to detect any NO-azobenzene adducts; low temperature measurements were performed in a Wilmad low temperature dewar insert filled with liquid nitrogen.

To gauge the turnover capacity of NO, a 1.71 mM solution of azobenzene in toluene was purged, sealed, saturated with the test gas by injecting with 1 mL of pure gas at atmospheric pressure, and irradiated with 365 nm UV light for 17 hours. After this extended radiation the rate of *cis-trans* isomerization was measured by UV-Vis spectrometry and compared to the baseline thermal rate.

2.3) Theoretical methods:

All of the calculations were performed using Gaussian 03.¹⁹ Computations were carried out at the restricted Hartree-Fock (RHF),²⁰ and Density Functional Theory (DFT) levels. DFT calculations used the hybrid B3LYP functional and triple zeta 6-311++G** basis sets.^{21,22} The calculated molecular geometries were fully optimized and correspond to minima on the potential energy surface as confirmed by the absence of imaginary vibrational frequencies. All transition states were confirmed by reaction path (IRC) following calculations.

2.4) Experimental Results:

All -N=N- bonded molecules investigated showed increases in rate of isomerization when in the presence of NO, except for DNAzo. Stilbene did not respond under these conditions (Table 1). Control tests were performed with oxygen, dipropylamine, and nitrogen dioxide. Nitrous oxide was included in the tests with azobenzene and HMA, when it was observed that solvent polarity had a measurable effect (dipole moment of NO is 0.1595 D, vs. 0.166 D for N₂O and 0.289 D for NO₂).²³⁻²⁵

Table 2.1: Pseudo-first order rate of *cis* to *trans* isomerization of various species under different gas exposures.

Species	Conditions of Thermal <i>cis</i> to <i>trans</i> isomerization	k of CTI ^a s ⁻¹
Stilbene (28 μ M)	With oxygen	2.05(8) x 10 ⁻⁵
"	No oxygen	2.05(9) x 10 ⁻⁵
"	Dipropylamine	1.50(4) x 10 ⁻⁵
"	Nitric oxide (excess)	3.0(7) x 10 ⁻⁵
"	Nitrogen dioxide (excess) ^b	~2(1) x 10 ⁻⁵
Azobenzene (760 μ M)	With Oxygen	1.69(6) x 10 ⁻⁵
"	No oxygen	1.72(2) x 10 ⁻⁵
"	Dipropylamine	1.7(2) x 10 ⁻⁵
"	Nitric oxide (1 NO:2 dye)	1.81(7) x 10 ⁻²
"	Nitrogen dioxide (1 NO ₂ : 2 dye)	4.23(1) x 10 ⁻⁴
"	Nitrous oxide (large excess)	1.72(2) x 10 ⁻⁵
ADS (50 μ M)	No oxygen	1.9(2) x 10 ⁻⁵
"	No oxygen, in 50% ethanol	1.68(1) x 10 ⁻⁴
"	Nitric oxide (1 NO: 2 dye)	4.5(8) x 10 ⁻⁴
"	Nitric oxide (1 NO: 2 dye), in 50% ethanol	1.35(1) x 10 ⁻³
BBZ (50 μ M)	No oxygen	8.3(2) x 10 ⁻⁵
"	Nitric oxide (1 NO : 2 dye)	2.4(9) x 10 ⁻⁴
HMA (50 μ M)	In Ethyl acetate, No oxygen	3.94(2) x 10 ⁻⁴
"	In Ethyl Acetate, (1 NO: 2 dye)	1.16(6) x 10 ⁻²
"	In Ethyl Acetate, with NO ₂ (1 NO ₂ : 2 dye) ^c	3.29(3) x 10 ⁻²
"	In ethyl acetate, with ethanol (1 EtOH:2 dye ratio)	1.58(8) x 10 ⁻³
"	In ethyl acetate, with N ₂ O (large excess)	3.9(2) x 10 ⁻⁴
DNAzo (50 μ M)	No oxygen, 50:50 Ethanol/Water	1.04(1) x 10 ⁻⁴
"	Nitric oxide (1 NO :2 dye)	9.6(3) x 10 ⁻⁵
"	Nitrogen dioxide (1:2 ratio), in ethyl acetate ^c	1.7(4) x 10 ⁻⁵

a. Number in parentheses indicates the error in the last reported digit.

b. NO₂ injection confounds accurate measurement of stilbene isomerization via UV, due to overlap and possible side reaction, but the observed change is within the limits of error for the thermal rate.

c. The solubility of nitrogen dioxide in ethyl acetate was set to be that of NO in ethyl acetate, as the gases have similar solubilities in polar solvents.

Unsubstituted azobenzene responds most dramatically to the introduction of NO, and to a lesser extent NO₂. The substituted azo dyes appear at first glance to have had a meager response, but at slightly higher dose levels, they clearly show the same behavior, DNAzo excepted. Taking ADS as representative, we see: (Fig. 2.4) the spectrum of a 50 μ M sample at equilibrium (effectively 100% *trans*) and after 5 minutes of exposure to UV (69% *cis*), (Fig. 2.5) the same *cis*-enriched ADS exposed to 100 μ M NO, and (Fig. 2.6) a kinetic trace of the peak at 320 nm when exposed to a range of solvated NO gas concentrations.

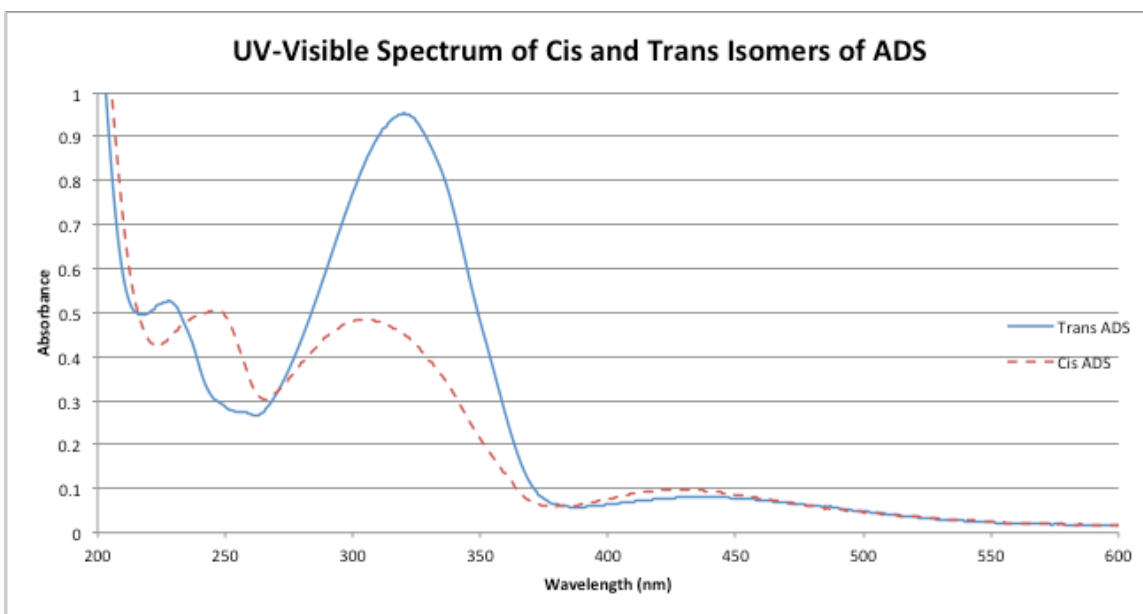


Fig. 2.4. UV-Vis spectrum of 50 μ M ADS in water, before and after UV exposure.

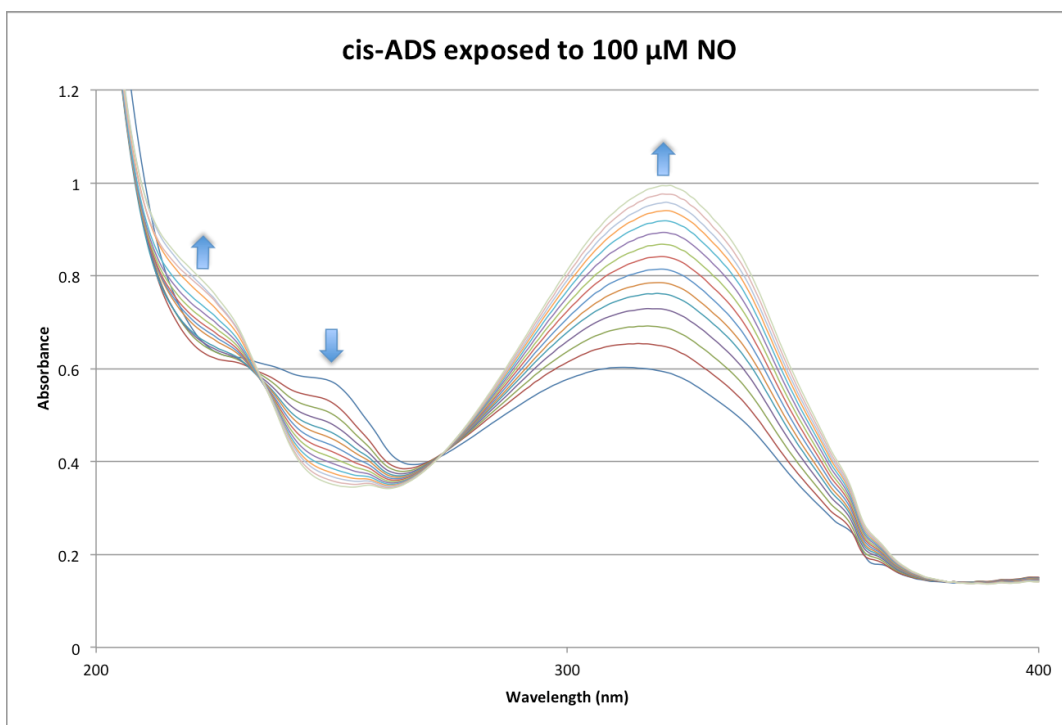


Fig. 2.5: UV-Vis of *cis*-enriched ADS after exposure to 100 μM NO. Measured over 15 minutes, every 60 seconds. Lowest signature at 300 nm is at time 0.

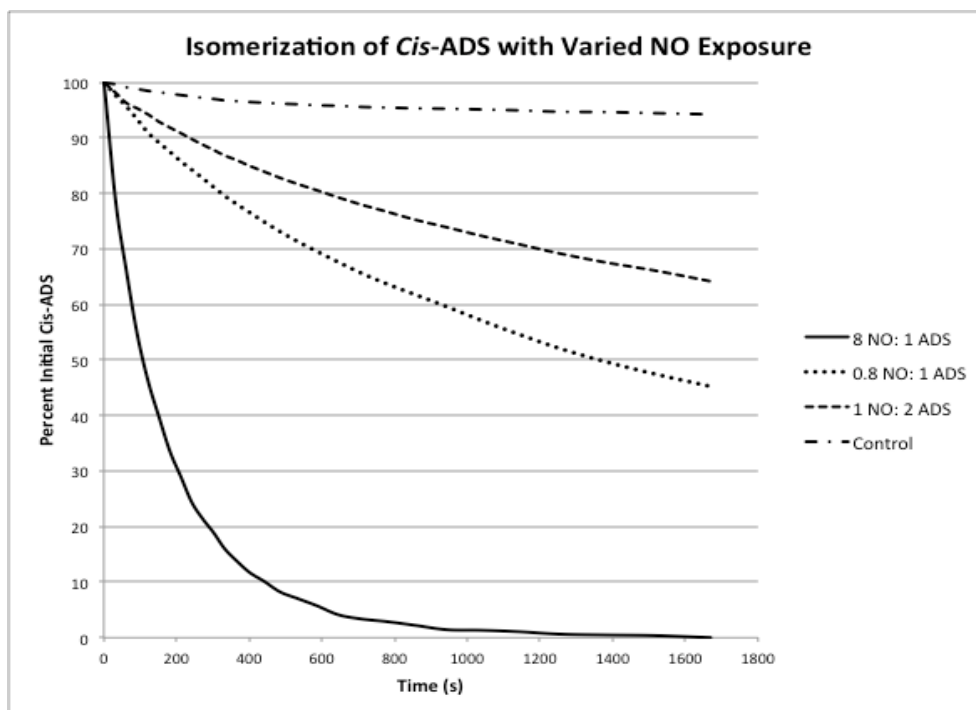


Fig. 2.6: Azobenzenedisulfonate (ADS) dye response to NO exposure in water (50 μM , 25°C).

The normal *cis-trans* thermal decay rate for ADS is a typical first order reaction, with $k = 1.9 \times 10^{-5} \text{ s}^{-1}$. The initial rates for the samples exposed to NO follow first order kinetics; the overall reaction is thus pseudo-first order. The generalized standard formula for reversible first order reactions (Eq 2.1) was used:

$$\ln ((A_t - A_\infty)/(A_0 - A_\infty)) = -(k_1 + k_{-1})t$$

Eq 2.1: Integrated reversible first order rate law.

Where A_t is the absorbance at time t , A_0 the absorbance initially and A_∞ the absorbance at equilibrium. A_0 and A_∞ were determined independently from the kinetics runs, as they were found to vary slightly with extended UV exposure. The back reaction k_{-1} is small enough that it can be neglected, as evidenced by the final steady state ratio of *cis/trans*, which is essentially 100% *trans*. The curves were fitted to this first order model using a least squares approach, and k was calculated at different dose levels. Plotting the logarithmic factor k versus time gives a linear dose/response curve (Fig. 2.7).

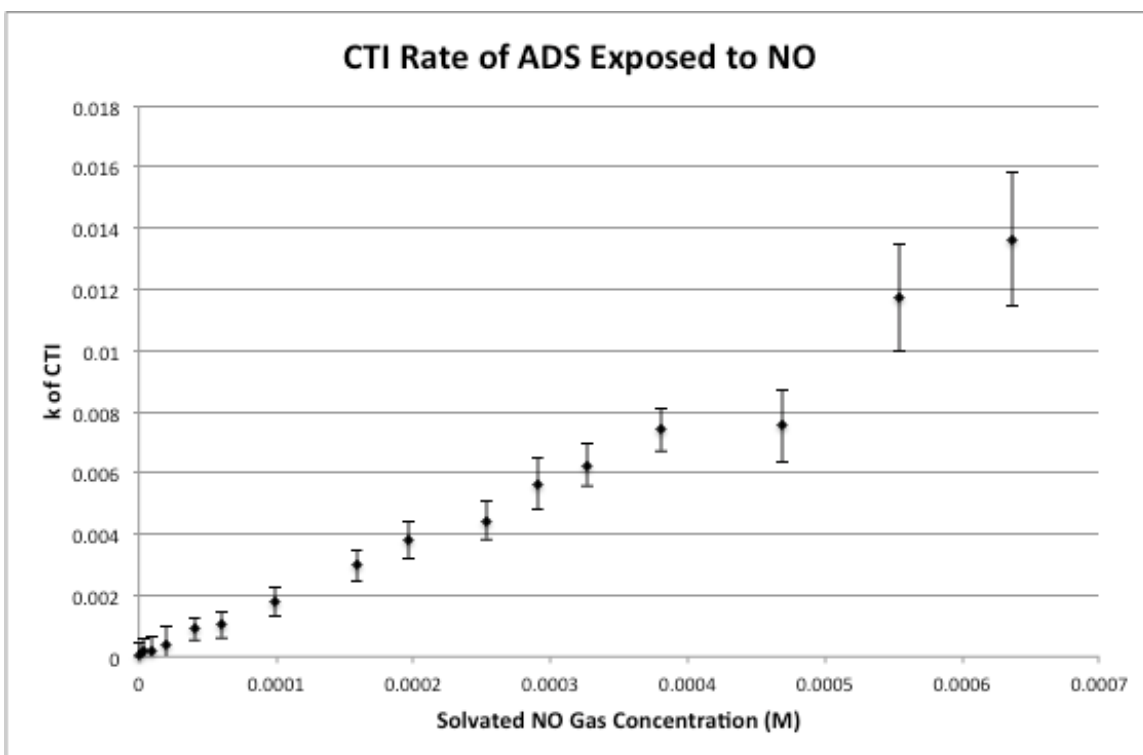


Fig. 2.7. Dependence of first order rated constants for *Cis-Trans* Isomerization (CTI) of ADS as a function of [NO]. Error bars represent 1 standard deviation.

Performing this operation for the three compounds in which a significant change was found, the second order rate constant (k) for the relation $d[\text{cis-Dye}]/dt = -k[\text{NO}][\text{cis-Dye}]$ was calculated:

$$\text{Azobenzene: } k_{\text{azo}} = 47 (\pm 4) \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$$

$$\text{ADS: } k_{\text{ADS}} = 18.1 (\pm 0.1) \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$$

$$\text{BBZ: } k_{\text{BBZ}} = 16.0 (\pm 0.6) \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}.$$

HMA is a special case, in that its isomerization can be provoked by the presence of certain solvents (ethanol, pyridine, dichloromethane, and water, for example). Ethanol has one of the most potent effects, so it was chosen for comparison with the gases, as seen in Table 2.1; NO_2 and NO can be seen to have a

greater effect than does ethanol, but the effect due to electronic interaction with the solvent cannot be distinguished from spin catalysis, and further kinetic determinations were not carried out for HMA.

Long-term irradiation tests were carried out to test whether catalysis decreases with time (i.e. due to NO consumption). The rate of *cis*-azobenzene formation when no NO is present can be estimated by measuring the amount formed in the first minute of exposure (true rate will be a first order process, so this will be an underestimation of the true rate at 100% *trans*), making use of Halpern's UV-Vis extinction coefficients²⁶ of the two isomers to gauge the concentration of each. This rate was found to be 1.4×10^{-7} moles of *cis* formed per minute, in a 1.72 mM toluene solution. The system was then treated with NO and exposed to 17 hours of continuous irradiation, which should allow 41.9 complete turnovers of all azobenzene present from *trans-cis* due to UV radiation (and *cis-trans* reconversion due to the presence of NO). After this period the rate of *cis-trans* isomerization was monitored by UV-Vis and was found to be the same as when the NO was first introduced. Azobenzene degrades with extensive UV exposure, showing the development of a broad undefined absorption band between its major ($\pi - \pi^*$) and minor ($n - \pi^*$) peaks, but a control sample demonstrated that these photoproducts do not interfere with the uncatalyzed rate of *cis-trans* isomerization, and presumably do not interfere with NO-mediated *cis-trans* isomerization.

EPR measurements of azobenzene/nitric oxide solutions show a weak anisotropic signal centered at 3493 G when frozen at -196°C, extending from 3460-3515 G. This shifts to an isotropic triplet at room temperature. This signal is

attributable to trace amounts of NO₂ trapped in solution. No other EPR signals are detectable.

2.5) Theoretical Results:

Table 2.2: Key Ground and Transition State Energies (B3LYP/6-311++G) for Azobenzene and its NO adducts**

	Cis	Trans	Δ
GS + NO	A -702.815283	-702.8397537 G	15.36
Adducts	C -702.816978	-702.8188314 E	1.16
Tstate to adducts	B -702.810431	-702.815107 F	
Tstate between adducts		-702.80503 D	

Energies are given in Hartrees except for the differences, Δ, which are given kcal/mol. Letters correspond to geometries shown in Figure 2.8 and Table 2.3.

To model the possible mechanisms for the observed spin catalysis, DFT calculations (UB3LYP/6-311++g**) were performed for the most likely ground and transition states for nitric oxide interacting with azobenzene. The absolute gas phase energies for the stationary points are collected in Table 2 with letters **A** to **G** given to the successive points in the *cis* to *trans* isomerization. The relative energies (in kcal/mol) and their relationships are diagramed in Figure 2.8, and information about the key metric parameters are collected in Table 2.3.

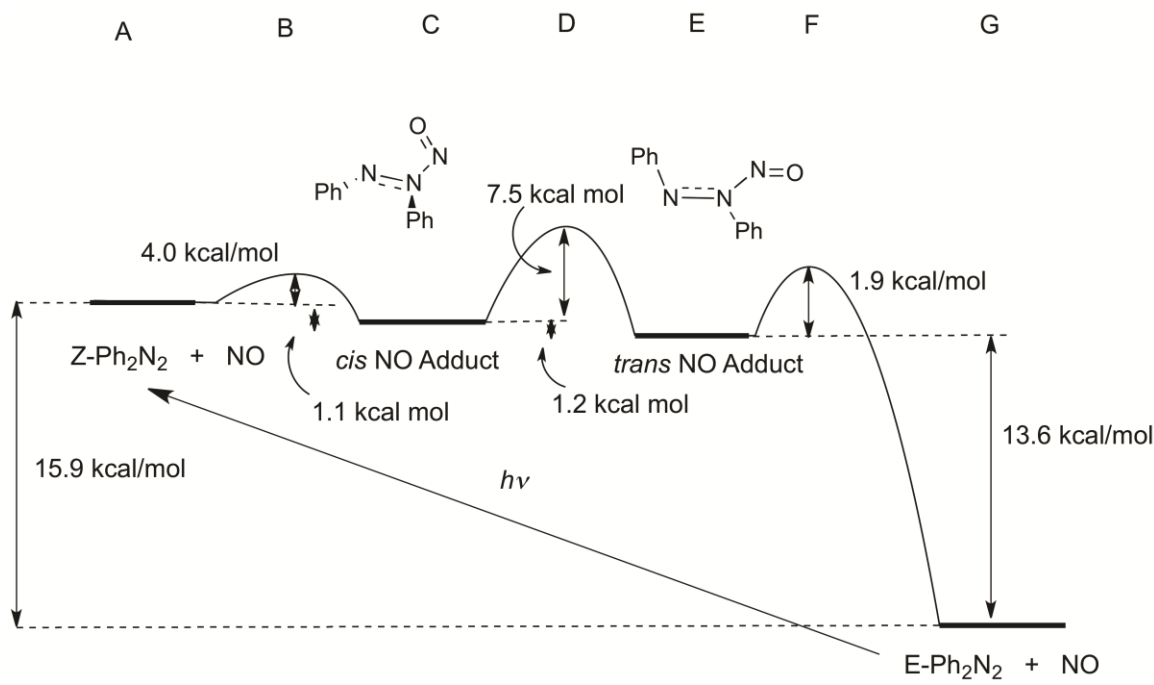


Fig. 2.8 : Relative gas phase energies for the ground states and transition state present in the NO catalyzed isomerization of azobenzene (*cis* isomer is labeled Z-Ph₂N₂, *trans* is E-Ph₂N₂).

2.6) Discussion:

That nitric oxide catalytically converts *cis*-azobenzene to *trans*-azobenzene is unequivocal. The conversion of *cis* to *trans* occurs rapidly on exposure to NO, and further irradiation will not produce a population of *cis*-azobenzene. In a prolonged test, azobenzene treated with NO was afforded complete immunity to UV light (that is, *cis* reconverts to *trans* as quickly as it forms) for 17 hours. Purging the solution with argon to remove NO restores normal functionality, and *cis*-azobenzene can develop at its original uncatalyzed rate. Were this the result of a typical chemical reaction which consumes one mole of NO for each mole of azobenzene transformed, this would have required, at minimum, the use of 351% more nitric oxide than was injected. Though catalysts are typically used in much lower concentrations than

their substrates, the necessity of using low concentrations of dye for measurement made it impractical to handle even lower concentrations of NO; nevertheless, this system fulfills the definition of catalysis in how NO accelerates reactions without itself being consumed, and it is still effective in sub-stoichiometric amounts.

Though continued UV exposure will eventually cause the dye to break down, regardless of the presence of NO, it is found to be stable throughout the 30-60 min interval of these experiments.²⁷ Careful examination of the system by UV-Vis and NMR before and after short term UV and NO exposure reveals no side products, either from organic decay or the formation of nitrites, nitrates, etc. Attempts to observe the interaction of NO with azobenzene by freezing a solution of *cis* with injected NO and measuring the resulting radical shift under EPR showed no new signal, which is consistent with free nitric oxide; the presence of a signal would suggest NO interaction with another molecule (due to a change in the radical's symmetry). IR of the headspace gas detects no change in composition (production of N₂O₃ or NO₂, for example). Litchfield *et al.* suggested that the spontaneous formation of NO₂ in NO injections is the active principle for CTI catalysis, but in our case, the greatly reduced response of azo bonds to injected NO₂ rules this out.⁵ Furthermore, NO₂ has a distinctive spectrum under UV, and when both nitrogen oxides are present with dipropylamine, they are known to react to produce nitrosamines (through the intermediate formation of N₂O₃), whose derivatives usually produce strong peaks in the 230 nm and 350 nm region, but these were not observed. A weak signal attributable to NO₂ was seen under EPR, but given the extreme sensitivity of this technique this is likely no more than a trace. We are thus confident

in ruling out an interaction between NO and NO₂ as being responsible for the catalysis, and attribute it solely to NO.

Mode of NO Association: If nitric oxide is associating with, but not permanently bonding to the N=N moiety, how can this association be modeled? Spin catalysis may proceed by outer sphere like associations, in a mechanism akin to Eyring's sticky collisions.²⁸ In this case transient structures and intermediates would dominate and direct the reaction pathway, but allow for the key *cis* to *trans* isomerization. This interaction would be similar to the way in which solvents are thought to interact with molecules-- weakly and transiently-- but with the added possibility of spin exchange.

Alternatively, an inner sphere like mechanism may operate, without necessarily involving spin catalysis, where discreet but weak bonds reversibly form between the nitric oxide and the diazene. This mechanism is similar to how thiyl radicals are proposed to catalyze E/Z isomerizations in lipids.²⁹

Any proposed mechanism must account for the observation that in the EPR no observable intermediates build up or are trapped out in the course of the reaction. Any adducts that do form do not accumulate to detectable levels by either EPR or UV spectroscopy. Thus the NO + diazene adduct equilibrium should be reversible and rapidly established, and also not particularly favor the adduct formation. Between an outer sphere or inner sphere reaction, the latter is well poised for modeling by modern density functional ab initio calculations, and the results of these are shown in Figures 2.8 (above) as well as in Tables 2.2 and 2.3.

Theoretically, both *cis* and *trans* azobenzenes form weakly stabilized adducts with NO, structures **C** and **E** in Table 2.8, shown in 3D in Fig 2.9 below.

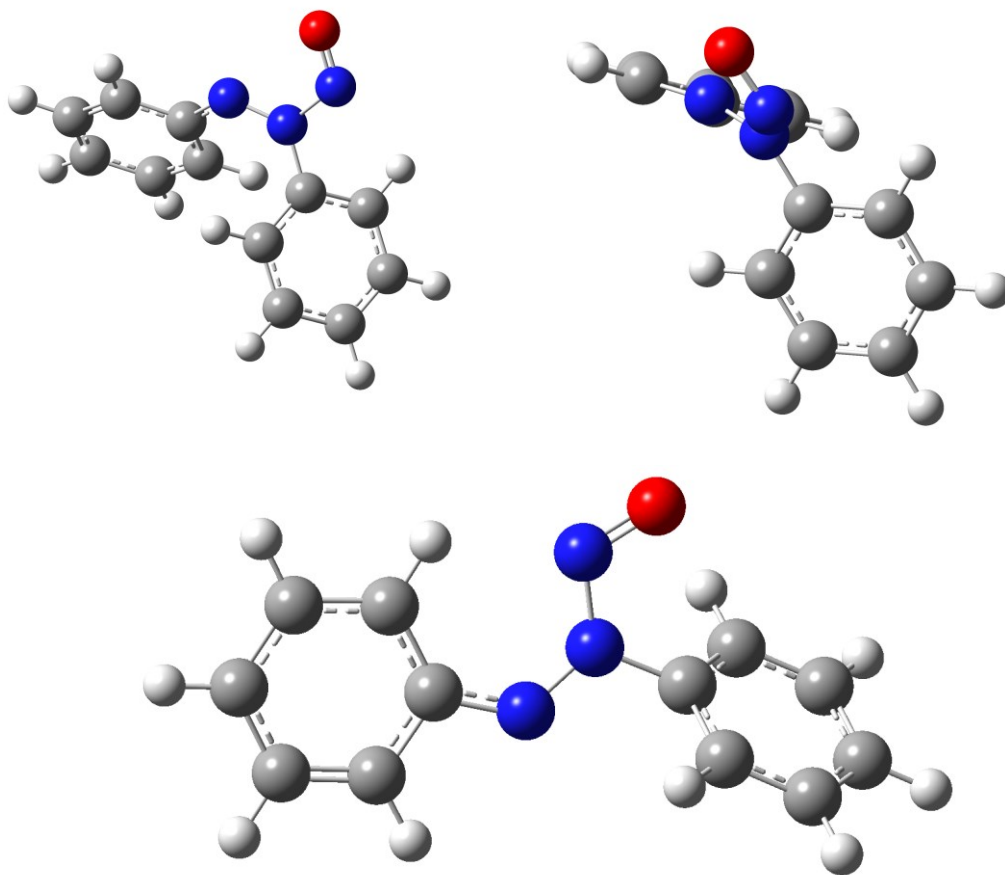


Fig 2.9: Model of possible NO association with azobenzene: (Top two) in the *cis* form (structure **C** from Fig 2.8), (bottom) in the *trans* form (structure **E** from Fig 2.8).

Both adducts offer only ~ 1 kcal/mole of electronic stabilization and the barriers that separate them from *cis* and *trans* azobenzene, **B** and **F** are very low (2-3 kcal/mole). The crucial features in this scheme are the final loss of NO from the *trans* adduct **E** which favors the free diazene by 13.6 kcal/mole and the highest barrier **D** in this system, 7.5 kcal/mole, is the critical Z to E isomerization in the

adduct. Although these calculations are for the gas phase and are not zero point corrected they suggest that an inner sphere mechanism is possible.

Given the energies of isomerization and association given in Figure 2.8, it is possible to estimate the expected reaction rate for this mechanism. Using the Arrhenius equation ($k=Ae^{-E_a/RT}$) for the known isomerization of azobenzene ($E_a \sim 150$ kJ for a *cis-trans* isomerization, $k=1.72 \times 10^{-5}$) to obtain the pre-exponential factor A, then applying this to the isomerization of the Azo-NO adduct C ($E_a= 31.38$ kJ) one obtains $k= 3.38 \times 10^{21}$. Clearly such a reaction should occur almost instantaneously, and it must be the association of NO with the azobenzene that limits the reaction. However, modeling the collision frequency by the equation:

$$\text{Rate} = d^2\pi(8kT/\pi\mu)^{1/2} (n_A n_B/V^2) e^{-E_a/RT}$$

Eq 2.2: Gas phase collision model for NO and azobenzene.

Where d is the average diameter of the two molecules (volume expressed as a sphere, azobenzene = $249 \text{ \AA}^3$, NO $\sim 36 \text{ \AA}^3$), k is the Boltzmann constant, μ is the reduced mass of the two molecules, n_A and n_B are the number of each species in a volume V (1 L) of liquid, and E_a is the activation energy for adduct formation given in Fig 2.8, in joules. The result is found to be 6.22×10^{11} , which is still far in excess of what is seen. While a solution phase reaction will be somewhat slower than modeled here, this suggests that NO does not form adducts nearly as easily as the models suggest, and this casts some additional doubt on the inner sphere mechanism.

The intermediates in Figure 2.8 are similar to some of the theoretical results that De Mare found for the photosensitized $^4\Pi$ NO isomerization of 2-butene.^{7,8} In particular the excited state of NO adds to the olefin to give an adduct similar to **C**. Unlike the diazene results in Figure 2.8, De Mare also proposed that $^4\Pi$ NO can add to the olefin to give highly active cyclic nitroxide-like intermediates such as **I**, for which the diazene-like analogue would be **H** (Fig 2.10).

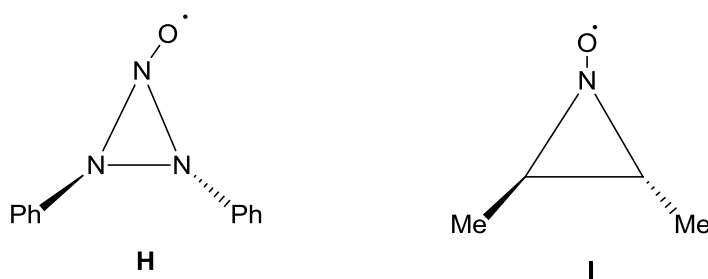


Fig 2.10: Possible cyclic NO-Azo CTI intermediate (**H**), compared to De Mare et al.'s proposal for the olefin intermediate.

A stable stationary state with a geometry like **H** has been theoretically located with the basis set and methods used in this paper but the resulting radical is 54 kcal/mole higher in energy than the adduct of NO and *trans* azobenzene. This energy makes these triazene oxide intermediates like **H** very unlikely in these conditions. However if this reaction were photosensitized, then radicals like **H** may have a role in that chemistry.

Table 2.3: Metric Parameters Calculated for Azobenzene and its NO adducts.^a

Structure ^b	N-O (Å)	N-NO (Å)	N-N(Å)	C-N (Å) ^c	O-N-N (°)	N-N- N(°)	τ N-N- N-O(°)	τ C-N- N-C (°)
NO	1.1481							
Cis GS	-	-	1.24345	1.43606	-	-	-	9.30178
B (Z TS)	1.15973	1.90016	1.25049	1.41609 1.41157	107.35	112.22	-4.29	-17.09
C (Z·NO)	1.19396	1.44864	1.31773	1.43511 1.37918	113.84	117.36	-9.96	-34.5
D (Z/E TS)	1.21393	1.36704	1.41491	1.43385 1.34846	115.67	113.17	168.15	-97.96
E (E·NO)	1.21875	1.39828	1.32077	1.45103 1.37660	114.05	123.78	176.20	177.34
F (E TS)	1.17679	1.67542	1.29081	1.43000 1.38651	112.35	122.23	164.36	-177.62
Trans GS	-	-	1.25219	1.41927	-	-	-	180
H Cyclic Radical	1.228721	1.43970 1.45430	1.49637	1.43580 1.43670	125.29 125.10	61.32 ^d	117.08	145.83

a. All values were calculated with Gaussian 2009 with B3LYP Density Functional Theory and 6-311++g** basis set.

b. Letters correspond to structures in Figure 2.9 and in Figure 2.8 with results for NO and *cis* and *trans* azobenzene. GS is the ground state structure.

c. Where two values are listed the longer is for the phenyl on the NO bearing nitrogen.

d. N-N(O)-N angle. That is, the acute angle at the NO between the two diazene nitrogens.

Thus in theory, NO may form a transient association with the lone pair of one nitrogen in the N=N bond, placing it close enough to the double bond to effect a spin transfer.

Mechanisms of N=N Bond Isomerization: To completely understand the pattern of NO_x activity discovered here requires an understanding of the mechanism of azobenzene isomerization; unfortunately, there is still controversy around this issue.³⁰⁻³⁷ It is thought to proceed either by rotation around the N=N axis, or by inversion, in which one nitrogen will rehybridize to *sp*, putting its lone pair into a *p* orbital and thus becoming linear; both pathways may compete, or even combine. Several points argue for rotation: for example, the degree of electron donation from benzene ring substituents is known to lower the barrier to isomerization, while theory expects it to raise the barrier to inversion (which would otherwise be the expected isomerization mechanism in the ground state). Push-pull systems (one donating, one withdrawing group) weaken the double bond and are known to accelerate isomerization, which supports a rotation mechanism. It has been suggested that the solvent chooses the mechanism: polar solvents allow rotation by stabilizing intermediates, whereas inversion would be expected in a non-polar solvent.³⁸ Early work by Rau *et al.*³⁴ suggests that energy is the deciding factor: they associated rotation with the S₂ ππ* transition, while the inversion comes about from the S₁ state, a spin-forbidden nπ* transition which makes use of the lone pair.

Ring-locking and steric hindrance can be used to make rotation impossible, and isomerization will still occur; most researchers conclude from this that

inversion is the dominant mode. However, Cembran³³ *et al.* point out that if this were true, then stilbenophanes would not isomerize, since both inversion *and* rotation would be impossible for them; they argue that the inversion pathway actually necessitates some rotation, and the two states actually mix to some degree. On consideration, it makes sense that molecular motion would not be rigidly confined to certain modes, but that the molecule can sample large regions of the potential energy surface with its different vibrational modes that will allow it to exploit the lowest available path. In their calculations, the lowest energy isomerization is by the short-lived and commonly ignored S₀-T₁ triplet pathway, involving rotation and the $n\pi^*$ transition coupled with an intersystem crossing (thus creating a long lived intermediate in which the π bond is weakened by the electron in the π^* orbital, and thus is more easily twisted). Spin-orbit coupling is calculated to be significant enough to make this viable, due to the high electron density on the nitrogen centers, and the modeled energies match up well with experiment.

Proposed Model: There are four key results of this research which bear on the possible mechanism of catalysis:

1) Nitric oxide is an order of magnitude more catalytically active than NO₂ for azobenzene, but slightly less effective for HMA (which has electron donating substituents). Neither is effective for azobenzenes with strongly electron withdrawing derivatives. Note that NO has a more available unpaired electron (based on an ionization potential of 9.25 eV, compared to 11.7 eV for NO₂³⁹); this

electron resides in the π^* orbital and hence is delocalized over the molecule. NO_2 , by contrast, has its unpaired e- localized on the nitrogen in a non-bonding orbital.

2) NO *cis-trans* catalysis is highest for azobenzene, less so for derivatives with moderately electron donating groups and moderately electron-withdrawing substituents, and ineffective for those with strong electron-withdrawing groups.

3) Provided that CTI is possible, NO is more effective in less polar solvents (as seen in Table 2.1, ADS undergoes a three-fold increase in CTI rate in 50% ethanol vs. pure water), which cannot be fully explained by a difference in NO solubility. Note that ethanol is also a protic solvent, which Kessler⁴⁰ suggested should *slow* thermal isomerization by tying up the lone pair with H-bond interactions.

4) No side products or signs of intermediates are detected, not even in EPR at liquid nitrogen temperatures.

Taken together these results suggest a catalytic mechanism whereby NO first interacts with the diazene non-bonding nitrogen lone pair. This is an extremely weak outer sphere transient interaction, in which the proximity to the -N=N- double bond nevertheless allows a spin transfer, and hence the bond can undergo a $n\pi^*$ transfer into the lower energy (in the twisted intermediate) T1 state (in preference to the S1 state). Whether the promotion to the T1 state is then followed by rotation about the weakened π bond or inversion by rehybridization of the single remaining electron is unclear, but the slightly increased activity in less polar solvents, which

cannot stabilize polar transition states and hence are thought to favor non-polar transition states, suggest that it may proceed by inversion. Substituents that donate electron density interfere with this process, as that density partly occupies the π^* orbital. Electron withdrawing species, however, delocalize the lone pair into orbitals with considerable arene ring character, thus making them inaccessible to NO_x interaction. The difference between NO and NO_2 activity is perhaps a question of steric effects. The HMA system, and the rough parity of activity for NO and NO_2 , suggests some interesting alternative interpretations (i.e. the more positively charged N of NO_2 may be better able to associate with the partially filled π^* of HMA, or the transition state of HMA may be energetically more similar to the non-bonding radical that NO_2 carries) but this estimation is too crude to make firm conclusions.

In contrast, stilbene is unaffected by NO under these conditions. Olefinic bonds isomerize only via a rotation and lack a localized lone pair (although it has been recognized for some time⁴¹ that rotation can occur through either a singlet or triplet state, in much the same pattern as azobenzene), and this supports the interpretation that NO catalysis proceeds by lone pair association. Plachkevitch⁴² et al. have calculated that, in theory, nitric oxide should spin-couple to this system and help it proceed via the triplet pathway. The fact that no effect is seen (not even the acceleration of a glacially slow to a very slow process) suggests that the mechanism of interaction is fundamentally different, and that either gas phase conditions, high temperatures, or high concentrations are needed to promote olefin CTI catalysis. Perhaps this involves another intermediate NO_x species, such as a dimer. There is evidence⁴³ that at higher temperatures, NO catalyzes olefin isomerization by formal

electron transfer mechanisms, which would generate transient charge separated species.

Conclusion:

Although nitric oxide has complicated reactivity patterns that reflect its accessible redox potentials as well as its electrophilicity,⁴⁴ we have shown that it is a surprisingly robust *cis-trans* isomerization catalyst for diazenes. Previous research into its spin catalytic quality has focused, understandably, on the gas phase, where nitric oxide is most commonly found in the laboratory and in industry. But this study has demonstrated that it maintains this behavior in solution, even in water, and can act to isomerize double bonds to a significant degree at low concentrations. Furthermore, it does so quite well with azo bonds, a previously unreported effect. Though the integrity of azo bonds specifically is not a concern in much of biochemistry, there are numerous and growing applications for diazenes in biomedical probes and materials. Any application of these materials to physiological conditions with even a minor nitric oxide flux needs to consider these findings.

Indeed, there are many other applications of diazenes, and questions about the stability of these materials in the presence of NO (as an atmospheric pollutant for example) needs to be considered as well. Diazenes are used extensively in organic chemistry as stereospecific electrophiles and oxidants.⁴⁵ Furthermore, the unique facile E/Z structural photo-isomerism of diazenes has led to many creative uses, for example in fuel cells,⁴⁶ fuel additives,⁴⁷ liquid crystals,⁴⁸ non-linear optical

materials,⁴⁹ anti-retroviral (HIV) drugs,⁵⁰ antibiotics,⁵¹ and anti-fungal agents.⁵² Diazene interactions with the GST family of enzymes⁵³ has led to their incorporation into other drugs, such as chemotherapy treatments.^{54 55 56 57} In all of these situations, potential spin catalyzed isomerization by low concentrations of nitric oxide will interfere or modulate their function.

A particularly intriguing biochemical consequence of these findings is that nitric oxide may qualify as a cofactor for enzymatic activity. Enzymatic transformations which generate triplet intermediates or progress through triplet excited states would also be facilitated by this type of “spin cofactor”. Although applied magnetic fields are able to alter the kinetics of these types of processes^{58,59} albeit to only a modest degree, nitric oxide's reversible Lewis acidity allows it to introduce spin into enzymatic active sites to a much higher degree. When this feature is combined with its near universal permeability to all organelles and cells, along with its being a compact diatom, it suggests there may be a large array of possible enzymes in which it could be such a cofactor.

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Chapter 3: Organic Solutions of Dinitrogen Trioxide

Dinitrogen trioxide is most commonly encountered as the vivid (and often alarming) azure blue condensate in liquid nitrogen cold traps when one has been working with nitric oxide on a vacuum line. It forms by the combination of NO and NO₂, and at normal terrestrial conditions it melts and quickly boils away; Mason¹ notes that N₂O₃, if it is kept in a sealed container and thus can achieve equilibrium, is 80% dissociated into NO/NO₂/N₂O₄ at room temperature. However, she also noted in her 1959 work that N₂O₃ can be stabilized by various solvents, particularly toluene, and she made measurements as to the degree of dissociation at low temperatures. This would have come as no surprise to Freiburg and Mandel², who as far back as 1890 had had some success in dissolving 'nitrous anhydride' in carbon disulphide, and reacting it with a handful of other organic molecules, obtaining mostly nitration products. Addison et al. had also noted³ that dissolving some NO in liquid dinitrogen tetroxide (creating, in effect, N₂O₃ dissolved in a solvent of N₂O₄) greatly enhanced the reactivity of the solvent towards zinc metal. Following Mason's work, A.J. Vosper published several articles⁴⁻¹⁵ concerning dinitrogen trioxide as a stable substance when dissolved in organic solvents, and he spent the better part of the 1960s and 1970s elucidating the composition of these solutions, noting that they consisted of a variable equilibrium between dinitrogen trioxide and dinitrogen tetroxide. In his last publication on the subject, he used them as a reagent for the nitration of primary and secondary amines, performed at -85°C, with some success, and promised that other reactions would be described at a later date (these were

either never published or never written). Though this research established that dinitrogen trioxide could be handled as a reagent in solution, the matter was never pursued, and his work remains largely uncited; a few papers have received a handful of mentions, often for tangential reasons, and the others have not been cited at all. Perhaps because of dinitrogen trioxide's mercurial nature (it can easily become gas or tetroxide depending on conditions), these solutions have never found a use or been given an adequate exploration. N_2O_3 has been studied in theory¹⁶, on surfaces¹⁷, and there is abundant work done on it in aqueous solutions as nitrous acid^{18,19}, but seldom are organic solutions mentioned. A group of pharmacists in Okayama came across the phenomenon of organic solvents trapping N_2O_3 in 2009, and they used it to acetylate (via nitrosylation) a guanosine derivative²⁰, but gave the matter no closer chemical scrutiny. Other groups have nitrated alcohols by bubbling NO into organic solutions²¹, or indoles by forming nitrous acid in benzene²², but the idea of forming organic dinitrogen trioxide solutions explicitly has become a piece of chemical arcanum.

In the course of experimentation I have rediscovered this phenomenon and expanded upon this research. What would normally be a somewhat exotic and unstable oxide of nitrogen, most often a transient intermediate, can in truth be prepared quickly and reliably using only basic laboratory materials, affording the researcher the use of a surprisingly versatile chemical agent. Dinitrogen trioxide solutions are solvatochromic and (contrary to some past results) thermochromic when at warmer temperatures, and can deviate substantially from Beer's law. Furthermore, they can be prepared in high purity even at 0°C, and by dint of

supersaturation, remain at high purity even at room temperature or above. Since these solutions are prepared in aprotic media, they can perform functions that would not be possible in the standard aqueous nitrous acid solutions. In the chapters to follow I will discuss their chemical reactivity with a suite of standard organic reagents (chapter 4) followed by an exploration of some select inorganic reactions (chapter 5). This chapter will serve as a discussion of their properties as well as a guide to produce, analyze, and handle these solutions.

Except where otherwise noted, 'trioxide' will denote dinitrogen trioxide, and 'tetroxide' will refer to dinitrogen tetroxide.

3.1. The Composition of Trioxide Solutions

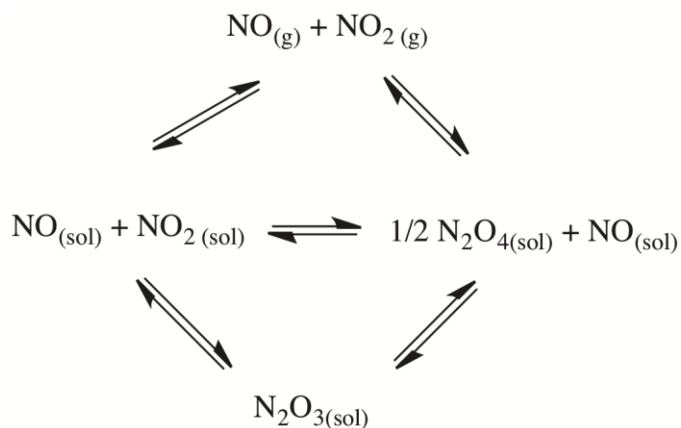
Chemists understand that the notion of purity is a theoretical idea, not a reality, and this is never more true than with dinitrogen trioxide. Composed of two gases notorious for their variable speciation, a solution of dinitrogen trioxide can potentially also contain solvated nitrogen dioxide (NO_2), nitric oxide (NO), dinitrogen dioxide (N_2O_2), dinitrogen tetroxide (N_2O_4), and dinitrogen pentoxide (N_2O_5). Furthermore, the nature of the molecule is such that contamination is impossible to fully rule out; where a symmetric species composed of identical parts has few opportunities to be other than what it is, an asymmetric species joined by a long labile bond can always disproportionate into two different species; that is, $\text{O}_2\text{N}:\text{NO}_2$ can only give more tetroxide, while $\text{ON}:\text{NO}_2$ is always potentially $\text{ON}:\text{NO}$ and $\text{O}_2\text{N}:\text{NO}_2$. Lastly, it is known that the trioxide has an isomeric form with C_{2v} symmetry ($\text{O}=\text{N}-\text{O}-\text{N}=\text{O}$ in place of $\text{O}=\text{N}-\text{NO}_2$) that can form when exposed to certain

wavelengths of light²³, at least within cold temperature matrices. Thus dinitrogen trioxide can only be said to be 'functionally pure', in that it behaves in one specific way chemically speaking. Nevertheless, we can go a long way to saying that a given solution, at the moment, is essentially the trioxide.

Fortunately, two components can be ruled out as being significant: the N_2O_2 dimer and the pentoxide. The former is a volatile gas at the working temperatures, which while an important intermediate in a lot of nitric oxide chemistry, is typically considered to exist in vanishingly small quantities at any given instant, except at extremely low temperatures (N_2O_2 mp: -163.67°C , bp: -151.8°C)²⁴. Of course, given that a supposedly volatile molecule like N_2O_3 is found to be stable in organic solutions, it is possible that the NO dimer is as well; still, rigorous solution studies of the dimer²⁵ and its asymmetric red form ($\text{O}=\text{N}-\text{O}=\text{N}$)²⁶ conducted at 77 K have thus far not turned up any anomalous solution based stability. Perhaps it has an expanded role in the chemistry of these solutions, but there is no evidence that it is a major role. Meanwhile, the pentoxide is a solid at room temperature, and while it could conceivably form from a surfeit of NO_2^+ reacting with transiently formed NO_3^- (two possible products of the self-ionization of N_2O_3 and N_2O_4 , respectively), electrochemical studies²⁷ of both trioxide and tetroxide solutions²⁸ find that there is negligible amounts of such activity, and it can be dismissed as an important species. Thus, trioxide solutions can be said to consist of NO, $\text{NO}_2/\text{N}_2\text{O}_4$, and N_2O_3 itself.

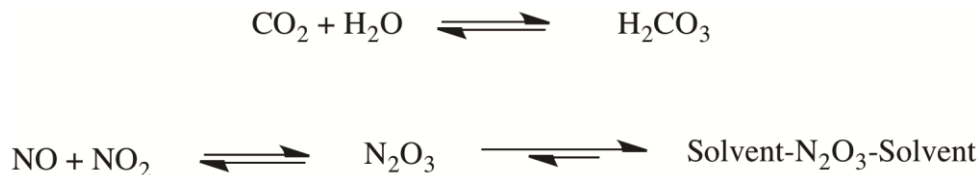
Another point that must be understood at the outset, which is always true but becomes frustratingly clear with trioxide solutions, is that the substance cannot be considered in isolation from its system: specifically, the headspace above the

liquid must be taken into consideration. Since NO, NO₂, N₂O₄ and N₂O₃ can all pass into the gas phase, and the level of NO in solution depends on the partial pressure of the atmosphere (by Henry's law), two identical trioxide solutions in two different vessels will soon obtain two different concentrations. These solutions exist as a complex set of equilibria (Eq 3.1), and failing to consider one phase can lead to serious error.



Eq 3.1: The significant equilibria of the solvated trioxide system.

Furthermore, it is not merely that N₂O₃ can be found in solution, but that it can be found in high concentration. An apt way to understand these mixtures is as super-saturated nitric oxide solutions, much the way that carbonated beverages are super-saturated carbon dioxide solutions (Eq 3.2). Both can be driven into their solvated form by higher pressures, and both can be further stabilized in that form.



Eq 3.2: Super-saturated solutions of carbon dioxide and nitric oxide.

Carbon dioxide would not be very soluble in water but for its ability to form carbonic acid. High pressures of CO_2 drive this reaction forward; a release of the pressure allows the gas to slowly reform and bubble back out of solution, just as a carbonated beverage fizzes when opened. The carbonic acid serves as a reservoir of CO_2 that is slowly depleted; shaking, stirring, or adding nucleation sites (such as the infamous 'Mentos in a Pop Bottle' experiment) can deplete this reservoir more rapidly. Similarly, nitric oxide normally has a fairly low solubility in organic solvents²⁹, but when it has nitrogen dioxide to interact with, it can be held as N_2O_3 , which has a higher solubility. Additionally, the solvent stabilizes the trioxide, such that even modest partial pressures of NO can accumulate as N_2O_3 . Releasing the pressure will eventually deplete the N_2O_3 , but just like beverages, these solutions also take some time before they go 'flat'.

Thus the breakdown of a trioxide solution can be stymied by keeping the atmosphere above it suffused with nitric oxide, maintaining the equilibrium. Kept in this way, trioxide solutions can theoretically be kept intact indefinitely. In practice, a stoppered bottle will maintain N_2O_3 for days at room temperature (NO attacks rubber and plastics and diffuses easily, so greater care is necessary to contain it), while the same solution unstoppered would fade in an hour. Furthermore, as shaking a can of beer before opening it demonstrates, the pressure exerted by a super-saturated solution will be far less than what it could exert were all the gas contained therein to escape at once. As an illustration, it is a simple matter to prepare trioxide solutions in which 10 mL of solvent has absorbed 1500 mL of total gas, without any noticeable pressurization of the system.

It may seem that only a precise confluence of factors produces trioxide solutions, but in fact the first such solution made in our lab formed by accident: a pale blue tint in an iced acetonitrile solution as it was being flushed with nitric oxide gas. Further experimentation showed that if any of a range of solvents is bubbled with NO gas while open to the atmosphere (or under a flow of air), it will take on a distinct tint almost immediately, deepening to an intense blue or green colour in less than a minute (the products of such a treatment can be seen in Figure 3.1).

Interestingly, purposefully mixing NO/NO₂ gas in equimolar amounts and then introducing them to a solvent produced only an NO₂-yellowed solvent. Both Vosper¹⁵ and Addison et al.³⁰ reported something similar: even in low temperature baths, attempting to form an N₂O₃ solution from equimolar NO and NO₂ produced no more than an ~80% solution of N₂O₃, the balance made up with N₂O₄.

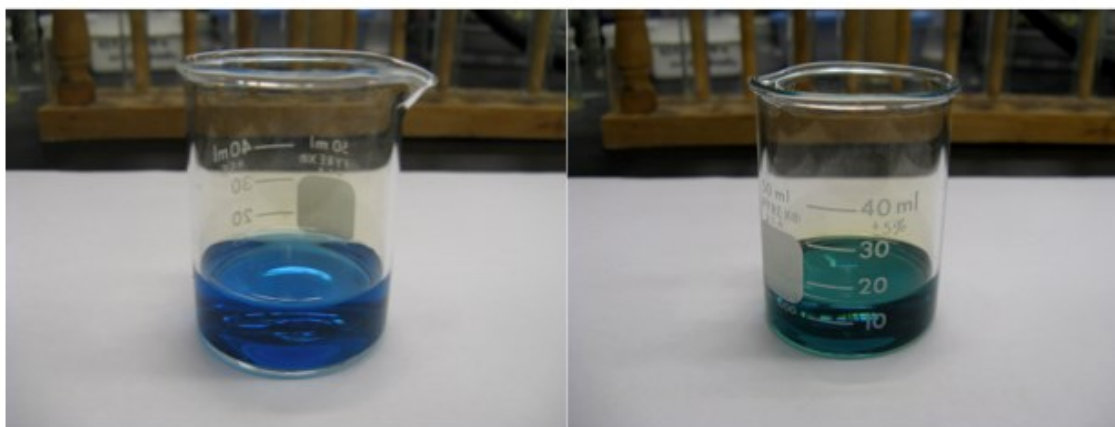


Fig 3.1: Acetonitrile (left) and toluene (right) bubbled with NO gas on ice, then warmed to 25°C.

Why this should be can be appreciated by considering the nature of the precursors. N₂O₃ is made up of two dissimilar gases; of the two, NO is more volatile and less soluble in most situations. NO will not dimerize much at these

temperatures, but the dimer of NO_2 , dinitrogen tetroxide, is a solid at -11.6°C and a stable liquid until room temperature. While NO_2 is stable in air, NO readily becomes NO_2 when exposed to oxygen. Thus while the unstable trioxide can easily become the stable tetroxide either by the loss of volatile NO or the oxidation by oxygen, the inverse is not true. So even at temperatures that favour trioxide formation, at best 80% of the NO/NO_2 will combine in this way; some NO_2 will dimerize instead, and the balance of volatile NO will diffuse into the gaseous phase. An excess of NO is necessary to produce trioxide in high yield. Vosper reports that using an 8:1 ratio of NO to NO_2 at -60°C , it was possible to produce N_2O_3 that was 98.6% pure¹⁵. At ratios less than this the trioxide slowly converts to tetroxide.

This does not, however, account for the ease with which these two combine in solvents, even in situations in which oxygen and NO_2 far exceed the levels of NO . The key is the stabilization offered by the solvent to both the N_2O_3 and to the N_2O_4 .

3.2 Preparation of Trioxide Solutions

Freely bubbling toxic NO gas through solvents and venting it to the atmosphere is not a practice that should be encouraged, and if trioxide solutions are to be useful in a chemical laboratory they must be easily and reproducibly synthesized. Methods by which this can be done are described in detail in the Experimental section of this chapter; general information with regards to gas sources, solvent preparation, handling etc. can be found in the General Experimental section, and the dynamic absorption method is included there as well. In brief, there are two approaches that work well:

Exp 3.1: Cold Condensation: A source of NO gas mixed with a small amount of oxygen is passed into the upper reaches of a cold trap cooled to -78°C by a dry ice/ethanol slurry. N_2O_3 will condense and pool in the bottom, while any N_2O_4 will freeze on the sides until sufficient NO transforms it into the trioxide. This method produces very high purity ($\sim 99\%$) N_2O_3 that may be subsequently dissolved in a solvent of choice.

Exp 3.2: Dynamic Absorption: A solvent is flushed with NO gas, and then a measured amount of oxygen is introduced with a gas-tight syringe. The mixture is gently stirred while a positive pressure of NO gas is allowed to flow into it, until absorption ceases. (Fig 3.2).

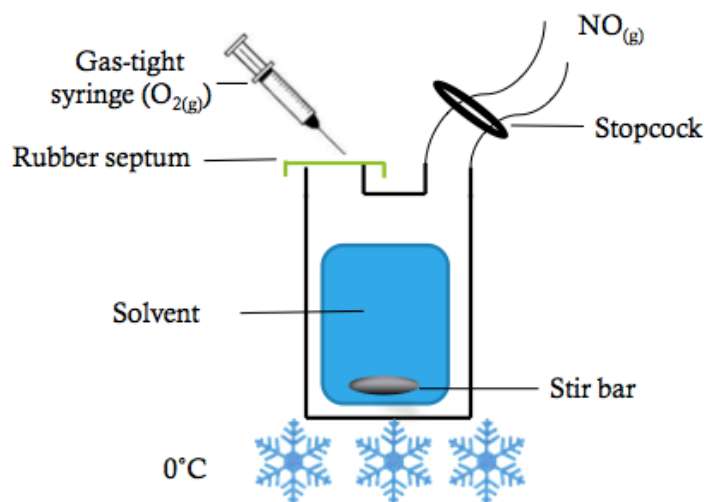


Fig 3.2: Diagram of basic dynamic absorption method.

The dynamic absorption method has been found to be simple, tunable, and easily controlled, and can be used to produce high quality solutions. However, the fact that the solutions can be made does not guarantee that one knows what is in them; pure trioxide made at -78°C may not be pure once in solution, or after that

solution has been warmed to 25°C. The dynamic absorption method tells us how much oxygen is present, and hence how much NO₂, but not what the ratio of tetroxide to trioxide will be. Even knowing the amount of NO introduced may not tell one about the nature of the solution under different conditions. Thus some analytical methods must be discussed, with the end of quantifying the trioxide in mind.

3.3 Analysis of Trioxide in Solution

Four detection methods were employed to study the trioxide in solution: visual inspection, IR, UV-Vis, and NMR.

Visually: The colour of trioxide can be seen at moderate concentrations (approximately at 0.01 mol/L, or 500 ppm in an acetonitrile solution), such that for decades, researchers working under the most exacting conditions believed that the colour of solid nitric oxide was bright blue, and argued emphatically³¹ that this was not due to trioxide contamination (which it was). Any blue, green, straw-green or similar colours are signs of trioxide formation. The tetroxide is more difficult: NO₂ in solution can be colourless, yellow, or even a red-orange colour, and concentrations too low to be chemically significant can sometimes be picked out by eye. At colder temperatures, tetroxide is a clear white solid. Mixtures of tetroxide and trioxide at -80°C can be gauged visually: the trioxide is a rich blue liquid that runs freely, beads, and pools, where any significant tetroxide component will give it an icy, dull or discoloured appearance and it will cling to the vessel walls, being more viscous and semi-crystalline.

Infrared: At low concentrations, the oxides of nitrogen in the liquid phase can be identified by their key IR bands; these are listed in Table 3.1. This technique is useful for detection of tetroxide in a trioxide solution, but not for quantification, and the loss of volatile NO is so easily accomplished that IR will almost always detect tetroxide in a mixture, limiting the practicality of this method.

Table 3.1: Strong IR Bond Stretches of Dinitrogen Trioxide³²

	Tetroxide (cm ⁻¹)		Trioxide (cm ⁻¹)
Antisymm. NO stretch (in phase)	1733	NO stretch	1841
Antisymm. NO stretch (out of phase)	1699	Antisymmetric NO ₂ Stretch	1611
Symmetric NO stretch (in phase)	1359	Symmetric NO ₂ Stretch	1291
Symmetric NO stretch (out of phase)	1257		

UV-Vis: For quantification of the trioxide vs tetroxide, the best technique is UV-Vis spectroscopy. Like tetroxide, the trioxide absorbs strongly in the UV range (ca. 230 nm), so much so that chemically insignificant amounts can be seen, but it has a broad, distinctive spectrum in the visual range which tetroxide lacks. The visible spectrum for N₂O₃ in acetonitrile is typical for both the solutions and the pure compound (Fig 3.3). Thus if the visible extinction coefficient of trioxide in a given solution is known, this method can determine the trioxide concentration (calculating what this extinction coefficient is in the first place, when trioxide and tetroxide are in equilibrium with each other, is a problem taken up in section 3.5).

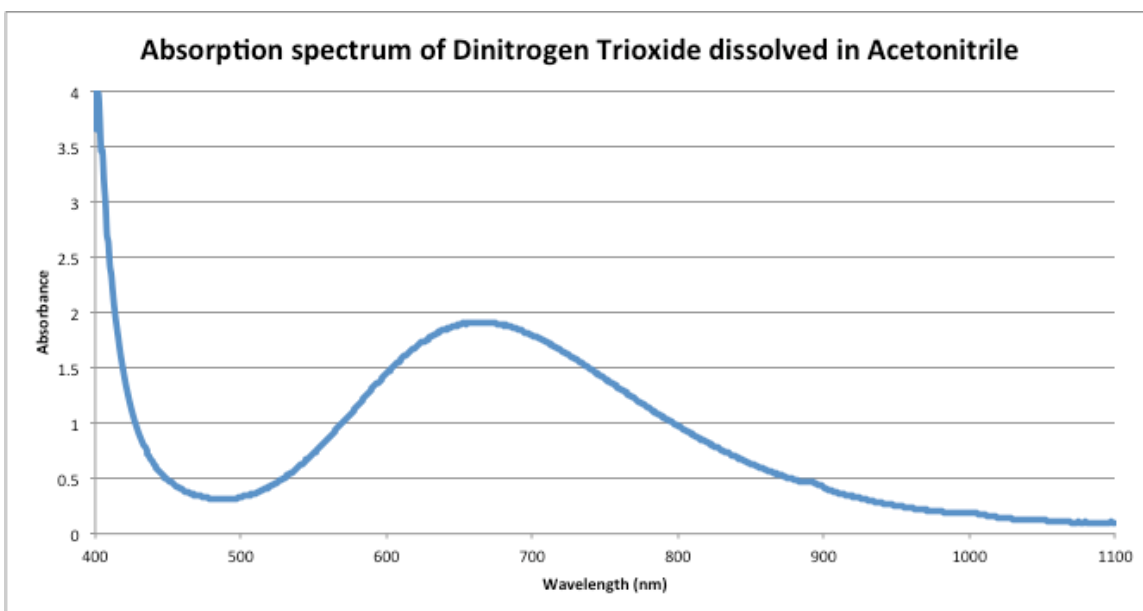


Fig 3.3: Visible absorption of dinitrogen trioxide in acetonitrile.

This general shape is found in all solvents in which N_2O_3 is stable, but it is distorted by solvent (the Table 3.2 in section 3.4 provides a range of observed visible λ_{max} for N_2O_3 in different solvents) and temperature (described in Section 3.6).

As the concentration of the N_2O_3 increases, the visible λ_{max} will shift to shorter wavelengths, evidence of an interaction between the N_2O_3 molecules themselves. In the range <100 mM, N_2O_3 roughly obeys Beer's law. Preparing a series of solutions by the dynamic absorption method yields a linear relation (within the range of experimental error). Below (Fig 3.4) is a typical example, in toluene.

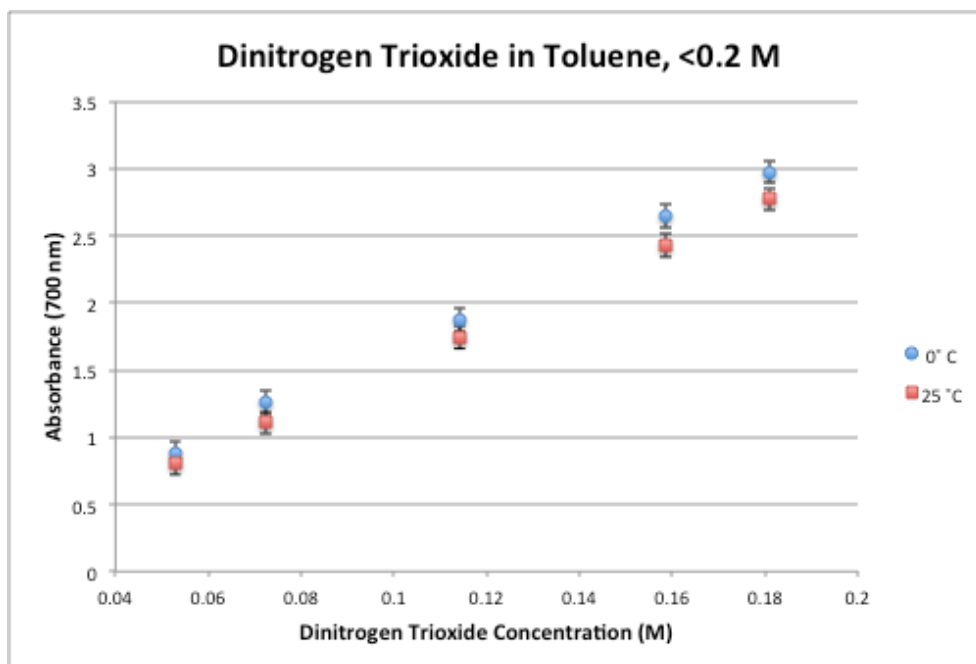


Fig 3.4: Relation of absorbance at 700 nm and N_2O_3 concentration, in toluene. The x-axis is given as moles of O_2 , which theoretically corresponds to twice this amount of N_2O_3 . Samples measured in a 1 cm path length cell. Error bars represent experimental error.

However, it distorts significantly at higher concentrations (Fig 3.5): at 1 M, the absorption is only 41.7% of what an extrapolation by Beer's law would predict.

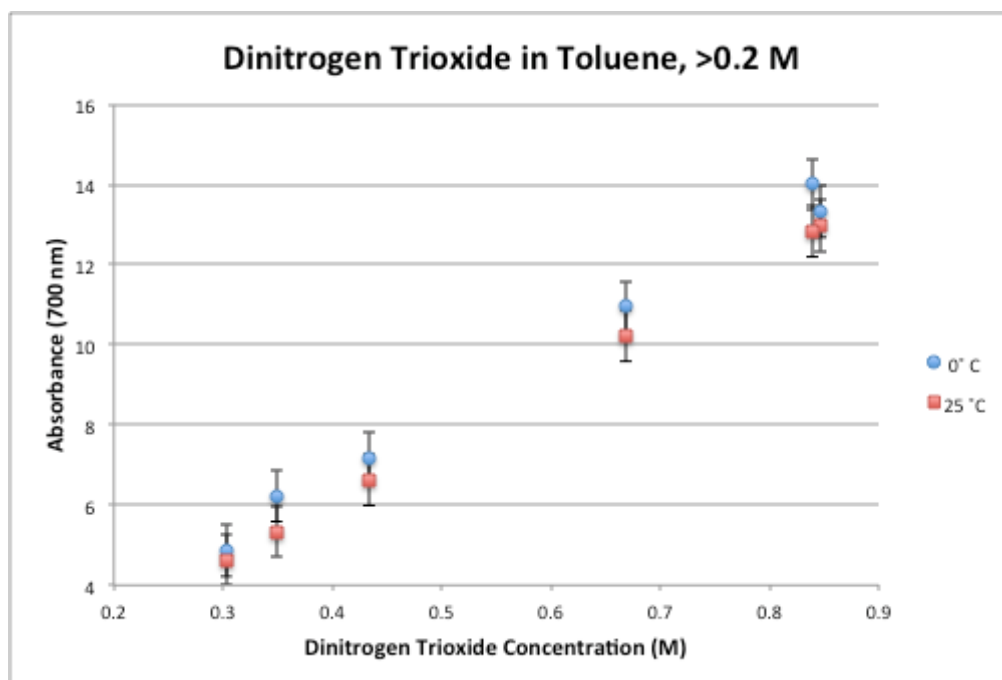


Fig 3.5: As in Fig 3.4, at higher concentrations. Samples were measured in 1 mm path length cell, and the values extrapolated to 1 cm, for comparison. Error represents 1 standard deviation.

Similar behaviour is seen in dichloromethane solutions, and across different temperature regimes (Fig 3.6).

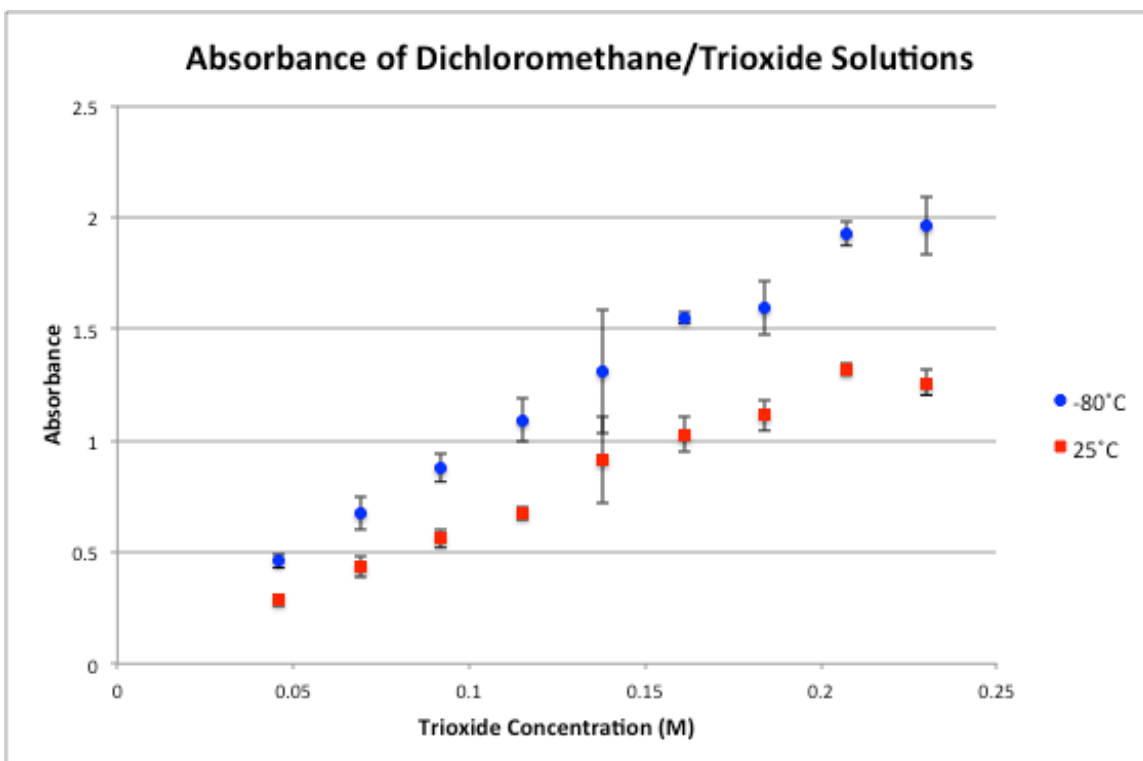


Fig 3.6: DCM/Trioxide solutions measured by UV-Vis at 690 nm. Error is given as 1 standard deviation.

The deviations from Beer's law can be explained by aggregation (i.e. to N_4O_6), which would be reasonable given the tendency of nitroso species in general ($R-N=O$) to undergo dimerization, though dimerization is generally inhibited by electron withdrawing groups, which NO_2 surely is. Alternatively, higher concentrations could induce clathrate-like formations, achieving an aggregation without necessarily being due to trioxide-trioxide interactions.

Another possibility is that the deviation from Beer's law is due to isomerization. It is well known that dinitrogen tetroxide may isomerize³³ at room temperature, either by autoisomerization or by interaction with other species³⁴. It has been noted by Varette and Pimentel²³ that when trapped in frozen nitrogen matrices, the normal C_s symmetry N_2O_3 can be isomerized under 720 nm light into a

C_{2v} symmetry form ($O=N-O-N=O$). Low temperature deposition of NO/ NO_2 displayed an absorption at 720 nm (assigned to the normal C_s form), which vanishes upon prolonged near infrared radiation due to photoisomerization to the C_{2v} form; radiation restores the original isomer. Though the deep blue colouration of trioxide is thought to be due to the $n_N \rightarrow \pi^*$ transition¹, and this would still be possible in the C_{2v} trioxide, the atom attached to the nitroso group greatly alters the energy of the transition. In this case, the long, labile bond to another nitrogen puts the energy of the transition in the visible region. Some monomeric C-N=O compounds will absorb in this region as well, but N-N=O species normally do not, nor do O-N=O species (NO itself and nitrite are colourless). It is possible that high concentrations of N_2O_3 aid in auto-isomerization (Fig 3.7).

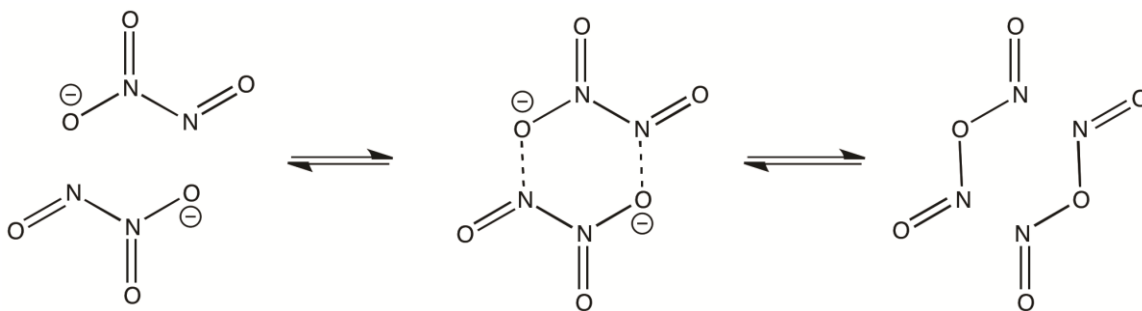


Fig 3.7: Possible concentration based mechanism for N_2O_3 isomerization.

Since the antisymmetric form was calculated by Pimentel and Varetto to be only slightly more stable, by approximately 4.4 kcal/mol, it is possible that as the concentration falls again, simple thermal agitation or low levels of ambient UV light would be enough to convert the isomer back to the normal C_s form.

NMR: Most early research in this field was done at low temperatures, where it could be claimed that dissociated gas was not a pressing concern, but my work at higher temperatures demands a better accounting of the free radical component. Both Vosper and Mason agree that the amount of dissociated radical is small, based on painstaking stoichiometric differential work, but since both free gas constituents are radicals, this allows for an in situ determination of the ratio of free gas to bound radical pair by use of the Evans method³⁵. This method measures the paramagnetic susceptibility of a solution in comparison to a pure solvent by means of NMR: the more paramagnetic species present in a solution, the more the solvent peak will be shifted upfield relative to the pure solvent (NOTE: The paramagnetism gives the bulk fluid a larger effective paramagnetic susceptibility, making it exaggerate the applied magnetic field; in older spectrometers this meant a downfield shift. Newer spectrometers produce the external field parallel to the sample tube rather than perpendicular, which necessitates a change in the correction factor due to sample shape; the end result is an upfield shift instead).

The standard formula for the Evans determination (corrected for modern superconducting magnets)³⁶ is:

$$\chi_g = -3\Delta f / 4\pi f m + \chi_o + \chi_o(d_o - d_s) / m$$

Eq 3.3: Mass susceptibility change as a function of radical concentration (the Evans effect).

Where χ_g is the mass susceptibility in cm³/g, χ_o is that of the solvent, f is the frequency of the spectrometer, Δf is the observed peak shift in Hz, and m is the mass

of solute in 1 mL of solvent. The final term accounts for the change in the density between solvent and solution, but in this case it can be safely omitted. NO has a mass susceptibility of 4.86×10^{-5} (cgs units)^{37,38}; owing to the dimerization of NO₂, its mass susceptibility is less certain, but Havens' determination is the most rigorous, and so his value of 2.966×10^{-5} for NO₂ was chosen³⁹. For determinations of the dissociation of N₂O₃, which produces one of each gas, a theoretical diradical with the mass of N₂O₃ and the sum of these susceptibilities was used for the purposes of calculation. The mass susceptibility of most solvents is on the order of 1% of these values, and so the term χ_0 was also omitted for this calculation.

This is a highly sensitive technique, and when applied to small amounts of a volatile gas that reacts with oxygen and can attack plastics, in low-boiling solvents, the experimental error can be large; in this case, an error in the shift of ± 0.015 ppm was seen, which translates to ± 3 μ M of NO. Nevertheless, control runs to verify the technique, which used mixed argon/NO atmospheres to dissolve pure NO into the solvent, obtained values that were within this margin of error of the theoretical NO concentration.

Trioxide solutions prepared in dichloromethane (Exp 3.3) exhibited the Evans effect, shifting the peak by ~ 0.05 ppm. Solutions prepared either *in situ* (by dynamic absorption) or from pure N₂O₃ displayed indistinguishable peak shifts. The dissociation as a percent of the initial N₂O₃ concentration (measured by UV-Vis, and assuming a theoretical 100% N₂O₃) was calculated, and was seen to increase with temperature (Fig 3.8):

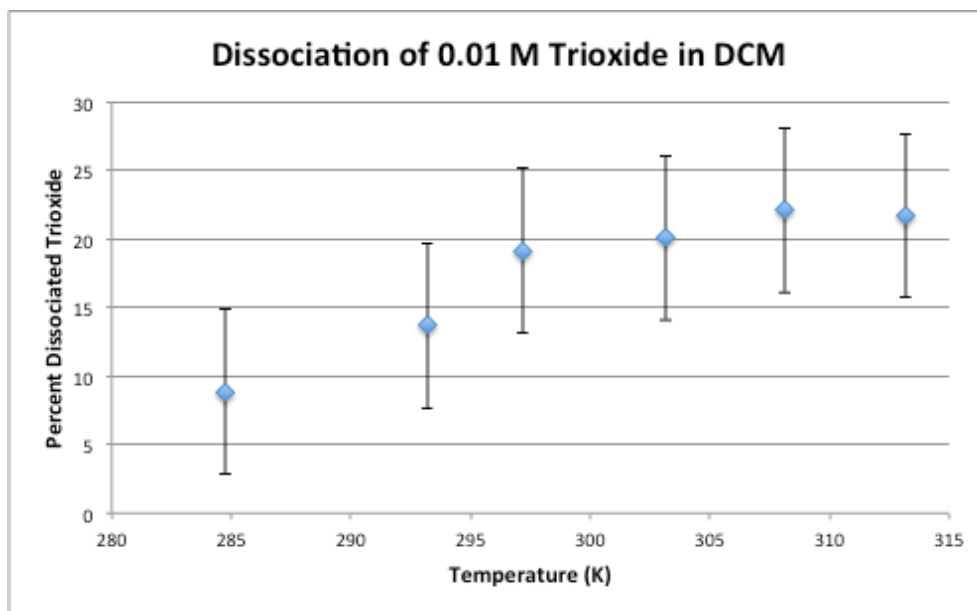


Fig 3.8: Dissociation of 0.01 M N_2O_3 in DCM solution, as calculated from the Evans effect.

The relationship levels off significantly as the solution approaches 40°C, which is the boiling point of dichloromethane. This stands to reason: as the solvent warms a greater portion of the trioxide/tetroxide dissociates into radical species, but at the same time the increasing heat causes these free radical gases to come out of solution. At near the boiling point, the amount of radical in solution actually begins to drop. Repeating this experiment using more concentrated N_2O_3 and acetonitrile (bp 82°C) yields a smoother relation (Fig 3.9).

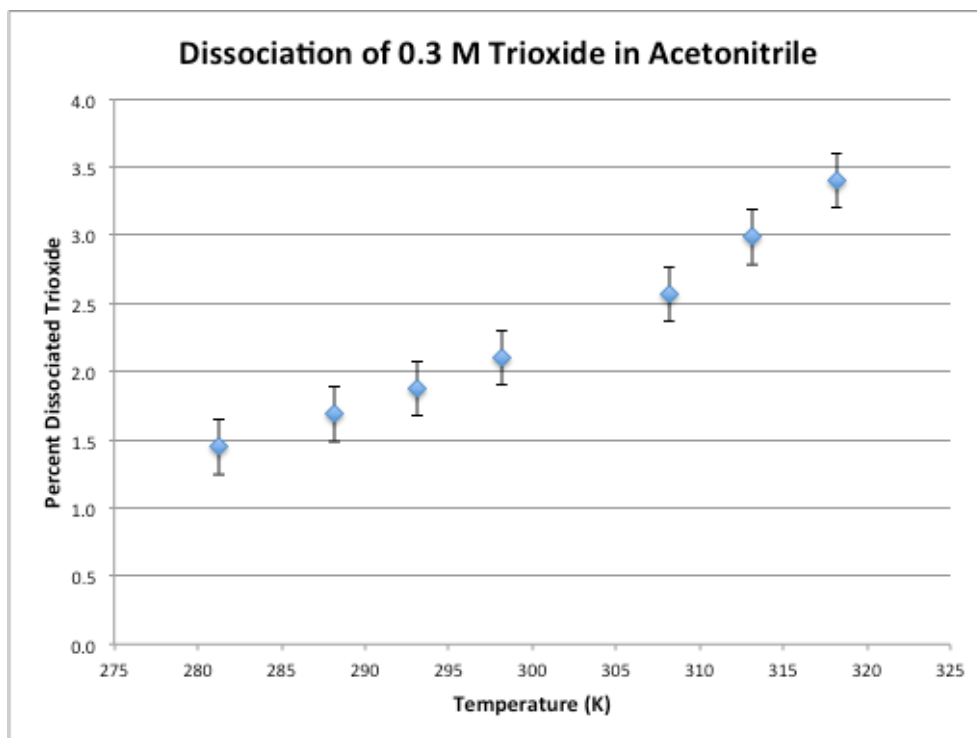


Fig 3.9: Dissociation of N_2O_3 into NO in acetonitrile solution, as calculated by the Evans effect.

In this case, the effect increases almost linearly with temperature, but with a slight upward curve, even though the liquid medium remains intact. This suggests that there may be two considerations to stability, which are being disrupted to different degrees as the temperature rises.

Notably, the degree of dissociation is markedly less in the more concentrated solution (i.e. this is seen in high concentration dichloromethane solutions as well) and the explanation is evident: the solubility of NO in solutions is limited and it depends, by Henry's law, on the partial pressure of NO in the gas phase. The highest theoretical concentration of NO under 1 atm of gas is 0.014 M in acetonitrile, and so the fact that a 0.3 M solution maintains less than 5% of itself (i.e. 0.015 M) in a dissociated state is just about right. In the lower concentration solution, a much

greater percentage is able to dissociate; at higher concentrations, the relative percentage falls.

This result confirms past research; Vosper writes¹²:

"Thus in equilibrium conditions and with a partial pressure of nitric oxide equal to 1 atm, dinitrogen trioxide will be less than 1% dissociated at -40°C. The partial pressure of nitric oxide necessary for stability rises rapidly as the composition approaches [pure] dinitrogen trioxide, proving that nitric oxide has low solubility in dinitrogen trioxide."

What becomes noteworthy about this is that these measurements are taken at temperatures 40-85°C higher, and yet the level of dissociation is still quite low. Even at temperatures well above room temperature, NO and NO₂ are minor species in solution, and the trioxide remains intact.

3.4 Mechanism of Solvent Stabilization

The standard expectation⁴⁰ for the dissociation of gaseous species in solution is that in non-coordinating solvents it is less favourable than in the gas phase due to entropic effects. A species breaking apart in the gas phase has access to a large free volume, whereas one in solution will be restricted, making for less of a gain in entropy due to dissociation. Furthermore, two particles disrupt the solvent-solvent interactions more than one, and the total free energy loss must compensate for this. However, Vosper and Shaw¹⁴ point out that this is insufficient to explain the stabilization by solvents, and that a further enthalpic explanation is needed to account for the evident preference for the dimer form in certain solvents.

Quite a broad range of solvents are found to stabilize trioxide (Table 3.2):

**Table 3.2: Properties of Dinitrogen Trioxide Solutions at Room Temperature
(prepared by dynamic absorption)**

Solvent	Visible Colour	Visible λ max (nm)	Violet Wall* λ (nm)	\$Solvent Dipole (μ)	\$Relative Permittivity (ϵ_r)
None	Muddy green	720	$\sim 500^{**}$	--	--
Acetonitrile	Bright blue	660	401	3.92	39.0
Dichloromethane	Blue	710	428	1.60	9.08
Tetrachloroethane	Turquoise	700	412	1.32	7.46
DMSO	Navy blue	600	437	3.96	49.0
Ethyl acetate	Blue	668	415	1.78	6.02
Acetic Anhydride	Blue	663	412	2.82	22.4
Acetone	Blue	655	425	2.88	20.7
Chlorobenzene	Mint green	718	408	1.69	5.708
Benzene	Icy green	705	408	0	2.284
Toluene	Green	700	421	0.36	2.438
Xylene	Emerald	694	441	0.62	2.374
Mesitylene	Dark green	685	457	0.047	2.27
Anisole	Lime Green	675	510	1.38	4.250

* Violet-Wall: The approximate position (varies slightly with concentration) of absorption cut-off of the intense UV absorption as it impinges on the visible region. Taken at the wavelength at which the absorption slope is nearly vertical (Absorption > 2), for ~ 0.05 M N_2O_3 .

** Violet-Wall in pure trioxide at room temperature will be mostly that of the tetroxide.

\$-Solvent dipole and relative permittivity values taken from the CRC Handbook⁴¹, except ϵ_r for acetonitrile⁴², tetrachloroethane and anisole⁴³, DMSO⁴⁴, and the dipole moments of acetic anhydride⁴⁵ and mesitylene⁴⁶.

The criteria seem to be that the solvent must be polar and/or aromatic, and that it not react with the trioxide itself (at least not at an appreciable rate). Thus trioxide is stable even above room temperature in acetonitrile or toluene, whereas hexane allows it to decay immediately (in fact, pure dinitrogen trioxide is insoluble in hexane). Water and alcohol are poor solvents because they react, but benzaldehyde is quite a good solvent (it will eventually react, however, see Chapter 4). DMSO, acetone, and acetic anhydride can all serve, but due to their tendency to absorb

water they are not very practical. What is particularly noteworthy is that either polarity or aromaticity is sufficient: benzene has no dipole moment yet it does a fine job of holding trioxide, whereas cyclohexane does not.

Between polarity and aromaticity, the latter seems to be the most stabilizing. Trioxide forms in aromatic solutions readily and endures longer (we will look at this in more detail in the next section). This suggests two different modes of stabilization. First, polar environments stabilize polar compounds. Non-polar bodies in a polar mixture disrupt the dipole-dipole interactions, and so these interactions are optimized (the most stable state is achieved) when these less polar bodies are contained together; this is why oil droplets in water collect and combine. While NO and NO₂ are both somewhat polar (0.160 D and 0.289 D)^{47, 48}, and N₂O₄ is nearly non-polar⁴⁹, trioxide is significantly polarized (2.572 D)⁵⁰. It is as though the oil droplets can combine in two ways, one of which makes them oilier, and the other transmutes them into water; over time, such a scenario would lead to the elimination of the oil. Since in this case entropic effects favour the formation of the bound radical pairs, in polar environments the trioxide species will dominate.

The pattern seen in the UV-Vis spectrum for polar solvents is that increasing polarity leads to a blue shift in both the visible and UV absorptions. This matches well with DFT calculations that model the N₂O₃ in different polar environments (Table 3.3), in which that general pattern is observed.

Table 3.3: DFT calculations of N₂O₃ properties in solvent

Solvent	Dielectric Constant	Theoretical λ_{max} (nm)	Observed λ_{max} (nm)	N-N Bond (Å)	Energy (a.u.)
Gas phase	1	827.8	720	1.87951	-335.086896312
Benzene	2.247	772.49	705	1.890795	-335.0903849
Toluene	2.379	769.35	700	1.89165	-335.0905898
Cl-benzene	5.621	731.75	718	1.90328	-335.0931746
CH ₂ Cl ₂	8.93	718.47	710	1.9084	-335.0941292
Acetonitrile	36.64	699.97	660	1.914721	-335.0954784
DMSO	46.7	700.17	600	1.916099	-335.0955366

Where this pattern breaks down is in predicting the effects of aromatic groups, confirming that a second mechanism is at work. Interestingly, these calculations predict that the N-N bond in fact *lengthens* as polarity increases and the molecule stabilizes. This is counter-intuitive, though it may account for the observation that polar solvents generally maintain lower levels of N₂O₃ than aromatic solvents can.

In aromatic solvents, increasing the degree of electron donation to the benzene ring results in the blue shift of the N₂O₃ peak, suggesting a similar interaction between the N₂O₃ HOMO and the π orbitals of the solvent. However, to gauge by the movement of the 'violet wall' (the cut-off of the more intense UV absorption), this is accompanied by the red-shift of the UV peak. As the aromatic solvents themselves have a strong absorption in this same region it is not possible to view the UV peak directly. Thus one cannot say with certainty that these peaks are shifting in different solvents, or if the apparent shift is caused by a change in peak intensity (which would also cause the intense absorption to advance somewhat into the violet region). However, by examining how this violet wall changes with concentration, we can compare it to the changes seen by a change in solvent (Table 3.4):

Table 3.4: UV absorption of N₂O₃ in aromatic solvents, at two concentrations

Solvent	Chlorobenzene	Benzene	Toluene	Xylene	Mesitylene
Violet wall* at 0.026 M (nm)	397	395	409	435	448
Violet wall* at 0.052 M (nm)	408	408	421	441	457

*Wavelength is reported at the point where the absorption slope becomes nearly vertical (Absorption > 2)

In each of the solutions seen in Table 3.4, doubling the concentration of N₂O₃ will increase both the visible and UV absorptions. At this concentration this means that the visible peak will double in intensity, while the violet wall will shift ~6-13 nm to the right, reflecting the growth of the large UV peak which is obscured by the solvent absorption. Thus on average, a doubling of concentration should shift this absorption wall ~10 nm to the right. The largest difference in extinction coefficients, from Table 3.3, is between xylene and chlorobenzene (17.4 and 10.9, respectively). If we assume that this ratio holds for the UV peaks, then a 0.026 M N₂O₃ solution in chlorobenzene should absorb 1.6 times more intensely in xylene. Applying this to the observation that a doubling of the UV peak results in a 10 nm shift in the observed absorption, and given the absorption for a 0.026 M N₂O₃ solution in benzene at 395 nm, we would expect a similar solution in xylene to be found at 403 nm. Since the xylene absorption is found to be red-shifted a full 32 nm beyond this (and mesitylene is even further along), it is likely that this represents a true red-shifting of the peaks themselves, rather than an increase in intensity.

Shaw and Vosper understood the shifting with polarity⁹ to be due to interaction with the lone pair of the -N=O, while the interaction of trioxide with the aromatic solvents was described as due to the formation of weak adducts¹⁰. An extra

absorption band (of unspecified wavelength) appears in the UV for these solutions, which is believed to be a contact charge transfer band between the trioxide and the π cloud of the aromatic ring. Trioxide in mesitylene solutions has also been observed to freeze at higher temperatures than expected, suggesting that an adduct formation provokes the solidification. The exact nature of this interaction is unknown at this time, but a crucial observation is that N_2O_4 has also been observed to benefit from solvent stabilization⁴⁰. Addison et al.⁵¹ have noted that tetroxide becomes red when mixed with some aromatic solvents at low temperatures, due to orbital overlap with the π cloud, and this may be the mechanism for trioxide as well.

Theoretical studies of the molecular orbitals of N_2O_3 by Doonan and Maclagan⁵² suggest that only two orbitals contribute bonding density to the N-N bond (one low lying orbital and the HOMO), and these are partly cancelled by another orbital, intermediate in energy between the two, which is anti-bonding between the N atoms. Furthermore, both the S1 and S2 excited states, as well as the first doubly excited state, are all into N-N anti-bonding orbitals, which accounts for the weak N-N σ bond. Models produced by Kishner et al⁵⁰ show that one of the lone pairs on the nitrosyl oxygen, which is almost wholly p_x in nature, donates to some extent into the anti-bonding p_x^* orbital of the adjacent N atom, and they credit this interaction as the source of the weakened N-N σ bond. Both models leave more negative charge on the nitrogen than oxidation states would indicate (Doonan and Maclagan further claim that the excited states involve charge transfer to the NO_2 side of the molecule), and thus electrostatic repulsion further weakens the N-N bonding.

In an attempt to visualize these interactions, DFT calculations were performed for N_2O_3 to produce the following diagrams (Fig 3.10):

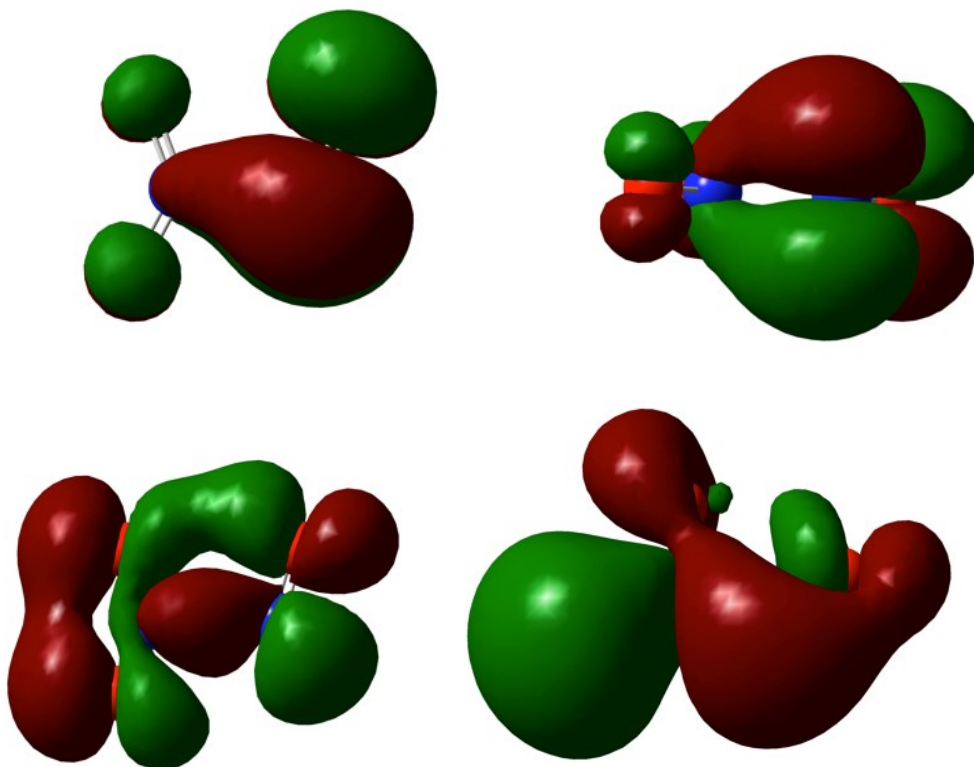


Fig 3.10: MO diagrams of N_2O_3 (oriented left to right as $\text{O}_2\text{N}-\text{NO}$). Top: Two views of the LUMO. Bottom left: HOMO. Bottom right, HOMO-1.

These results were not entirely consistent with Doonan and MacLagan's (here the LUMO seems clearly bonding between the N atoms), but the HOMO is seen to be weakly σ bonding, as their work predicted.

The UV-Vis behaviour and stabilization of N_2O_3 in solution can thus be rationalized thusly: both polar solvents and π donation from aromatic solvents interact with the bonding HOMO orbital, decreasing its energy and stabilizing it, thus protecting the long $\text{O}_2\text{N}-\text{NO}$ bond from dissociation. This increases the HOMO-LUMO gap and thus the energy of the visible transition. The red-shifting of the UV absorption in aromatic solvents suggests that the HOMO-1 π orbital (which is

mostly anti-bonding or non-bonding with regards to the N atoms) is rising in energy, lowering the gap between it and the LUMO. In effect, aromatic interaction moves the HOMO and HOMO-1 orbitals towards degeneracy. Thus a solvated trioxide molecule is, on an electronic level, a different species from a gas phase one. Interestingly, these effects can work at cross purposes: chlorobenzene is more polar than benzene, so one would expect a blue shift of the peak, and yet the electron withdrawal from the ring red shifts the peak so far that it appears at longer wavelengths than benzene.

One final observation must be made about the role that the solvent can play in the initial trioxide formation. When a trioxide solution is produced by gentle bubbling of NO, the blue colouration does not begin at the air/solvent interface (where the NO could encounter O₂), but forms uniformly throughout the solvent. This could be because it is reacting with solvated oxygen, but performing this operation in a constricted vessel will not produce appreciable amounts of trioxide--the oxygen must come from the atmosphere. What this suggests is that what primarily forms at the interface is the colourless tetroxide, which is more stable at these temperatures and can then spread throughout the solution and further react with the NO as it bubbles through (Eq 3.4):



Eq 3.4: Reaction of solvated tetroxide with solvated nitric oxide.

This can be better appreciated by reviewing the reaction by which NO becomes NO₂. As discussed in Chapter 1 (Fig 1.3) NO₂ is formed from NO by reaction

with the NO dimer, N_2O_2 . In the gas phase, subsequent reaction with oxygen would then immediately lead to dissociation. In other words, the initial product of the oxidation is better represented as N_2O_4 (Fig 3.11). In cooler temperatures and in a stabilizing solvent, this would be the primary product.

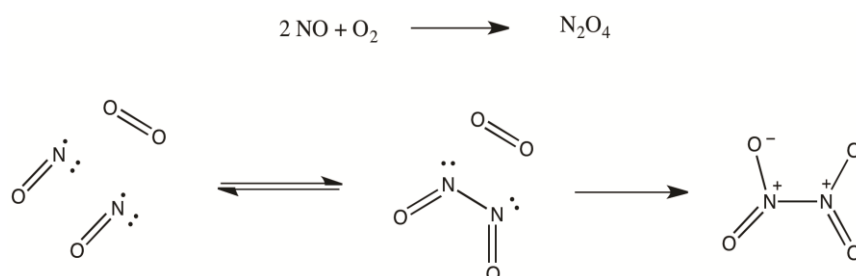


Fig 3.11: Formation of dinitrogen tetroxide from NO and O_2 , where dissociation is prevented by solvent stabilization.

It is thus the tetroxide which is most likely present in solution at room temperature, and most research suggests that NO reacts more readily with N_2O_4 than with NO_2 . Vosper's preferred method of N_2O_3 formation¹⁵ involves condensing tetroxide in the upper reaches of a cold trap, then passing NO gas over it such that N_2O_3 drips down; he reports that this method yields better than 99% pure trioxide.

What this highlights is the fact that the solvent is not merely a medium in which to dissolve N_2O_3 as it forms, nor even just the basis for its stabilization, but that the solvent is an active component in N_2O_3 formation. The interface of liquid and gas appears to act as a substrate in which trapped NO and O_2 can form N_2O_4 . The solvated $\text{NO}_2/\text{N}_2\text{O}_4$ then reacts with further NO, and the final product is stabilized by the solvent cage and solvent interactions. Hence this phenomenon is well primed to be discovered and rediscovered by successive generations of chemists being careless with their NO gas.

3.5 Quantifying Trioxide vs Tetroxide:

With the level of radicals in solution thus established to be minor, the complexity of the initial equilibrium can be reasonably modeled as having three components: the trioxide in solution, the tetroxide in solution, and the nitric oxide in the gas phase (the NO_2 in the gas phase can also be seen to be minor except in systems above room temperature). Since the volume and pressure of the headspace is easily known, the problem becomes knowing the level of trioxide versus tetroxide, and for that we can make use of the analyses above.

The simplest way to quantify the trioxide is also the most robust: since trioxide is visible to the naked eye, it may be used as its own titration indicator. Titrations with known amounts of oxygen will decrease the trioxide by a ratio of one oxygen to two trioxide, and the amount of trioxide in solution can be calculated. This method is detailed at the end of the chapter (Exp 3.4). Thus the mole percent of trioxide for solutions formed at both 0°C and 25°C were determined. With the trioxide concentration so established and the absorption measured by UV-Vis, a series of extinction coefficients can be calculated for solutions at room temperature (Table 3.5), measured at the maximum visible absorbance listed in Table 3.2. These can be compared to the published extinction coefficients, most of which were measured at -78°C ⁹ (benzene and acetonitrile were measured close to their melting points of -45°C and 5.5°C), taken at the maximum visible absorbance at this temperature (which will be blue-shifted somewhat; I will return to this issue in the next section).

Table 3.5: Trioxide content of solutions prepared by dynamic absorption

Solvent	Mole % N ₂ O ₃ (0°C)	Mole % N ₂ O ₃ (25°C)	ε (25°C) (L/cm•mol)	ε from lit. (L/cm•mol)
Acetonitrile	91.7(6)	73.6(5)	9.8 (7)	10.7
Dichloromethane	76.8(5)	59.1(4)	8.5 (7)	9.2
Chlorobenzene	91.5(7)	55.7(4)	10.9(9)	15.2
Benzene	88.7(4)	66.5(3)	14.0(8)	16.3
Toluene	99.8(7)	69.0(3)	15.3(7)	18.7
Xylene	98.5(8)	69.0(5)	17.4(8)	20.3
Mesitylene	100.7(7)	71.1(5)	16.4(8)	20.8

What is found, first of all, is that the yield of trioxide for these solutions is quite high when prepared at 0°C under 1 atm of NO, in some cases what might be termed 'reagent grade' dinitrogen trioxide, and even at room temperature are significant. Secondly, the extinction coefficients at room temperature are noticeably lower; the error ranges in the literature values are not reported, but if we assume that it is in the range of the last reported digit, then the two values are mostly outside the margin of error from each other.

This second issue will be taken up again in the next section, but first the yield must be more closely examined; the results for trioxide formation appear to contradict earlier research. Vosper et al, throughout the various works so far cited, maintain that at temperatures above 0°C the equilibrium favours dissociation and the formation of tetroxide. Using their notation for N-O ratios (where 1.5 denotes pure N₂O₃ and 2.0 denotes pure N₂O₄), they stated that it is impractical to form solutions at a ratio much below 1.7, or a 60:40 mixture trioxide/tetroxide mixture at 0°C.¹² At room temperature, the values will be even lower.

The disagreement in the N_2O_3 concentration is only apparent, however, as can be appreciated by examining Vosper and Shaw's method. They formed their trioxide solutions from solutions of commercial tetroxide of known concentration, into which NO from a gas burette is allowed to flow, while the vessel is violently agitated. However, they note that while pure tetroxide quickly absorbs NO at first¹⁵, it slows down radically thereafter; they note as well that NO is very slow to absorb into a still (i.e. unstirred) column of tetroxide solution, and hence the violent agitation in these preparations. This slow diffusion of NO and/or N_2O_3 is not unique to tetroxide absorption; N_2O_3 diffuses very slowly through all organic solutions. Narrow vessels of concentrated trioxide solution that have been left open to the air will bleach yellow to a depth of a centimetre or so, while the lower layer remains dark green. Stirring to facilitate the mixing is required.

The crucial fact to remember, however, is that equilibrium is achieved when the flux of a species in one direction equals the flux in the other, howsoever that flux is achieved. Thus for a tetroxide solution absorbing NO, the NO absorption will cease when the rate of NO entering solution equals the rate at which it is leaving, which will come from both solvated NO and from N_2O_3 . What must be understood is that N_2O_3 achieves stability by being surrounded by solvent; when pushed to the surface or ejected from solution, it is put into a state in which the equilibrium is driven towards dissociation; that is, the NO flux out of solution comes from solvated NO, surface trioxide, and gas phase trioxide, and these last two populations are greatly increased when the solution is agitated (Fig 3.12).

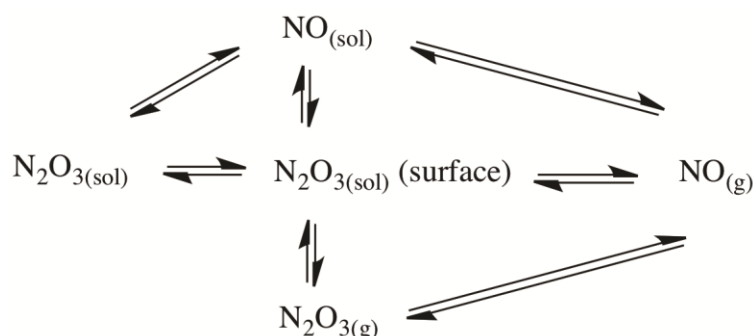


Fig. 3.12: The equilibrium of NO with a trioxide solution.

Slow stirring and formation at cooler temperatures thus allows for solutions to form that are super-saturated, and hence the greater values seen in Table 3.5. The ratio of 1.7 thus represents solutions at an agitated equilibrium, like a can of root beer with most of its 'fizz' shaken out. This illustrates once again the peril of trying to understand these solutions apart from their system: there is no single value that can be given for the 'true' equilibrium of trioxide/tetroxide/nitric oxide.

Results more in keeping with Vosper's can be reproduced by the simple addition of measured amounts of gas and solvent into evacuated vessels, followed by vigorous shaking. In Table 3.6, we see the results of such an experiment (Exp 3.5). Here, 40 mL of NO and 10 mL of O₂ (at 1 atm, 298 K) have been introduced to a 54 mL vessel along with 3 mL of solvent, then shaken for 5 minutes. Measuring the resulting solutions by UV-Vis, trioxide yields between ~20-50% are found (ratios of 1.8 to 1.9), using their extinction coefficients.

Table 3.6: N₂O₃ Formation in solvent by violent agitation

Solvent	* ϵ_{max} (cm ² /mol)	25°C Formation (mmol/L)	-78°C Formation (mmol/L)	*% Yield warm/cold
Dichloromethane	9.2	50 (2)	145 (15)	18/52
Acetonitrile	10.7	51 (3)	129 (8)	19/47
Benzene	16.3	35.1 (0.1)	**	13/**
Chlorobenzene	15.2	25 (2)	119 (7)	9/43
Toluene	18.7	32 (2)	130 (11)	12/47
Xylenes	20.3	32 (2)	130 (9)	12/47
Mesitylene	20.8	81 (5)	127 (12)	29/46
Anisole	17.9	28 (7)	138 (4)	10/50

* ϵ_{max} values obtained from Shaw and Vosper (1972), and used to calculate %Yield.

** Benzene is solid at this temperature.

A note must be made about anisole, which breaks the pattern in extinction coefficients established for increasing ring donation. It is likely that the interactions here become so strong that dinitrogen trioxide begins to break down; a very concentrated solution will slowly turn an inky black, and hence any calculations are likely to be inaccurate.

If super-saturated solutions are thus being formed, to what extent do they endure? Will the high grade solutions prepared at 0°C remain so when warmed to 25°C? To gain a quantified idea, in Experiment 3-6, solutions are prepared and left in open cuvettes to vent into a large inert atmosphere vessel. The inert atmosphere was necessary to prevent water and oxygen from being absorbed from the air, which would thus destroy rather than release N₂O₃; also, the escaping vapours are hazardous. Monitoring by UV-Vis, the loss of N₂O₃ is measured over a period of hours. This is compared to a sealed control, and clearly contrasts with the behaviour

of pure, exposed N_2O_3 (which boils away in mere moments). Chlorobenzene solution provides a typical example (Fig 3.13):

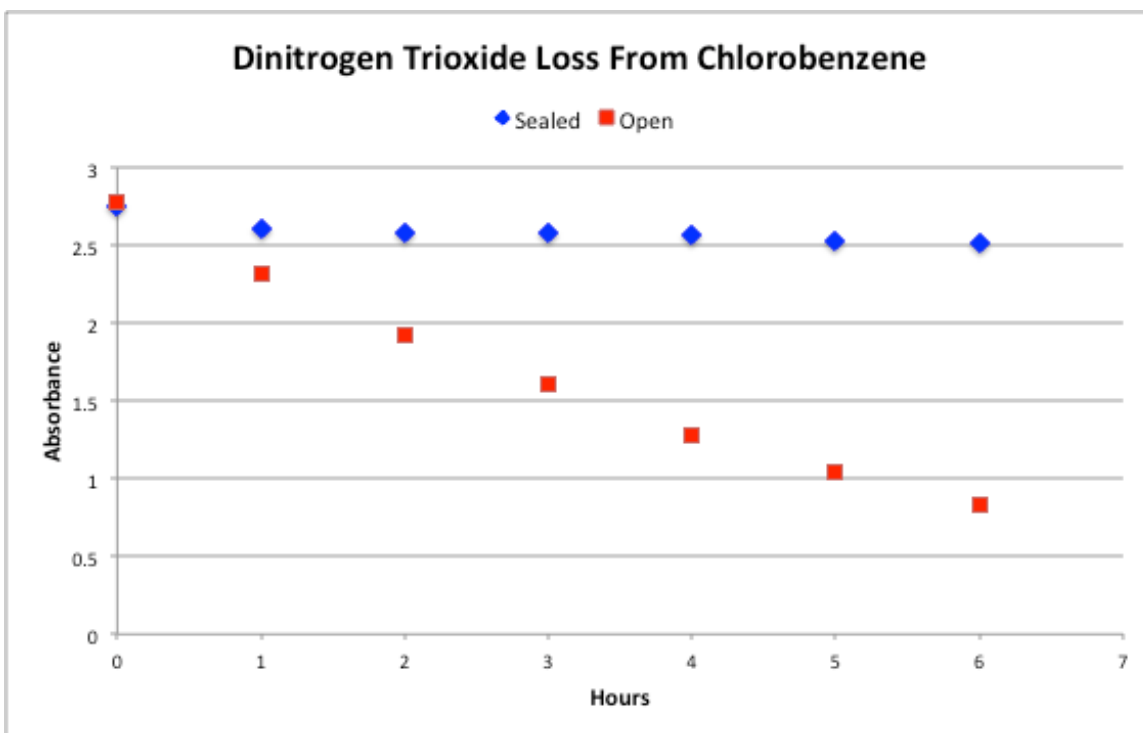


Fig 3.13: Trioxide loss from 1 cm² surface area of a 3 cm³ volume.

This measurement can in fact be extended to 24 hours, where the open solution is found to have 13% of its original N_2O_3 , while the sealed vessel has continued a linear course (representing a slow leak). The loss follows the standard first order decay, and hence a rate constant can be easily calculated for each solvent so tested (Table 3.7):

Table 3.7: Rate of trioxide loss from a still solution (1 cm² surface)

Solvent	k_{loss} (s ⁻¹)	Solvent Viscosity ³⁹	Boiling point (°C)
Acetonitrile	1.93×10^{-4}	0.345	82
Dichloromethane	3.77×10^{-4}	0.393	40
Toluene	7.33×10^{-5}	0.526	111
Chlorobenzene	5.21×10^{-5}	0.799	131

To be sure, a part of this effect is due to the sluggish diffusion of N_2O_3 in solution and the static environment: the upper layer of the sample will bleach yellow much more quickly while the lower layers will retain their intense colour. Before each measurement, the cuvettes are mixed by gentle inversion, and so the decrease represents, specifically, the loss from a total volume of 3 cm^3 through a surface area of 1 cm^2 . Stirring will speed this, while bubbling with argon gas can remove all the N_2O_3 in minutes. From the four cases in Table 3.5, it might be inferred that viscosity is the determining factor in trioxide retention, but on further analysis the relationship is loose, at best. DCM is more viscous than acetonitrile, yet loses trioxide at almost twice the rate. The 0.1 viscosity difference between DCM and toluene amounts to a five-fold increase in rate, but the ~ 0.3 viscosity difference between toluene and chlorobenzene makes almost no difference at all. There is a rough correlation (Fig 3.14) between the rate of loss and the boiling point (and hence the vapour pressure), but as the sharp change between toluene and chlorobenzene shows, this alone is not predictive.

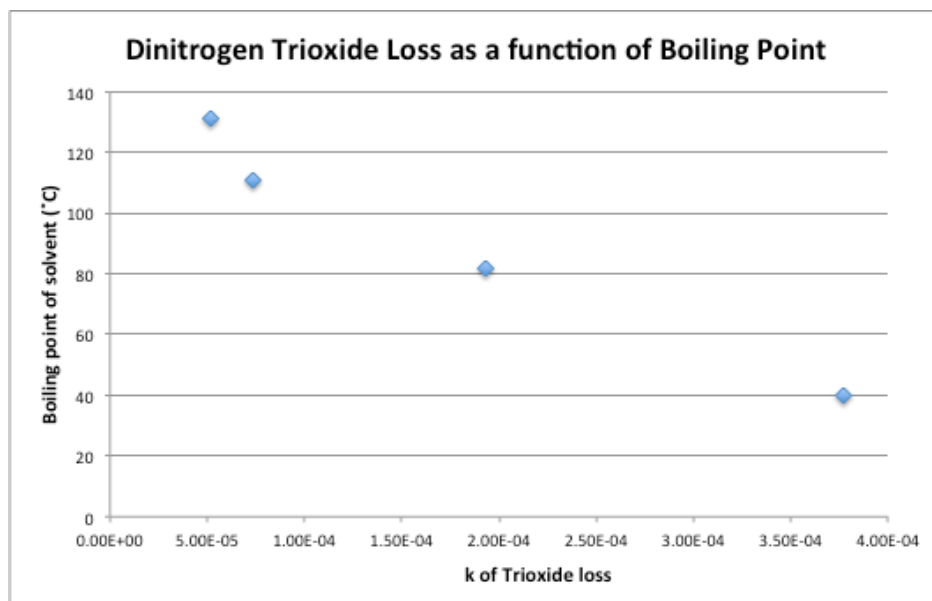


Fig 3.14: The rate constant (k) of N_2O_3 loss from a given solvent, compared to the boiling point of that solvent (points from left to right: chlorobenzene, toluene, acetonitrile, dichloromethane).

We thus see that trioxide solutions with a concentration in the millimolar range ($\sim 0.25 \text{ M}$) do not immediately degrade. A solution prepared at 0°C may be warmed and used without measurable loss, so long as the atmosphere above it remains flushed with NO . Nevertheless, there are changes significant enough to frustrate analytical work.

This returns us to the second disparity with the published results, that of the extinction coefficients of N_2O_3 in aromatic solutions. This phenomenon of the absorption being significantly lower at room temperature in aromatic solutions, even when losses for N_2O_3 decay are accounted for, bears upon the question of thermochromism.

3.6 Solvatochromism and Thermochromism

That dinitrogen trioxide solutions are solvatochromic is beyond question, as can be seen Table 3.2. Different solvent-solute interactions cause remarkable shifts in the UV-Vis peak position and hence the colour. The difference between the interactions of polar solvents versus aromatic solvents is also evident, as the case of chlorobenzene vs. benzene makes clear, and the narrowing of the $n/\pi \rightarrow \pi^*$ gap attests. Aromatic solvents in particular seem to have a close interaction with trioxide and stabilize it to a greater degree, as was seen by their slightly greater ability to retard trioxide loss to the atmosphere. Anisole seems to be the limiting case of this interaction, since at this degree of ring donation the solute and solvent begin to react chemically. Finally, the fact that the extinction coefficient of dinitrogen trioxide is so radically different in different solvents, by a factor of two, shows that this interaction is significant; the highest extinction coefficients are also found in aromatic solvents. Solvent interactions do not merely change the energy of absorption (peak position); they also change the degree of the absorption (peak intensity).

Thermochromism, by contrast, is regarded as an artifact. Mason¹ and Vosper¹² agree that trioxide solutions are not thermochromic at low temperatures, and Vosper insisted that this was so at all temperatures. Dinitrogen trioxide, the thinking goes, is simply blue and any deviation from this is due to contamination as the solution warms. The pure trioxide at low temperature is commonly reported as azure blue ($\lambda_{\text{max}} \sim 660 \text{ nm}$), almost identical to how it is found in acetonitrile; by contrast, the pure trioxide at room temperature is a brownish-green, and is

reported as having an absorption maximum of 720 nm (near where it is found in chlorobenzene), which is thought to reflect its state of near full dissociation into NO and brown NO₂.

There is some truth to this claim, as dissociation is seen to increase as solutions are warmed. Consider, however, that greater substitution on the aromatic ring leads to green colours even at low temperatures, and thus a xylene solution is always green. Interpreting this by the logic that green colours stem from nitrogen dioxide would suggest that these solvents have difficulty maintaining the trioxide, which is breaking apart and liberating NO₂. It would be strange, however, to imagine that solvated trioxide is 'breaking apart' even at temperatures where it would normally form spontaneously, in a solvent that stabilizes it. A closer look at the spectra in acetonitrile and xylene (Fig 3.15) reveals some important details of the colour shift:

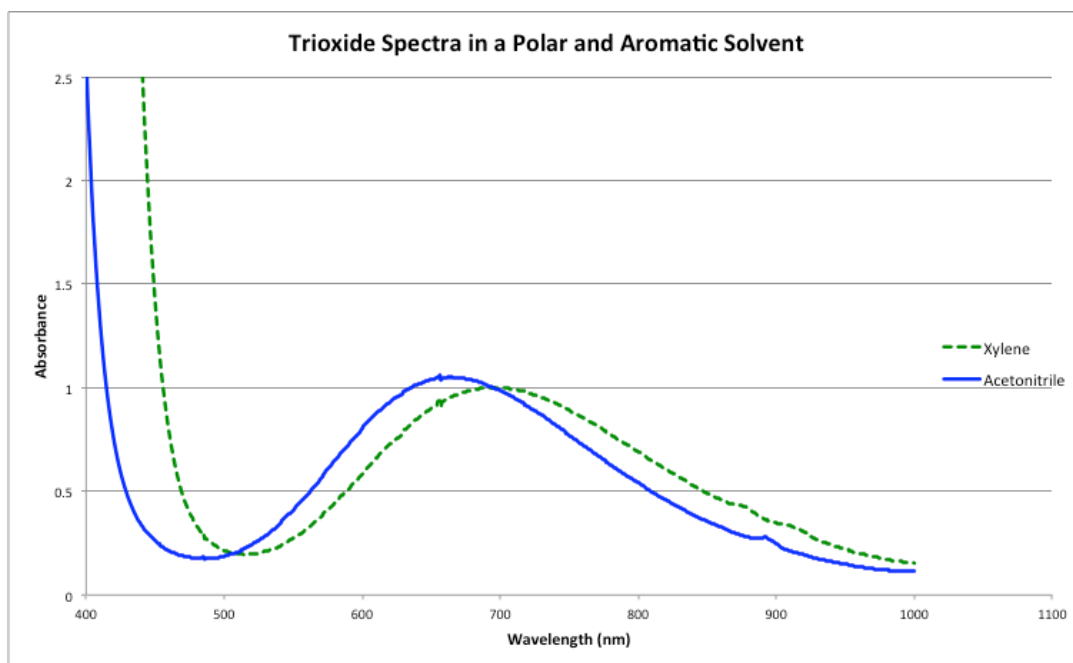


Fig 3.15: Trioxide in xylene and acetonitrile at 25°C (concentrations chosen for best overlap).

The resulting colour difference (green xylene vs blue acetonitrile) arises from two main factors. First, the maximum of the visible absorption is blue shifted in acetonitrile by 30 nm. However, both of these peaks are still in the 'red' region, meaning our eyes would perceive them as different shades of green, were they a single narrow band. Naturally the broad slopes absorb some of all the colours, but this absorption predominates. The second aspect, easily ignored, is how the cutoff of the intense UV absorption impinges on the visible region: deep violet is absorbed in both (giving a bit of yellow character), and in xylene, this absorption (which I will refer to as the violet wall) advances into blue absorption. Thus acetonitrile solutions absorb predominately red and deep violet, leaving primarily blue-green, which ends up looking blue. Trioxide in xylene is similar but loses much of its blue character to the advancing violet wall, while its visible peak is shifted more into the red region, and so ends by looking green. Thus a change from blue to green is accomplished by a) absorption in the violet/blue region, and/or b) absorption in the red region.

How can the presence of $\text{NO}_2/\text{N}_2\text{O}_4$ effect a colour change? Dinitrogen tetroxide is considered colourless⁵³, with an extremely intense band at ~ 220 nm and a moderately intense broad absorption at 343 nm ($\epsilon_{\text{max}} \sim 200$ depending on the solvent) that should be covered by trioxide's own absorption. It is in equilibrium with nitrogen dioxide, however, whose spectrum Hall and Blacet⁵⁴ managed to untangle from tetroxide to show an extremely broad, detailed absorption curve, starting around 300 nm and extending well into the 500 nm region, with a maximum around 400 nm and an absorption coefficient similar to tetroxide (~ 200), and still absorbing strongly (~ 100) in the minimum of the trioxide absorption (the

trough around 500 nm). In practice, because NO_2 is only present in minute amounts, it is evident only by a small 'foot' which creeps into the 500 nm trough; this absorbs some light the way that the violet wall does, such that small amounts of NO_2 can also give a green colour by absorbing more blue/violet light.

Thus the apparent thermochromism of dinitrogen trioxide solutions can be partly explained by increases in NO_2 concentration. The claim that the thermochromism can be *entirely* explained in this way seems to be in frank disagreement with the evidence, however. While it is true that solutions below -40°C do not vary much in appearance, and also true that at temperatures above this dissociation becomes more important, it is plain that a solution prepared at 25°C and sealed without headspace (preventing any gas from entering or leaving the solution) will, when cooled to -78°C , change its spectrum. This transformation may be repeated as many times as desired. Indeed, as seen in Fig 3.16, a vial containing toluene can be turned different colours by dipping one end in a cold bath. The shift seen in the UV-Vis spectrum of toluene (Fig 3.17) is typical for all aromatic solvents, and the shift for acetonitrile (Fig 3.18) is typical for non-aromatic, polar solvents.



Fig 3.16: A toluene N_2O_3 solution at 25°C (left), then dipped into a -78°C bath (right).

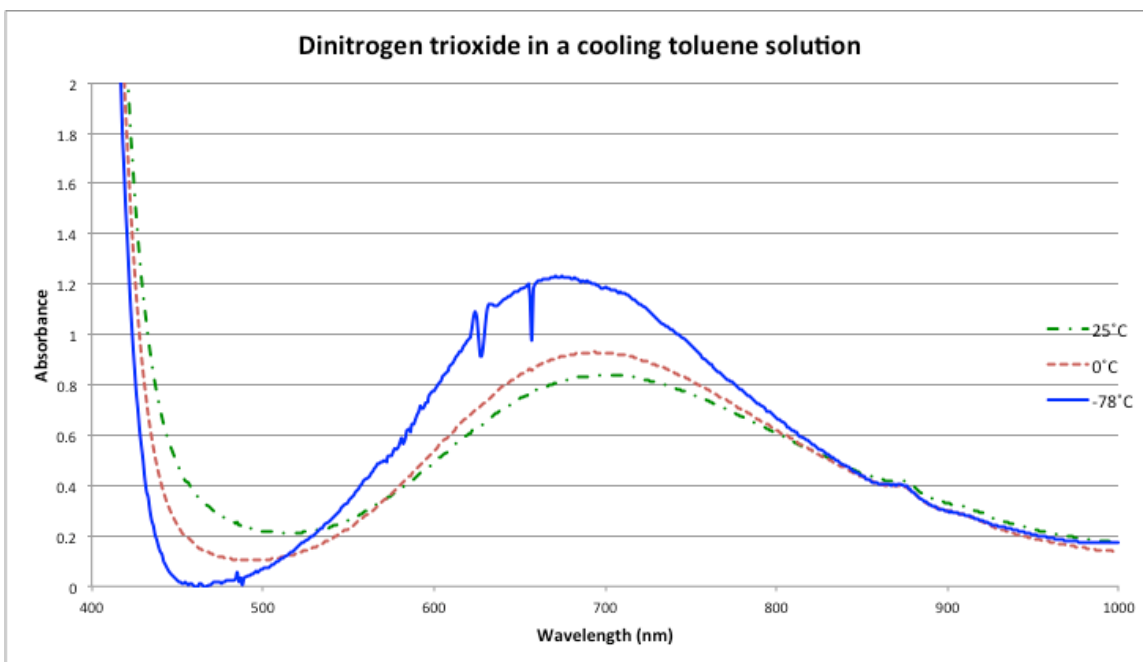


Fig 3.17: A 0.08 M trioxide solution in toluene cooled from 25, to 0, then -78°C.

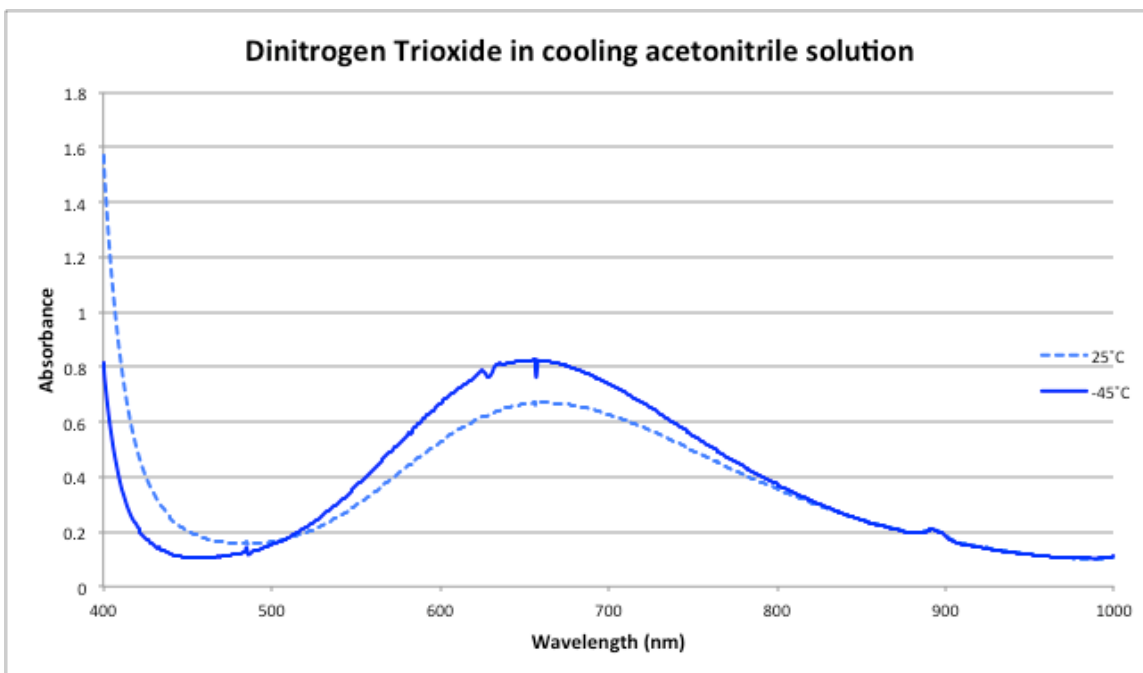


Fig 3.18: A 0.08 M trioxide solution in acetonitrile cooled from 25 to -45°C.

The blue shift of the visible peak is quite minor for non-aromatic polar solvents, and more pronounced for aromatic ones. The change in the strength of

absorption is likewise far greater in aromatic solvents. Visibly, acetonitrile solutions merely deepen their blue colour, whereas toluene shifts dramatically from green to blue.

The obvious movement of the visible peak is difficult to square with the claim that there is no thermochromism. An examination of Vosper's paper¹² on the subject shows two spectra. In one, warming a solution from -10°C to 30°C produces no serious peak changes until the NO_2 peak begins to cover it at 30°C , because this is a solution of nearly pure tetroxide (N-O ratio 1.996). Of course, at this concentration, any decrease or shift in the peak will be difficult to spot as it is swallowed up by the NO_2 . In a second series of traces, recorded at -10°C , there is a small blue shift, but not from temperature; rather, it is as the N-O ratio is decreased by NO addition, from 1.946 to 1.735. Vosper credited this to the greater polarity of the trioxide, also remarking that:

" There is also, apparently, a small increase in the extinction coefficients as the concentration of dinitrogen trioxide increases. This could be due to some systematic error, but it is naive to expect the Beer-Lambert law to be exactly obeyed when the nature of the solvent is continually changing."

This apparent increase is exactly the opposite of what I have found at room temperature (where deviations from the Beer-Lambert law lead to a *decrease* in extinction coefficients at higher concentrations), although the blue shifting of the peak is in accord with my results. If the formation of tetroxide causes the peaks to red shift due to decreased polarity, then the shift in Fig 3.12 could be caused by half of the trioxide dissociating on warming to give a half-equivalent of tetroxide. This is a prediction easily tested by diluting one trioxide solution by half with pure toluene,

and a second solution with an equimolar amount of tetroxide/toluene solution (this will be over twice the relative level that would be present should a trioxide solution dissociate by half upon warming). The result is seen in Fig 3.19: a small increase in the violet region occurs due to the addition of NO_2 (and by the principle of additivity, much of this absorbance is from the trioxide that was already present) but the visible peak at 700 nm does not change. It is clear that $\text{NO}_2/\text{N}_2\text{O}_4$ does not cause the red shift that is seen when changing temperatures.

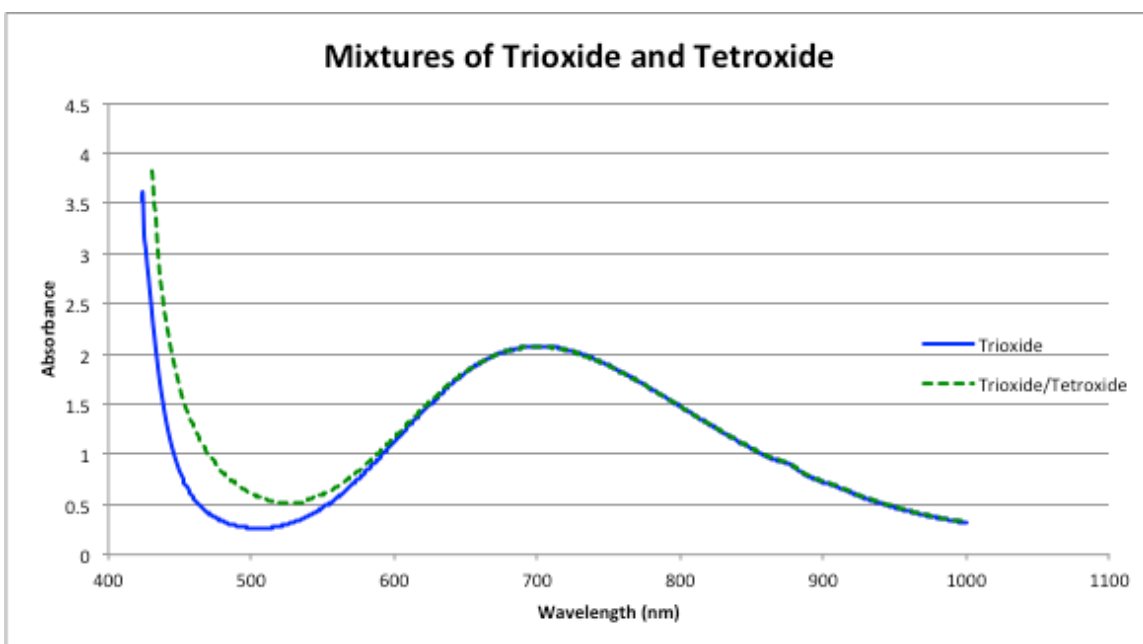


Fig 3.19: A 0.12 M trioxide solution diluted by half in toluene, and with a toluene/tetroxide solution, at 25°C.

The difference in the strength of the absorbance is presumed to be due to the dissociation of N_2O_3 into NO_2 and NO . This is a reasonable assumption, as this does indeed happen. However, this is inadequate to explain the degree of the change seen. Table 3.8 shows the shift in peak positions as solutions are cooled from 25°C to -78°C, as well as the ratio of the peak strength when measured at their λ_{max} , after

correction for the dilution factor due to thermal expansion. These solutions are formed at 25°C and are sealed without headspace; if we assume that at this point they contain the maximum possible amount of solvated NO gas, any increase in trioxide concentration must come from the solvated NO gas associating with NO₂/N₂O₄. This extra trioxide formed from cooling plus the trioxide present at 25°C is expressed as a percent of the trioxide necessary to account for the level of absorption found at low temperature, if the extinction coefficient were constant at the literature values. Benzene has such a narrow liquid range that it could not be used for this analysis. The extinction coefficient that would need to be found at 25°C to accommodate this shortfall is calculated from the ratio of the high and low temperature absorbances. Finally, this result is compared to the values taken from Table 3.5, which were found by experiment.

Table 3.8: Visible peak of trioxide solutions cooled to -78°C

Solvent	Blue Shift (nm)*	Peak Intensity Ratio	% Trioxide Accounted For	Calculated ϵ (25°C)	Found ϵ (25°C)
Acetonitrile**	19	0.838	100	10.9(2)	9.8 (7)
Dichloromethane	25	0.653	88	8.1(2)	8.5 (7)
Chlorobenzene	27	0.730	81	12.3(2)	10.9(9)
Toluene	33	0.711	87	16.2(3)	15.3(7)
Xylene	36	0.631	77	15.7(3)	17.4(8)
Mesitylene	34	0.612	74	15.4(3)	16.4(8)

*Calculated from the values in Table 3.2 and the published values at -78°C.

** Taken at the m.p. of acetonitrile, -45°C.

A pronounced shortfall is seen between the measured trioxide concentration and what the published extinction coefficients predict should be there; this effect is minor or non-existent in the polar solvents but becomes a serious deviation in aromatic ones. A change in extinction coefficients between 25°C and -78°C is thus

necessary to account for the increased absorption (or conversely, to account for why the absorption falls more quickly than it should when the solutions are warmed). The extinction coefficients that are theoretically necessary are found to be in fair agreement with the coefficients that are in fact found at 25°C.

Thus while dinitrogen trioxide may not be thermochromic in its pure form, and perhaps not in solutions at low temperature, there is a distinct thermochromism, especially in aromatic solvents. This should not seem strange, given that the solvent-solute interactions produce such dramatic solvatochromism as well as changes in the extinction coefficient. The deviations seen between the extinction coefficients at room temperature and the literature values (calculated at low temperature) are thus explained as part of this thermochromic effect.

It is an error to imagine that dinitrogen trioxide exists as a kind of Platonic ideal of a molecule. Consider the limiting cases: pure crystalline dinitrogen trioxide is a radical pair of nitric oxide and nitrogen dioxide, ON-NO₂, that absorbs strongly in the visible region to appear bright blue; warming it breaks the bonds apart, ON---NO₂, and it becomes colourless monoxide and strongly violet-blue absorbing dioxide. If solvated trioxide exists in a stabilized solvent intermediate form, it is not unrealistic to expect that as it warms without breaking, the nature of its interaction with the solvent molecule may change. It would absorb less strongly, and gain some of the absorption character of its two constituents.

3.7 Conclusions

The apparent stability or instability of any material thing is only one shade on a long spectrum that describes the dynamic nature of matter, and chemists deal with this fact every time they change the temperature of a reaction. It is one of the chief tools for the transformation of matter, and it can completely rewrite the nature of a substance. The only limit to the applicability of temperature as a tool for transformation is whether the species to be involved will exist together in this new temperature regime. No one thinks of wood and water as being particularly reactive together, but this is only because for the temperature regime in which they can exist together (0-100°C) they are not-- provided one keeps one's cool, one could sail a boiling sea in a wooden boat. But high pressure studies have shown that in super-critical water, which is liquid above 100°C, wood dissolves easily⁵⁵.

Extending the borders of temperature regimes allows exciting new possibilities in chemistry, and dissolving dinitrogen trioxide in organic solutions is one such extension. The types of reactions that may occur with this oxidizing, nitrating species at -78°C is quite different from those at 0°C, or 25°C. When N₂O₃ is stabilized in this way, it is not only possible to work with it at ambient temperatures, but also to use it at elevated temperatures. Sealing a toluene or dichloromethane solution in a high pressure Fisher-Porter vessel, it is possible to raise the operating temperature of N₂O₃ as high as 70°C, though at this temperature most solvents have begun to react considerably with the nitrogen species and

various side reactions become important. Nevertheless, the ability to work at these temperatures gives chemists an expanded toolbox.

This work demonstrates conclusively that dinitrogen trioxide, far from being a curiosity or merely a transient intermediate, can with a little care be prepared and employed like a common reagent. The nature of the molecule, unfortunately, prohibits the formation of rigorously pure trioxide solutions at elevated temperatures, but the solutions can be enriched in N_2O_3 substantially. Thus any chemistry that results must be interpreted as potentially being the result of tetroxide, and where ambiguities result, a comparison must be made to a pure tetroxide solution. Some reactions may even be the result of a trioxide/tetroxide interaction. Nevertheless, with these trioxide enriched solutions, we can begin to explore the chemistry of trioxide at elevated temperatures. In the next chapter, I will describe some of the results of its use in common organic chemical reactions, some of which are similar to known dinitrogen trioxide/nitrous acid reactions but are possible to carry out in aprotic environments, while others are unique to the warm, solvated version of this molecule.

3.8 Experimental:

(Exp 3.1) Cold Condensation: A Schlenk flask is flushed with argon gas, and then immersed in a dry ice/ethanol slurry to cool it to -78°C . A mixture of O_2 and NO gas (with NO in great excess) is passed slowly into the flask. This is best achieved by venting through the side arm while directing the mixed gas flow through a glass tube introduced through a septum in the neck. N_2O_3 will condense as a blue liquid

on the upper walls, which should drip down to the bottom. When the quantity desired is reached, oxygen flow should be halted and NO flow continued, to drive the reaction to completion. Allowing the vessel to warm slightly will cause dinitrogen tetroxide/trioxide slurry that has adhered to the walls to liquefy and aid in exposing it to the nitric oxide gas.

This condensation method produces the highest purity (99%) dinitrogen trioxide, which can then be solvated by slowly adding chilled solvent to the mixture. It may also be measured by weights or transferred as a neat liquid by mechanical micropipettes (plastic tips, once cooled, can transfer known volumes of liquid without significant error).

(Exp 3.2) Dynamic absorption: A sealed vessel equipped with a stir bar is evacuated under high vacuum, and is then flushed with nitric oxide gas. Solvent is then injected. Alternatively, solvent can be added first, then freeze-thaw-degassed or sparged with argon, before finally flushing with NO. A measured amount of oxygen gas is then injected with a gas tight syringe. The mixture is allowed to stir gently for 5 minutes while under a weak positive pressure of NO gas (~ 0.7 kPa above atmospheric pressure).

A solution prepared in this way will slowly absorb NO until it reaches a saturation point. The oxygen should be introduced slowly in steps, followed by some NO exposure, or else high pressures will develop; slow addition allows it to become tetroxide/trioxide and become solvated. Stepwise addition allows one to add liters of gas to only a few millilitres of solvent in a 50 mL vessel without developing any

overpressure. The nitric oxide atmosphere should be left intact to protect the solution, or replaced if the vessel must be opened or otherwise disturbed.

(Exp 3-3) Evans Determination: A 0.01 M dichloromethane/ N_2O_3 solution is prepared by dynamic absorption (as in Exp. 3-2) into 2 mL of deuterated solvent in a 54 mL vessel. The concentration is quantified by UV-Vis extinction coefficient values. A small amount of pure deuterated dichloromethane is placed in the inner tube and immersed in the N_2O_3 solution. The tube is then flushed with NO gas and sealed. A second tube is prepared using N_2O_3 produced as in Exp 3.1, using O_2 and excess NO, and the desired volume is transferred using a mechanical pipette. The literature density of 1.447 g/cm^3 for N_2O_3 is assumed. ^1H NMR measurements are performed on both a 400 and 500 MHz Bruker NMR instrument. This process is repeated for acetonitrile, to create a 0.3 M solution.

(Exp 3.4) O_2 Titration: The solutions are prepared by the dynamic absorption method at 0°C (cooled in an ice bath) and at room temperature, using 10 mL of solvent and 30 mL of oxygen. The stirring is halted, the atmosphere within the preparatory vessel is quickly removed with a flow of argon, and oxygen is introduced by increments (first by 10 mL, scaling down to 0.25 mL as the endpoint nears). As the lack of NO in the headspace allows dissociation, the remaining NO can be visualized by cooling the solution in a dry ice/ethanol slurry, which will reform any NO into N_2O_3 . The solution should be warmed to speed the reaction of O_2 . At low concentrations, the reaction can be very slow, and a minimum of ten minutes

between injections should be allowed, with vigorous stirring. The final solution should be compared to a prepared tetroxide solution in the appropriate solvent, as this can possess its own faint colouration; such a solution should become less coloured when cooled in dry ice.

(Exp 3.5) Equilibrium gas trapping: A 50 mL vessel (true total volume 54 cm³) is evacuated under high vacuum, and 40 mL of purified NO gas along with 10 mL of O₂ gas are injected. In the first run, these gases are then chilled to -78°C until they condense as N₂O₃; in the second they are left at room temperature. Next, 3 mL of dried solvent is injected, and the mixture is shaken vigorously for 30 seconds. The vessel is warmed (if necessary) then opened to an argon gas stream and the liquid is removed by pipette and measured by UV within 30 seconds inside a stoppered cuvette. The visible range maximum is recorded (varies by solvent) and concentration is gauged by established extinction coefficients.

(Exp 3.6) Trioxide Exhaustion: Quartz cuvettes are filled with saturated solutions of dinitrogen trioxide prepared at 0°C, then are allowed to warm to 23°C. A control cuvette is left tightly stoppered and parafilmed, while a second bearing the same solvent is sealed inside a 1 L jar flushed with inert atmosphere. This atmosphere is static but is replaced at every measurement. Solutions are monitored by UV-Vis at the appropriate $\pi_{\max}$ in the visible region.

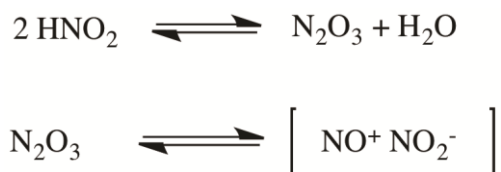
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Chapter 4: The Organic Chemistry of Solvated Dinitrogen Trioxide

Nitrous acid is a standard reagent in organic chemistry, commonly used for nitrosations (addition of NO_2^+), nitrosylations (addition of NO^+) and diazotizations (formation of N_2^+). Textbooks¹ cite dinitrogen trioxide as the essential intermediate in this reaction; as discussed in Chapter 1, it forms from the dehydration of nitrous acid (Eq 4.1), and in terms of reactivity, can be considered the ionic $[\text{NO}^+][\text{NO}_2^-]$ intermediate species.



Eq 4.1: Equilibrium of nitrous acid with the active 'nitrous anhydride' form.

The assumption one would make of the reactivity of pure or solvated dinitrogen trioxide is that it should perform the same function, and indeed in some cases it does. Vosper and Lovejoy² had used dinitrogen trioxide solutions at low temperature as a means of nitrosating primary and secondary amines, and found that they ably perform this function. On the other hand, it is by no means clear that this is the *only* way the molecule may behave. As noted in the preceding chapter, electrochemical studies³ of solvated dinitrogen trioxide suggest that it does not easily dissociate into its ions under these conditions. It is possible that the availability of protons is the key to allowing the trioxide to break down in an ionic rather than radical fashion.

A second reasonable assumption is that as a highly reactive, highly oxidizing volatile compound composed of two stable radicals, N_2O_3 should behave as an extremely harsh oxidant, and one might expect its reactions to be variable and 'dirty', with many side products. Again, in some cases this is true, but as we shall see, N_2O_3 reactions can be surprisingly selective. For a quick visual comparison, below is the ^1H NMR spectra taken of the crude reaction mixture between pentylamine and nitrous acid (Fig 4.1) (D_2O solvent):

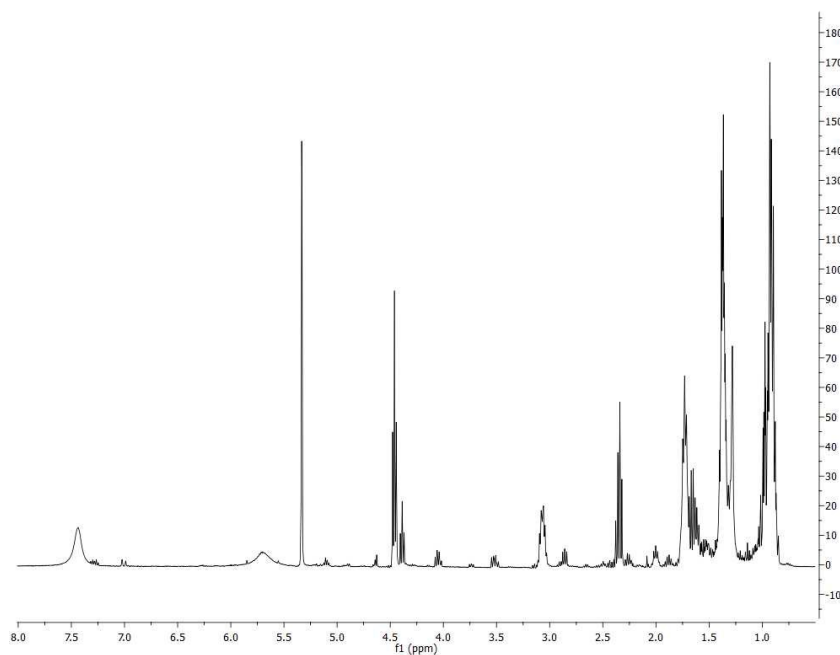


Fig 4.1: Crude product of pentylamine and nitrous acid.

Next, the same reaction carried out in an organic dinitrogen trioxide solution (CDCl_3 solvent):

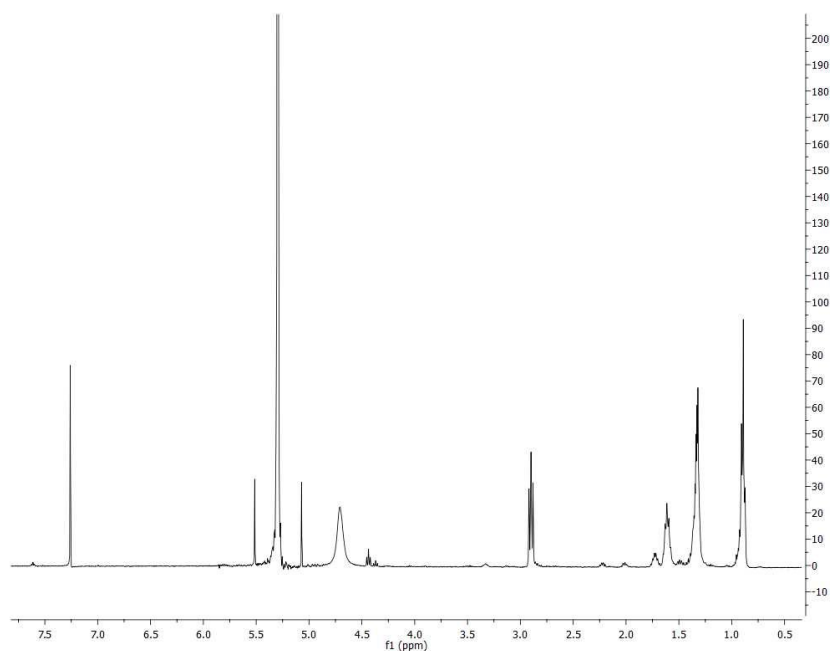


Fig 4.2: Crude reaction product of pentylamine and N_2O_3 in CDCl_3 .

While neither reaction is without side product, the difference in both the number and quantity of those side products is stark.

To examine in detail how dinitrogen trioxide behaves in solution, especially when it is deprived of proton sources and where solvent stabilization may alter its chemical character, reactivity studies were carried out for a range of reactive organic compounds, some known to react with nitrosating agents, and others unknown. Reactions with metals, inorganic compounds, and uncommon species will be discussed in the next chapter.

4.1: Experimental

This chemistry was carried out in accord with the methods outlined in the General Experimental section. Unless otherwise specified, 'trioxide' will be used in

place of 'dinitrogen trioxide' and 'trioxide solution' will designate an organic solution of same. Anhydrous trioxide solutions are generated using the dynamic absorption method and handled as described in General Experimental. 'Quenching with hexane' refers to the addition of hexane to cause the trioxide to break up and more easily boil out of the solution.

Most reactions were carried out in either dichloromethane or toluene. In no experiment did the choice of one over the other change the basic chemistry observed, but choice of solvent does affect the convenience of the work-up process and hence reported yield. The solvent indicated should be considered as the most practical. Reported yields are determined from the weight of the recovered and purified product, except where otherwise noted. Major products that have been identified are given in **bold**, as are important spectral peaks. Products are generally identified by comparison to a commercially obtained pure sample or to a sample prepared by literature techniques, and are cited as such. Further details and a discussion of the results will be given in Section 4.3, and general conclusions will follow in Section 4.4.

(4.1-a) Benzaldehyde: A 0.5 mol/L trioxide solution is formed in 10 mL benzaldehyde at 0°C. A 3 mL sample vial is filled completely with this solution, sealed, and left at room temperature for two weeks. Evaporating the solvent under reduced pressure yields crystalline **benzoic acid** (pure by NMR) in a yield quantitative to the amount of trioxide initially present.

(4.1-b) Hexanal: One mL of hexanal is added dropwise to 10 mL of an equimolar trioxide solution in toluene at 0°C. Three mL is withdrawn and sealed in a small vial with minimal headspace, and left at room temperature for three days. Evaporation of the solvent under reduced pressure gives **hexanoic acid** in quantitative yield. ¹HNMR (CD₂Cl₂): 0.95 (sx), 1.37 (sp), 1.64 (qn), 2.36 (qn), 9.65 (broad).

(4.1-c) Pyridine: Adding pyridine to a toluene/trioxide solution immediately produces a small amount of white precipitate, **pyridinium nitrate** (IR: 3105, 3068, 1636, 1535, 1487, 1354 (vs), 754, 678) in a yield dependent on the moisture content of the pyridine (1 mL of pyridine dried for 24 hours on molecular sieves and redistilled was found to produce a 2% yield of the nitrate). Dry pyridine will not react.

(4.1-d) 2-propanol: Two mL of isopropanol is diluted in 2 mL of toluene and added dropwise to 10 mL of 1.31 mol/L toluene/trioxide solution (2:1 ratio of isopropanol to trioxide) at 0°C and allowed to stir for 10 minutes. The crude mixture was then sampled and examined immediately by NMR spectroscopy; starting material was determined to have been consumed, and **isopropyl nitrite**¹, (H₃C-HC(O-N=O)-CH₃), was found to be the only product. ¹HNMR (CD₂Cl₂): 5.65 (sp, 1H),

1.41 (d, 6H). UV-Vis: 325, 336, 348, 360, 373, 390 (broad peak, fine structure). It is recovered as a greenish yellow liquid by three rounds of trap-to-trap cold distillation. Yield: 45%. Repeating the experiment at room temperature will produce a like amount of **acetone**, with the evolution of nitric oxide gas.

(4.1-e) t-butanol: The solid alcohol is dissolved in 2 mL of toluene, and the reaction is carried out as in 4.1-a). The product is purified using four rounds of trap-to-trap vacuum distillation. Product is **t-butyl nitrite**¹ as a greenish yellow liquid. Yield: 41%. ¹HNMR: 1.588 (s). UV-Vis: 340, 352, 365, 380, 398 (broad peak with fine structure).

(4.1-f) Mercaptoethanol: One mL is added to 10 mL of an equimolar trioxide solution in dichloromethane at 0°C immediately produces a bright, cherry red solution, which is stable on ice but at room temperature will slowly produce an atmosphere of nitric oxide, over a duration of days. Identified by UV-Vis as **2-nitrosothio-ethanol**^{1,4,5} (O=N-S-C₂H₄-OH) in 55% yield (calculated from the literature extinction coefficient). UV-Vis: 340, 515, 548 nm.

(4.1-g) Benzyl mercaptan: One mL of the reactant is added dropwise to 10 mL of a dichloromethane solution of trioxide in a 1:1 mercaptan to trioxide ratio at

0°C. Over a few seconds the solution will become red. The product is sampled in the mother liquor, and is identified by UV as **benzyl thionitrite**. Yield: 51%. UV-Vis: 340, 515, 548 nm. Yield is calculated from the solution concentration, using the literature value at 548 nm, $\epsilon_0 = 26 \text{ L}/(\text{mol} \cdot \text{cm})^6$.

(4.1-h) Phenol: One gram is dissolved in 2 mL toluene and added to 10 mL of an equimolar trioxide/toluene solution at 0°C; it is stirred for 5 minutes, then quenched with 50 mL of hexane. Products 1 and 2 are removed with the hexane, while the third settles out as a dark oil (the colour is due to unidentified impurity). Product 2 is separated from product 1 by chilling in hexane (crystallizes as scarlet red needles). The dark impurity precipitates from product 3 when the mixture is dissolved in CH_2Cl_2 and chilled. Further purification is performed by 4+ rounds of recrystallization from hexane/ CH_2Cl_2 .

1. **o-nitrophenol**: Yield 19%. These yellow crystals are recovered from the evaporation of pure hexane washes. $^1\text{HNMR}$: 10.57 (br s, 1H), 8.103 (d, 1 H), 7.575 (t, 1H), 7.161 (d, 1H), 6.995 (t, 1H).

2. **diphenol quinone**: Yield 4% (see Results). It appears as scarlet crystals that precipitate out of pure hexane. $^1\text{HNMR}$: 7.25 (t, 4H), 6.93 (t, 2H), 6.84 (d, 4 H), 6.78 (s, 4H). CNMR : 207, 162, 136.49, 129.59, 120.60, 115.14. IR: 3374, 3270, 1640, 1591, 1471, 1370 (w) 1354 (w), 1318 (w), 1221, 879,

911, 758, 690. It is unstable in pure form, sublimes and is easily lost to evaporation.

3. **p-nitrophenol**: Yield 13%. The brown powder is recovered from evaporation of 50/50 hexane/dichloromethane washes. ^1H NMR (CDCl_3): 8.181 (d, 2H), 6.926 (d, 2H), 5.886 (br s, 1H).

Use of dinitrogen trioxide in excess (2:1) ratio produces **2,4-dinitrophenol** as the major product (determined by NMR measurement). ^1H NMR: 9.064 (s, 1 H), 8.467 (d, 1H), 7.359 (d, 1H).

(4.1-i) 4-bromophenol: Dissolved in 3 ml dichloromethane and added to 10 mL of an equimolar trioxide solution in dichloromethane. An intense, clear yellow solution forms immediately. This is stirred for 5 minutes. A rich yellow powder was recovered by evaporation and separated by silica column filtration (hexane/ethyl acetate eluent). The first product to elute is the major product (60% yield), which dries to a bright yellow semi-crystalline powder and recrystallizes easily from DCM/hexane into large square plates. Confirmed by NMR, IR and X-ray crystallography to be **2-nitro-4-bromophenol**. IR (cm^{-1}): 3280, 3105, 1616, 1525, 1474, 1339, 1247, 1231, 1164, 1112, 1077, 882, 834, 769, 656, 628, 525. ^1H NMR: 10.455 (s), 8.278 (d, $J=0.06$ Hz), 7.708 (dd, $J=0.22, 0.06$ Hz), 7.10 (d, $J=0.22$ Hz). Three other products were recovered in only trace amounts (yellow solutions that dry dark orange), which were not fully characterized.

(4.1-j) Nitrosobenzene: A few grains of nitrosobenzene (0.01 g) is dissolved in dry acetonitrile, then treated with an excess of acetonitrile/trioxide solution, and immediately purged with argon on ice for 2 minutes. The samples are withdrawn and diluted sufficiently to be observed by UV-Vis spectroscopy. The 290-295 nm twin peak of nitrosobenzene is transformed entirely to a single 280 nm peak, identical to a pure commercial sample of **nitrobenzene**.

(4.1-k) Pentylamine: One mL of amine is diluted in 3 mL of toluene and added to 10 ml of toluene/trioxide solution at 0°C in a 1:1 molar ratio. Nitrogen and nitric oxide gas rapidly evolve and the solution becomes bright orange. The solution is chilled at -20°C for several hours and the product separates as an oil (the solvent can also be removed under vacuum to achieve the same result). The red-orange oil is washed three times with hexane and mixed vigorously to produce a cloudy suspension. On sitting for ~30 min, the supernatant clarifies and may be decanted. By the third wash the major product is present as a yellow oil. The minor product may be recovered from the supernatant as a red to magenta oil (colour from unidentified trace product; smells strongly of cut grass).

-pentylammonium nitrate (Yield: 31%): ¹HNMR (CD₂Cl₂): 7.0-7.5 (broad s), 2.91 (t), 1.61 (m), ~1.3 (m), ~0.9 (m). CNMR (CDCl₃): 40.96, 29.54, 28.65, 22.25, 13.86. UV λ_{max} at 220-225 nm in ethanol. IR (thin film on an NaCl plate,

can react with KBr plates): 3032 (br), 2960, 2931, 2871, 1768, 1559, 1467, 1354 (vs, br), 1028, 935 (w), 831(w).

- **1-nitropentane** (Yield: 10%): ^1H NMR (CD_2Cl_2): 4.461 (t), 1.8- 0.8 (m).

Three other minor products are found by GCMS, including **1,3-dipentyltriazene**.

Restricting the amine/trioxide ratio to 2:1 produces a 26% yield of **pentylammonium nitrite** (IR: 1378, 1277. UV-Vis stretch over 360 nm region), and a 14% yield of 1-nitropentane.

Using an amine/trioxide ratio of 1:2, reaction proceeds as above, but the solution remains blue and the oil is blue-green on drying (will become yellow after a few hours at room temperature). The major product is pentylammonium nitrate in 54% yield, with nitropentane in 14% yield.

The gas is trapped using a pneumatic trough (upended graduated cylinder in a dish, filled with water), and sampled using an IR cell. NO vs N_2 volume is estimated from difference in total volume and remaining volume after the slow introduction of oxygen (NO becomes NO_2 which dissolves completely in water). One mL pentylamine will yield 111 mL of NO and 144 mL of nitrogen. Yield of nitrogen to pentylamine: 68%.

(4.1-l) Aniline: Distilled and recrystallized from ether at -20°C, and stored over molecular sieves. It is added dropwise to a trioxide solution at 0°C in a 1:1 ratio to produce a dark colour; a white to yellow precipitate forms over a few seconds. Filtering and washing with cold acetone gives the product **benzenediazonium nitrate**^{7,8}, pure by IR. Yield: 40%. IR (cm⁻¹): 3060, **2292**, 1567, 1458, 1382 (vs), 1318, 1302, 1072, 823, 758 (s), 666, 517.

WARNING: Benzenediazonium nitrate is highly explosive and will detonate on warming to 80°C, from sufficient friction, or from a sharp blow. Synthesis in large quantities is not recommended, and even small quantities should be filtered using gravity and a filter paper; loosen the filtrate before drying. DO NOT allow to dry in a sintered glass frit. It is soluble in H₂O, EtOH, MeOH.

Reversing the addition, adding trioxide to an aniline solution, or carrying out the reaction with excess aniline will result in an orange solution only, with no precipitate. Condensing this by evaporation yields a small amount of an oily liquid that crystallizes spontaneously, **1,3-biphenyltriazene**^{9,8} (IR (cm⁻¹): 3443, 3197, 1603 (s), 1502, 1466 (s), 1442, 1412 (s), 1385, 1245 (s), 1200, 1175, 764, 749, 684, 642).

(4.1-m) Dipropylamine: One mL is diluted in 3 mL of dichloromethane and added to 5 mL of a half equivalent of trioxide in dichloromethane at 0°C. White mist results but no gas is evolved. The solution is reduced by rotovap to an oil and washed with hexane to precipitate a white powder, **dipropylammonium nitrite**

$[(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{NH}_2^+\text{NO}_2]$ in 30% yield. $^1\text{HNMR}$ in CDCl_3 : 2.928 (t), 1.570 (sextuplet), 0.840 (t). IR: 2972, 2815, 1354, 1269. UV-Vis: broad peak at 354 nm. The yellow oil is recovered from the hexane and identified as **dipropylnitrosamine**
 $^{10,11}[(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{N-N=O}]$ in 44% yield. $^1\text{HNMR}$: 4.03 (t), 3.49 (t), 1.82 (sextuplet), 1.57 (sextuplet), 1.02 (t), 0.92 (t).

NOTE: Two peaks are seen in the proton NMR for the CH_2 groups alpha to the nitrogen because the interaction of the lone pair with the nitroso gives the N-N bond some double bond character, making the protons of each propyl group magnetically inequivalent¹².

(4.1-n) Pyrrole: The addition of 1 mL of pyrrole to an equimolar solution of trioxide in toluene or dichloromethane at 0°C immediately yields a black, tar-like substance, qualitatively similar to what is known as **pyrrole black**^{13,14}.

(4.1-o) Benzotriazole: One gram is dissolved in 5 mL dichloromethane and added dropwise to 10 mL of an equimolar trioxide solution in dichloromethane. The solution immediately becomes lime green and a precipitate forms. Dried under vacuum without air exposure to yield a bright yellow powder (IR (cm^{-1} , hex): 3092, 2789-2412 (br, multiple fine peaks), 1909 (br), **1805**, 1354, 1209, 1032, 976, 939, 847, 778, 742, 654).

When exposed to air, yellow powder bleaches white, and was identified as the salt **benzotriazole nitrate** (pure by NMR). Yield: 63%. IR (hex): 3099, 2795-2412 (br, multiple fine peaks), 1905, 1354 (s), 1209 (s), 980, 855 (vs), 742 (vs). ^1H NMR (CDCl_3): 7.97 (2H), 7.52 (2H) (appears as two pseudo-quartets of equal integration). ^{13}C NMR: 138.09, 126.30, 126.20, 114.14.

(4.1-p) Triethylamine: Purified by drying over CaCl_2 , distillation and storage over molecular sieves. Added dropwise to ~10 mL of trioxide solution in toluene, in a 1:2 triethylamine/trioxide ratio. This results in rapid formation of red colour darkening to brown, with a steady evolution of nitric oxide gas (1 mL yields 130 mL NO gas); the precipitate forms after a few seconds of stirring. The supernatant decanted off within 5 minutes, and the precipitate is washed with cold ether under inert gas, then dried under vacuum. Gives ~50% yield of **triethylammonium nitrite/nitrate**¹⁵ (based on weight of dried product to initial triethylamine, using ratio of nitrate/nitrite determined by UV-Vis to calculate weight) as a light yellow to red semi-crystalline material. ^1H NMR: 10.79 (broad s, not always seen), 3.148 (q), 1.329 (t). IR: 2960 (w) 2944 (m), 2738 (m), 2678 (st), 2493 (w), 1475 (w), 1386 (vs), 1265 (w) 1169 (w), 1036 (w), 847 (w), 823 (w), 802 (w). EA %: Calculated for triethylammonium nitrate ($\text{C}_6\text{H}_{16}\text{N}_2\text{O}_3$): C-43.87, N-17.06, H-9.83%. Calculated for triethylammonium nitrite ($\text{C}_6\text{H}_{16}\text{N}_2\text{O}_2$): C-48.61%, N-18.90%, H-10.90%. Found: C-45.32% N-17.56% H-10.22% (thus ~67% nitrate salt and 33% nitrite).

Using a 1:1 ratio of triethylamine to trioxide, and repeating as above, produces white or off-white **triethylammonium nitrite**. Yield 48%. ¹HNMR (DCM): 10.79 (broad s, not always seen), 3.148 (q), 1.329 (t). IR: 2980 (w), 2674 (w), 2493 (w), 1478 (m), 1349 (m), 1192 (vs), 1168 (vs), 1072 (m) 1040 (s), 850 (m), 802 (m), 556 (w), 456 (w). NOTE: Pure triethylammonium nitrite is aggressively deliquescent, and will melt away entirely in normal atmospheric conditions in minutes; in warm, humid summer air¹⁵, it will dissolve in a few seconds. It must be handled under inert atmosphere and carefully dried. It is purified by sublimation. Greater quantities of water in the starting materials cause corresponding losses in yield due to dissolution and nitrate formation.

Analysis of crude reaction mixture shows minor yields of **diethylnitrosamine** (¹HNMR: 4.15 (q), 3.6 (q)) and three other trace products of similar nature (α -H NMR peaks in the 3.5-4.2 ppm range).

(4.1-q) Trihexylamine: Dropwise addition of 1 mL diluted in 3 mL of dichloromethane to an equimolar dichloromethane/trioxide solution at 0°C consumes the blue colour before half of the amine is added, with a small amount of nitric oxide gas evolution (<20 mL), forming a yellow solution which becomes pale red-violet within minutes. The solvent is removed under vacuum at 0°C and the crude product is a yellow oil, which is violet when re-diluted. UV-Vis (DCM) 330 nm (major), 552 nm (minor). IR (thin film): 2960, 2931, 2859, 1467, 1402, 1378, 1297, 1092, 951, 891, 730. Raman: 2879, 1661, 1444, 1341, 1321 (w), 1039, 890, 702.

Exposure to the atmosphere for a few minutes produces **trihexylamine n-oxide**¹⁶ (C_6H_{13})₃N⁺-O⁻) as a yellow oil (remains yellow upon dilution). Crude yield (from initial trihexylamine): 94%. UV-Vis: 330 nm, 370 nm. IR (cm⁻¹): 3447, 2960, 2931, 2859, 1700, 1640, 1467, 1390, 1088, 1020, 730. ¹HMR: 2.905 (t, 6H), 1.632 (br, 6 H), 1.328 (br, 18 H), 0.902 (t, 9H).

The use of excess trioxide (4x) in the initial synthesis will eliminate the violet colour, and the UV-Vis will become a single peak at 376 nm (addition of more trihexylamine to this product will reproduce the violet colour). Exposure to air will produce a single peak at 348 nm. This product is otherwise similar to the product of the 1:1 mixture in IR, Raman, and reactivity.

(4.1-r) DABCO: 1,4-diazabicyclo[2.2.2]octane is purified by sublimation, and 0.025 g is dissolved in 3 mL freshly distilled dichloromethane and added to 10 mL of trioxide solution. This immediately produces a dark colour and varying amounts of precipitation, depending on the ratio of trioxide to DABCO used (see Results). Use of an 8:1 ratio forms an intensely coloured orange precipitate that is recovered by removal of the solvent on a vacuum/inert atmosphere manifold; it is stable when well sealed and/or kept under positive argon pressure. Product is the adduct **1,4-diazabicyclo[2.2.2]octane (bis-dinitrogen trioxide)** ([N₂O₃]-N-(C₂H₄)₃-N-[N₂O₃]) in 89% yield (see Results). ¹HNMR (CD₂Cl₂): 2.972. IR (cm⁻¹, hex): 3004, 2782, 2585, 2472, **1897**, 1474, 1377 (vs), 1317 (sh), 1184, 1055, 1039, 971, 939, 842, 786, 649, 580. Raman: 1908, 1347, 1047, 973, 796, 682.

Momentary exposure to atmospheric moisture bleaches the product white, transforming it into **1,4-diazabicyclo[2.2.2]octanium nitrate** $[\text{H-N}-(\text{C}_2\text{H}_4)_3\text{-N-H}]^{+2} [\text{NO}_3]^{-2}$ salt, with evolution of nitric oxide gas. EA: Calculated for $\text{C}_6\text{H}_{12}\text{N}_4\text{O}_6$: C-30.20, H-5.90, N-23.50 %. Found: C-28.28, H-5.63, N-22.84%. IR: 3018, 2807, 2617, 2396, 1764 (w), 1383 (vs, br), 1188, 1040, 891, 851, 823, 803.

Quantification of the orange product is carried out in a one pot reaction; after the preparation (as above) the solvent is evaporated by 1 hour of drying under high vacuum on ice. A solution of excess mercaptoethanol in water is injected and stirred for 1 minute. A sample is withdrawn, diluted 10-fold, then examined by UV-Vis spectroscopy for the concentration of nitrosothiol (see mercaptoethanol descriptions).

(4.1-s) Triphenylamine: One gram is dissolved in 3 mL dichloromethane and added to an equimolar trioxide/dichloromethane solution at 0°C , which consumes the blue colour immediately and produces an intense amber yellow solution. The solvent is removed by evaporation, and the resulting solid is redissolved in a minimum of CH_2Cl_2 , diluted in 10-fold hexane, and then chilled on ice to give **(4-nitrophenyl)diphenylamine** ($(\text{O}_2\text{N-C}_6\text{H}_4)(\text{Ph})_2\text{N}$) as orange crystals in 42% yield. $^1\text{HNMR}$ (CDCl_3): 8.038 (d, 2H), 7.368 (t, 4 H), 7.193-7.172 (d overlapping t, 6 H), 6.922 (d, 2H). CNMR (CDCl_3): 129.93, 126.52, 125.73, 125.47, 118.15. IR: 3435, 1583, 1491, 1297, 1314, 1285, 1108, 843, 750, 604.

Repeating with a large excess of trioxide (>2 equivalents) and purifying on a silica column (hexane/ethyl acetate as eluent), produces **(4,4'**-

dinitrophenyl)phenylamine¹⁷ ($(\text{O}_2\text{N}-\text{C}_6\text{H}_4)_2(\text{Ph})\text{N}$) as yellow crystals in 90% yield. (¹HNMR: 8.15 (d, 4H), 7.15 (d, 2H), 7.44 (t, 1H), 7.32 (t), 7.18 (d) (the 7.17 doublet of nitrophenol overlaps with the 7.32 doublet of the unsubstituted ring; comparing the 8.15 (d) and the 7.44 (t) gives the correct integration of 2:1). IR: 1579, 1491, 1342, 1314, 1281, 1181 (w), 1108, 847, 750, 698.

(4.1-t) Tribenzylamine: One gram is dissolved in 3 mL toluene and added to an equimolar toluene/trioxide solution. After a few minutes a white precipitate forms. When precipitation ceases (~10 min, blue colour not entirely consumed), the precipitate is filtered and dried to a snow white powder. Recrystallizing from ethanol gives **tribenzylammonium nitrate** ($(\text{C}_6\text{H}_5\text{-CH}_2\text{-})_3\text{N-H}^+[\text{NO}_3]^-$), confirmed by X-ray crystallography. ¹HNMR (CD₂Cl₂): 7.473 (m, 15 H), 4.260 (s, 6 H). CNMR: 131.07, 129.97, 129.36, 30.56. IR: 3439 (br, w), 3040 (w), 3000 (w), 2734 (w), 2605 (br, w), 1454, 1390 (vs), 1297 (vs) 1277, 1040, 1016, 911, 758, 698, 501.

Repeating in dichloromethane and protecting from air contact yields a yellow liquid with no precipitate. Removing the solvent under vacuum produces a white solid. IR (Nujol mull): 2972, 2883, 2847, 1744 (w), 1712 (w), 1656, 1595 w), 1454 (s), 1378 (s), 1346, 1297 (s), 1040, 1012, 907, 823, 754 (s), 698 (s), 501. When exposed to air this product becomes the tribenzylammonium nitrate described above.

When trioxide is used in excess, the products are as before with increasing quantities of **benzaldehyde**.

(4.1-u) Triphenylphosphine: One gram is dissolved in 5 mL toluene and added to an equimolar trioxide/toluene solution at 0°C, causing the evolution of nitric oxide gas and the formation of a clear solution. Evaporation yields **triphenylphosphine oxide** (O=PPh_3), in 95% yield, as a snow white powder (pure by NMR). IR (cm^{-1}): 3057, 1589, 1482, 1436 (s), 1311, 1188 (s), 1121 (s), 720 (s), 696 (s), 538 (s).

This trial is repeated with trioxide in excess, and in rigorously dry conditions the results are as above. The presence of small amounts of moisture in the solvent (or atmosphere during reaction) will cause the formation of a second product as a waxy yellow, slowly crystallizing solid, an adduct of nitric acid and triphenylphosphine oxide, $[\text{Ph}_3\text{P=O}][\text{H-ONO}_2]$ (**Tranter's salt**^{18,19,20}). IR (cm^{-1}): 3084, 3060, 1635 (br), 1438, 1422, 1285, 1249, 1120 (s), 1051, 947, 725, 693, 536. ³¹PNMR: 34.18. mp: 79-80°C.

(4.1-v) Trimethyl Borate: Trimethyl borate is added as a pure liquid in a 1:1 ratio to a toluene/trioxide solution at 0°C; this forms a stable honey yellow solution within a few seconds. A trap-to-trap distillation is performed (crude mixture is kept on ice while under vacuum and the vapour is collected in a liquid nitrogen chilled vessel) to isolate a brilliant orange solid which becomes colourless upon melting. NMR (CD_2Cl_2): 4.058 (s), 3.558 (s). UV-Vis displays fine structure (311, 320, 330,

340, 352, 365 nm). The liquid rapidly decays and evaporates, releasing nitrogen dioxide gas. This NMR and the observed reactivity resembles a mixture of **methyl nitrite** ($\text{CH}_3\text{-O-N=O}$)²¹ and **methyl nitrate** ($\text{CH}_3\text{-O-NO}_2$)^{22,23}.

(4.1-w) Phenyllithium: One-tenth of a mL of phenyllithium is diluted in 5 mL of cold dry benzene, then added dropwise to 10 mL of equimolar benzene/trioxide solution at 0°C (at this concentration of trioxide, the benzene should not freeze). A dark precipitate of **lithium nitrite** forms rapidly (IR (cm^{-1}): 3439, 1640, 1354, 1269, 573), with a small amount of **lithium nitrate** (IR (cm^{-1}): 3439, 1644, 1382, 826, 564). (NOTE: lithium nitrite is deliquescent and must be protected from the atmosphere). A dark pigment is isolated by washing the solid with cold methanol, then drying the filtrate. UV-Vis displays sharp fine structure (238, 244, 249, 255, 261 nm). NMR shows a multitude of products; **nitrosobenzene** can be identified as a significant product by comparison of the NMR to a pure sample (¹HNMR (MeOD): 7.95 (d, 2H), 7.74 (t, 1 H), 7.65 (t, 2H).

4.2: Results

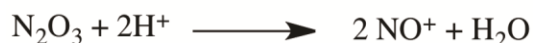
Twenty-two different compounds were examined for their reactivity with dinitrogen trioxide, all the reactions being carried out at 0°C (the temperature at which most nitrous acid chemistry is done), and most at the gram scale, where feasible. By and large observed chemistry is similar to that seen with nitrous acid,

but the absence of water and (in many cases) free protons allows for the formation and/or easy isolation of compounds that would otherwise not be seen. I shall group and discuss them according to what they illustrate about the behaviour of dinitrogen trioxide in solution.

Two preliminary notes: first, a major product in many of the reactions is a mixture of nitrite and nitrate; sometimes one, sometimes another. This will be discussed directly in the next chapter, but what can generally be seen is that reaction with trioxide (ONNO_2) will produce a nitrite (NO_2^-), which can further react with N_2O_3 to form the nitrate (NO_3^-). Thus the appearance of nitrate can be accounted for by the production of nitrite that is subsequently oxidized; this reaction is facile and it can compete with organic reactions, which can depress the yield of some reactions when a 1:1 ratio of trioxide to reactant is used. Use of excess trioxide in nitrite-producing reactions usually results in only nitrate being recovered. In a few cases to be discussed, the nitrate only forms when exposed to atmospheric water.

Second, the stoichiometry of these reactions is less straightforward than it appears. In the reactions to be discussed, the reactant and the trioxide were usually mixed in a 1:1 ratio. This is to be understood as 'one molecule of X to one molecule of N_2O_3 ', but in some cases, this is not the end of the story. When these reactions are performed in water immiscible organic solvents, and in quantities larger than the ~1 g typically performed here, a water layer will eventually form. This reveals an important facet of dinitrogen trioxide solutions: for N_2O_3 to donate a nitrosonium

ion (NO^+), nitrite ion (ONO^-) must be produced, which in systems where protonation is possible gives HONO , the nitrous acid. However, nitrous acid does not seem to be a favourable form in non-polar solvents; instead, the nitrous acid dimerizes and dehydrates, eliminating water into a separate layer and yielding more N_2O_3 . At times, a reaction that has gone colourless will become blue again after a short induction period, a visual confirmation of this trioxide regeneration. This can also be seen in the stoichiometry of reaction, where every N_2O_3 molecule is capable of nitrosating two other molecules. In essence:



Eq. 4.2: Stoichiometry of dinitrogen trioxide reaction with protic species.

Titration of an N_2O_3 solution with isopropanol based on this ratio (1 N_2O_3 to two isopropanol) results in the blue colour disappearing after half of the isopropanol has been added (indicating that the trioxide is no longer at visible concentrations) yet the reaction will nevertheless continue until two equivalents of isopropanol have reacted. In this case, the initial reaction forms HONO , which continues to form more trioxide, but it is consumed as it is made, and so it is not visible.

It is worth noting, however, that in reactions that do not involve proton loss or transfer, N_2O_3 is typically consumed on a one to one basis, since a nitrite formed will remain as nitrite, rather than forming nitrous acid. Thus for non-protic reactions, 'equimolar' denotes a reaction ratio of 1 N_2O_3 to 1 reactant molecule, whereas for protic reactions, it denotes 1 N_2O_3 to 2 reactant molecules, as each N_2O_3 can act twice. This too is a simplification, however, since in many reactions, the

presence of water or HONO can cause secondary reactions and other products, such that the reactant will still consume trioxide on a one -to- one basis, but produce only a half equivalent of one product, and a half equivalent of a second product by reaction with a protic species. Thus the reactions performed are a description of a baseline reactivity between N_2O_3 and other species, but do not tell the whole story.

Unreactive/Weakly Reactive Species (4.1 a, b, c)

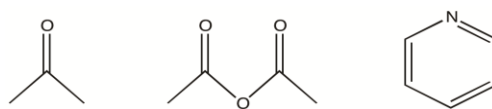


Fig 4.3 Compounds that do not react with trioxide solutions (left to right: acetone, acetic anhydride, pyridine).

In addition to the various solvents discussed in the preceding chapter, dinitrogen trioxide does not appear to react with any of the compounds shown in Fig 4.3. Mixing pyridine into a trioxide solution initially appears to form a white salt, but this proves to be pyridinium nitrate (Fig 4.4). Presumably the water causes the formation of some nitrous acid, which protonates the pyridine; the nitrite counter-ion is subsequently oxidized by the excess trioxide around, as discussed above. Rigorously drying both solvent and pyridine prior to the reaction all but eliminates this salt, a demonstration that even though dinitrogen trioxide is considered to be the 'active' component of a nitrous acid mixture, in some cases the reverse can be true. Without free protons, N_2O_3 is inert towards pyridine, and solutions of the two are actually quite stable (i.e. no loss is seen over 1 hour).

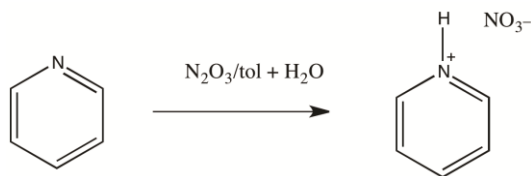


Fig 4.4 Pyridine to pyridinium nitrate in the presence of moisture.

Acetone and acetic anhydride were both considered as solvents in the previous chapter, but are weakly stabilizing, and acetone is difficult to render completely anhydrous. They are worth considering in comparison to aldehydes, which are weakly reactive with trioxide. Stable trioxide solutions can be formed in benzaldehyde as a solvent, but over a period of a few days it reacts to form benzoic acid. Hexanal mixed into a toluene/trioxide solution will behave similarly (Fig 4.5):

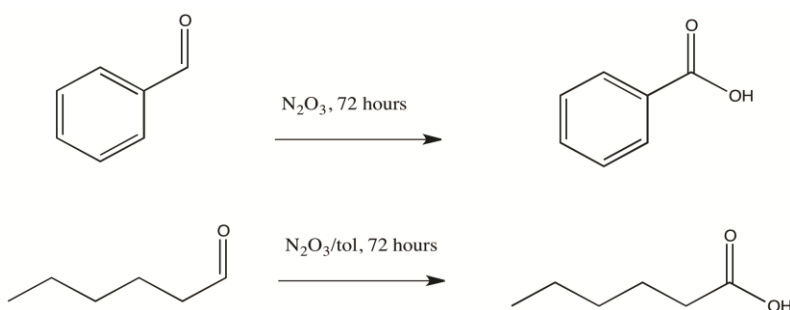


Fig 4.5: Slow oxidation of aldehydes by dinitrogen trioxide.

This transformation is accompanied by the slow evolution of nitric oxide gas. The sluggishness of the reaction did not permit accurate measurement of the escaping gas, but since no other products are detected (not even NO_2 gas), it is reasonable to expect that two moles of NO are forming for every mole of aldehyde oxidized (Eq 4.3):



Eq. 4.3: Oxidation of aldehydes.

Thus in this reaction, N_2O_3 behaves as an oxygen transfer reagent, rather than as an NO^+ donor, as is usually the case.

Alcohols and Thiols (4.1 d-g)

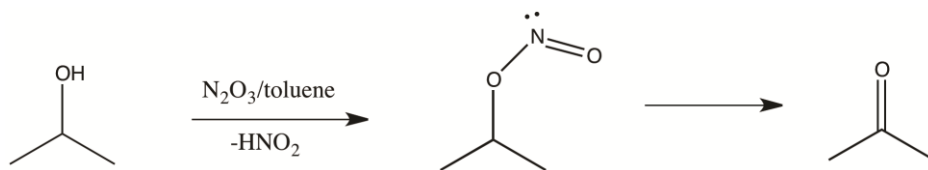


Fig. 4.6- Alcohol nitrosylation and subsequent decay.

Confirming some similar recent work done by Grossi and Strazzari²¹ (in which nitric oxide is bubbled through the reactant solution, presumably while still exposed to oxygen) trioxide solutions will react cleanly with 2-propanol to give 2-propyl nitrite (Fig 4.6). This is a classic reaction for nitrous acid, one in which the trioxide molecule donates a nitrosonium ion to the alcohol and abstracts a proton, forming nitrous acid (Eq 4.4):

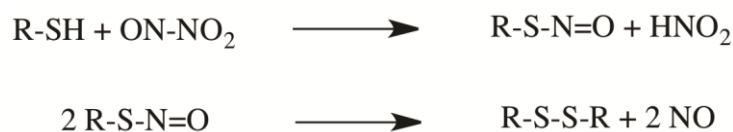


Equation 4.4: Formation of alkyl nitrites from alcohols.

Warmer temperatures (or sudden mixing of concentrated solutions) will instead produce acetone (Fig 4.6) (the reaction is slightly exothermic, so sudden mixing may cause rapid heating and subsequent breakdown). The stoichiometry of this requires the elimination of HNO , though neither this nor its reported byproduct of N_2O was

detected. No other products are seen spectroscopically, and it is likely that the reported yields are due merely to losses during work-up. Of note is that despite the harsh conditions, the alkyl nitrite is not further oxidized and good yields are achieved, provided that temperature is controlled. Likewise, t-butanol reacts to make t-butyl nitrite, though here the formation of ketones is prevented.

In an analogous way, thiols react readily to make the brightly coloured nitrosothiols, (Eq. 4.5) which have varying stability in solution but disproportionate when pure, releasing nitric oxide.



Eq 4.5: Formation and breakdown of nitrosothiols (R= alkyl, aryl groups).

As such, their formation was quantified while in the mother liquor by UV-Vis spectroscopy, using the 548 nm peak ($\epsilon_{548} = 34.3 \text{ L} \cdot \text{cm}^{-1} \cdot \text{mol}^{-1}$). This extinction coefficient was determined from the standard reaction between mercaptoethanol and a large excess of nitrous acid, and it compares reasonably well to the available literature⁴, which cites the value for this class of molecules as $\sim 20 \text{ L} \cdot \text{cm}^{-1} \cdot \text{mol}^{-1}$. This result is bolstered by comparison to the reactivity of benzyl mercaptan (literature value⁶ $\epsilon_{548} = 26 \text{ L} \cdot \text{cm}^{-1} \cdot \text{mol}^{-1}$), which gives nearly the same yield. The fact that only slightly more than half of the available mercaptoethanol produced the nitrosothiol is curious; while this suggests that the alcohol side of the molecule has reacted with the remainder of N_2O_3 , analysis of the crude NMR shows only traces of product that would correspond to ethylnitrosothiol nitrite. Benzyl mercaptan, which

does not have this alcohol functional group, also reacts to produce only about half of the expected nitrosothiol. These reactions are exothermic and are accompanied by NO gas generation, so clearly a secondary reaction is involved that depresses the yield.

Phenols and Nitrosobenzene (4.1 h,i,j)

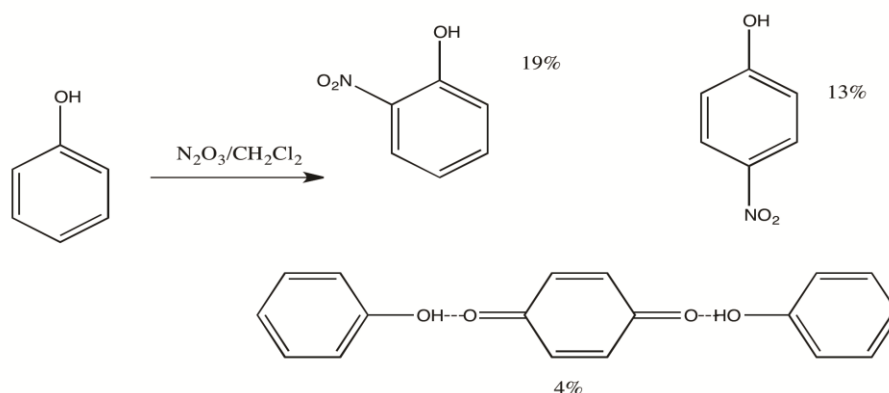


Fig 4.7: The recoverable products of phenol reaction with dinitrogen trioxide.

Phenols mixed into a trioxide solution will over time mature into an array of darkly pigmented compounds. When sampled by NMR immediately, however, only four products are seen: p-nitrophenol, o-nitrophenol, benzoquinone and phenol, which can be integrated to get a relative ratio of 1.4 to 1 to 0.25 to 0.9, respectively.

Prompt work-up allows their isolation, leaving behind a precipitate of poorly soluble dark pigments. The benzophenone and phenol will not separate, but will instead co-crystallize into a hydrogen bonded bis-phenol quinone molecule, as scarlet red needles (Fig 4.7). This molecule is known^{24,25} but not fully characterized;

its X-ray crystallographic structure appears here for the first time (Fig 4.8), which corresponds to the structure predicted by IR and NMR.

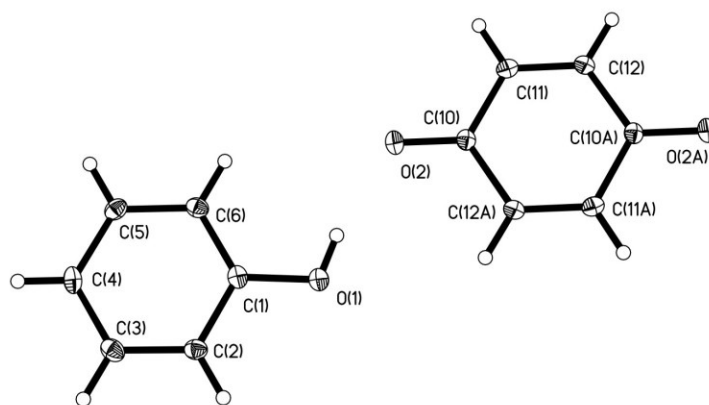


Fig 4.8: Phenol-benzoquinone hydrogen bonded adduct.

The phenol pictured is symmetry related to a second phenol on the other side of the benzoquinone. The molecule is not quite planar, each ring canting away from each other by 6.0° . The oxygen-oxygen distance is $2.370 \text{ \AA}$. This product sublimes easily at room temperature; hence its true yield is no doubt substantially higher than what was recovered.

The nitrosation of benzene rings comes as no surprise, as the hydroxyl behaves as an ortho-para director. It is probable that phenyl nitrite (Ph-O-NO) forms as an intermediate, due to direct attack on the alcohol group by trioxide, but this product was not detected, and it may act to direct the NO^+ to the ortho position,

accounting for the high final yield of the ortho product. The formation of benzoquinone confirms that there is some deprotonation followed by an oxidation at the para-position. Here it appears that N_2O_3 can act as an oxygen donor, as seen in the reaction with aldehydes.

The relatively small overall yield of products, and presence of starting material, suggests that in a 1:1 ratio of phenol to trioxide, it is the trioxide that is the limiting reagent, and that secondary processes are consuming the trioxide faster than it can react with the phenol. Here it is worth considering that nitrosophenol, which might be expected to form from NO^+ donation, is never seen, and it appears that the trioxide is acting as a nitronium (NO_2^+) donor. This is, however, contrary to the accepted model of trioxide reactivity, as well as the fact that no $\text{HNO}/\text{N}_2\text{O}$ is detected as a byproduct.

If it is the nitroso species that forms first and is then oxidized to the nitro, then one should be able to witness N_2O_3 acting in this way by mixing it into a sample of nitrosobenzene. Performing this experiment with an exposure time totaling less than five minutes, nitrosobenzene is oxidized entirely to nitrobenzene. Thus if nitrosophenol is the intermediate species, this demands the consumption of a second equivalent of trioxide to oxidize it, and accounts for the lower than expected yield, and the fact that a large excess of trioxide must be used before the di-nitrated species is seen. This requires that trioxide reacts faster with nitrosobenzene than with phenol, but this is consistent with the fact that nitroso species readily dimerize, and could be expected to interact with dinitrogen trioxide, which is essentially a

nitroso-nitro molecule. Dinitrogen trioxide itself is thought to interact through its non-bonding electrons (i.e. the lone pair)²⁶. Whether this oxidation proceeds by direct attack on an oxygen or pre-association through the lone pairs (fig 4.9) is uncertain: pathway B avoids a highly charged intermediate, but theoretical work²⁷ identifies the normal reaction pathway of N_2O_3 as occurring through the nitroso group. If the similarity between this as a nitroso-nitro species and other nitroso molecules is valid, then option A is the likelier of the two, despite the unusual Lewis structure, involving two dative bonds between nitrogen and oxygen.

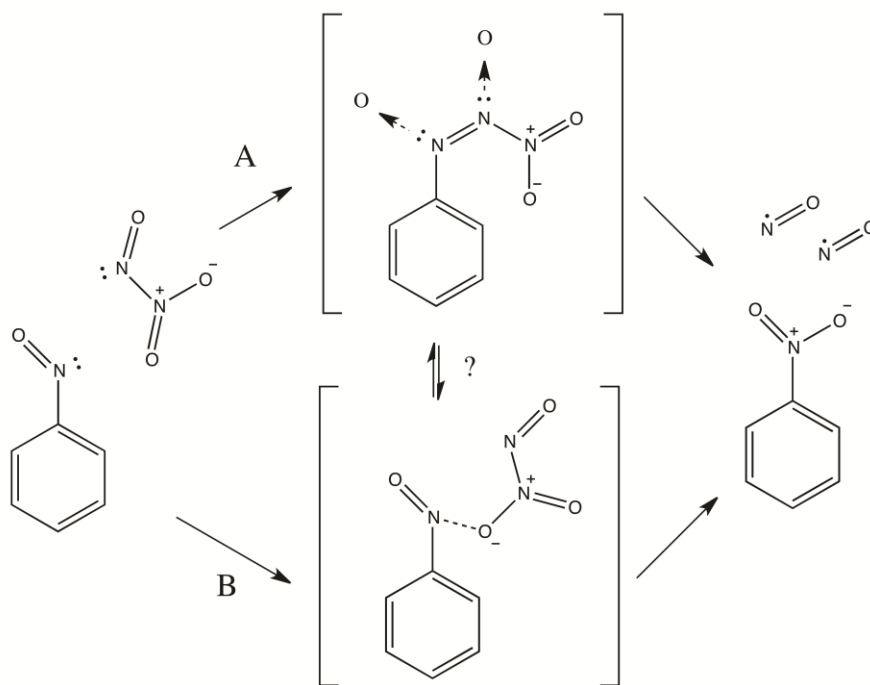


Fig 4.9: Possible mechanisms of nitrosobenzene oxidation by N_2O_3 .

The formation of nitrosophenol first, then further oxidation to nitrophenol, is further demonstrated by performing the addition of phenol to trioxide in a UV-Vis

cuvette and diluting 100x immediately afterwards. Trapped out in this way, one sees a broadened double peak in the 280-300 nm region, which is consistent with the formation of a nitrosophenol intermediate.

This behaviour is nevertheless still puzzling. Phenol is known to react readily¹ with dilute aqueous nitrous acid to produce nitrosophenol, in yields of up to 90% p-nitrosophenol and 10% o-nitrosophenol, with no sign of further oxidation to nitrophenol. An interesting facet of this reaction is that the stable product in solution is not the nitrosophenol, but its tautomer, the quinone-oxime (Fig 4.10):

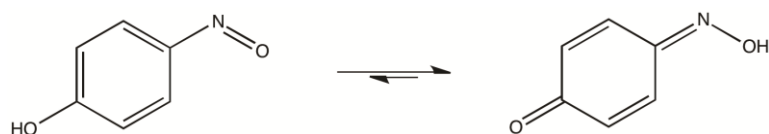


Fig 4.10- Tautomerization of nitrosophenol to p-oximequinone in aqueous solutions.

The complete absence of either product in organic trioxide solutions demands some explanation. One principal difference between the nitrous acid and organic trioxide solution reactions is concentration: though dinitrogen trioxide is thought to be the active species in the aqueous transformation, it is never present in large amounts. Most of the time, the product will thus only encounter increasingly dilute amounts of HONO, which evidently will not further oxidize the nitroso to a nitro group. Nevertheless, it would be strange if the N_2O_3 were simultaneously scarce enough that the nitroso group fails to oxidize, a reaction that happens readily, but at the same time the level is adequate to nitrosate the phenol, which occurs more slowly. It is likely that another factor is at work in the aqueous solutions that is not at work in the organic solutions. The quinone form may be the key: protons do not usually

move about on their own, requiring an agent capable of protonation to facilitate tautomerization. A high concentration of the nitrosophenol itself could perform this function, but in this case it is likely that abundant HONO in solution performs the role, protonating one side while a bare ONO^- anion deprotonates the other. In aqueous solutions then, one would expect large amounts of the quinone form, which would make encounters between a nitroso group and another N_2O_3 molecule a rare occurrence. In organic solutions, it is likely that most of the product remains in the vulnerable nitrosophenol form, and this explains both why the nitro predominates and the orange quinone form, or a product of its reaction, is not seen in the organic solutions. It is also possible that the quinone form is the precursor to the benzoquinone, which is detected.

It is worth noting that while the nitrosobenzene species seems vulnerable to further oxidation, this is not a universal rule. The nitrosothiols do not react with trioxide, seen by the fact that a small excess of trioxide does not seem to degrade them; nitrosothiols typically degrade by homolysis, especially in reducing conditions (seen in Eq 4.5). Alkyl nitrosothiols do not readily undergo this reaction, nor dimerize, and can persist over long periods¹⁴. Alkyl nitrites can be recovered from trioxide solutions, and thus they must be less reactive with trioxide than the parent alcohol, and one must appreciate the similarity between the two: R-S-N=O and R-O-N=O . If the oxidation does indeed proceed as described in Fig 4.9, through the lone pair of the nitroso, then it would seem that electronegative species (S, O) lower the energy of that lone pair and diminish its activity. The simplest case, however, is the nitrite molecule $^-\text{O-N=O}$, which is seen to oxidize when in contact

with dinitrogen trioxide. Here, however, there is free movement of a negative charge, and the lone pair is not similarly deactivated. N-nitroso species should follow this pattern, except that in most cases the N carries other species, such as hydrogen, which beget other chemistry. An N-nitroso species without hydrogens (i.e. $R_3N-N=O$) would thus be expected to be resistant to further oxidation from dinitrogen trioxide.

When the para-position of phenol is blocked by bromine, in p-bromophenol, then much higher selectivity is seen for the 2 position, and the product is mostly (>60%) 2-nitro-4-bromophenol; only faint traces of other compounds can be recovered by chromatography. The relative cleanliness of this reaction suggests that it is the para-nitro or benzoquinone species that leads to the formation of most secondary products, which is reasonable, as the presence of electron density on the 4-position (from an electron donating group on the 1-position) often leads to coupling reactions.

Primary Amines (4.1-k,l):

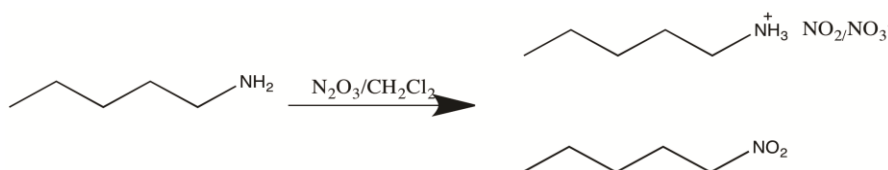


Fig 4.11: Major products of equimolar trioxide solutions with pentylamine.

The reaction of pentylamine, as a representative alkyl amine, with trioxide solutions at $0^\circ C$ is surprisingly clean, yielding mostly pentylammonium nitrite (or nitrate,

when the trioxide is present in excess) and nitropentane as yellow oils (fig 4.11). When the ratio of amine to trioxide is 1:1 or lower, a number of colourful side products result, from red to magenta, but they are present in only trace amounts. The fact that they are removed during washing with hexane suggests that they are the result of coupling between pentylamine chains, and their polar substituents are hidden in the center of two long alkyl chains; alkyl triazenes ($R-(NH)-N=N-R$) are the likely candidate.

This is similar to what was reported by Vosper and Lovejoy² for reactions carried out at -85°C , but they also saw traces of alkyl nitrites ($R-ONO$), and a number of products "that appear to result from the reaction with dinitrogen tetroxide" (not specified). Vosper proposes that nitrogen gas evolved during these reactions and that this carried away some amount of NO , rendering two N_2O_3 into one N_2O_4 . This gas evolution was also observed when I attempted this reaction using pentylamine at 0°C , but it must be noted that intentionally bubbling nitrogen through a cold solution, even at 0°C , does not quickly deplete the amount of N_2O_3 in solution. This suggests that the breakdown of trioxide to NO is part of the reaction itself.

This is observed by the large amount of gas evolved: 1 mL pentylamine will produce 255 mL of gas, 144 mL of which is nitrogen and ~ 111 mL NO (the water used in trapping will absorb some NO). This volume of nitrogen suggests that 68% of the pentylamine is breaking down with loss of N_2 , which is the standard decay path expected for primary amines in nitrous acid (fig 4.12). If we assume that the remaining 32% of pentylamine is being protonated by the nitrous acid formed when N_2O_3 reacts with amine, then a likely candidate for the formation of NO gas is the

subsequent oxidation of nitrite to nitrate; this amount of pentylammonium nitrite would, when oxidized, theoretically yield 133 mL of NO gas, almost precisely what is seen.

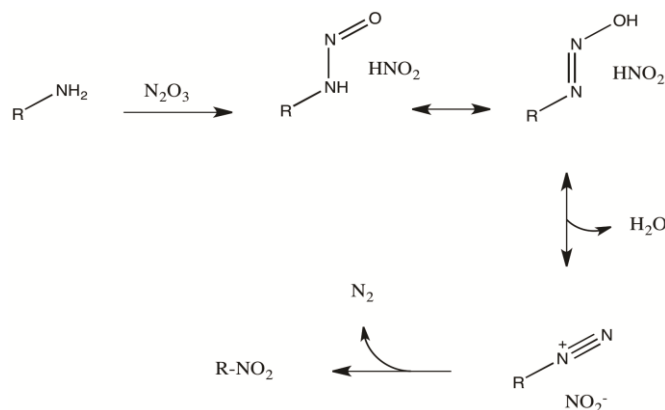


Fig 4.12: Standard breakdown of primary amines with dinitrogen trioxide.

The reaction with aniline proceeds precisely as with nitrous acid and according to Vosper's results at $-85^\circ C$, producing the explosive benzenediazonium nitrate; here the product precipitates immediately, and the anilinium nitrate is not seen. A broad range of intensely coloured aniline dyes will also result, but only in trace quantities; the only other product results when aniline is added quickly or in excess, in which case it will couple to form the orange diphenyltriazene (Fig 4.13):

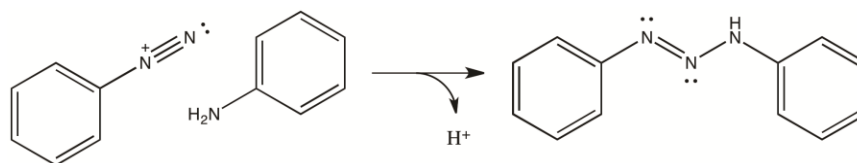


Fig 4.13: Formation of diphenyltriazene from a benzenediazonium cation.

Secondary Amines (4.1-m,n,o):

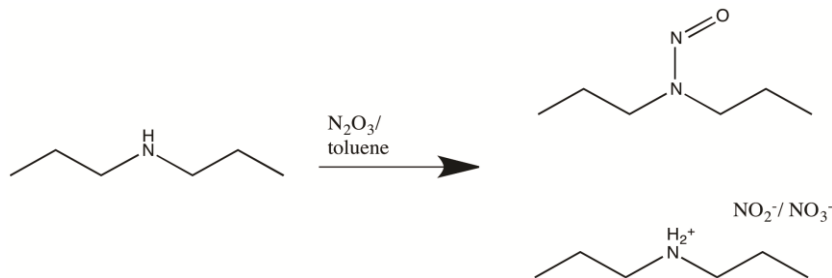


Fig 4.14: Products of secondary amines with trioxide solutions, at 0°C .

The reaction with dipropylamine proceeds as expected, forming mostly the nitrosamine, the production of which has been a major health concern and the chief area of research for nitrite mediated nitrosation reactions. These results match those of Lovejoy and Vosper (discussed above) working at -85°C . As with the primary amines, the reaction with trioxide produces the nitrosamine, whereas the reaction with the nitrous acid side product creates the ammonium salt (Fig 4.14).

An interesting point of difference lies in the yield. Vosper reported that at -85°C , he obtained nitrosammonium to nitrosamine in a 2:1 ratio, whereas my results at 0°C were 30% and 44%. If either value were to be depressed by the vagaries of work-up, it would be the nitrosamine. This suggests that at high temperatures, the dinitrogen trioxide is more reactive than the nitrous acid, or that warmer temperatures promote the equilibrium of nitrous acid and dinitrogen trioxide in favour of the trioxide. Warmer temperatures usually depress the level of trioxide by pushing for its dissociation, which makes its formation from nitrous acid less likely, but would also make it more likely to heterolytically cleave, and hence a better NO^+ donor. A third possibility is that the 2:3 ratio is the result of some nitrosammonium

product being subsequently deprotonated by trioxide still in solution; this last explanation seems the most likely, as it explains both the depression in the amount of nitrosammonium as well as in the overall yield.

Two other compounds related to secondary amines were tested: pyrrole and benzotriazole. The reaction with pyrrole is immediate and characteristic of the nitrous acid reaction: what forms is a poorly characterized mass known simply as 'pyrrole black', demonstrating that trioxide and nitrous acid have the same reactivity in this case. Benzotriazole, by contrast, does not react at room temperature with nitrous acid to any appreciable degree, but in an organic trioxide solution it rapidly produces a series of darkly coloured compounds. Most of these are only traces, and by NMR appear to be based on attacks upon the aryl ring. Analysis of the bulk product, however, shows that the basic structure of the benzotriazole is intact, and the main product-- a bright yellow compound that rapidly reacts with atmospheric water to form a white salt-- appears to be an adduct between the trioxide and the azole ring. This will be discussed in more detail in the next section.

Tertiary Amines (4.1-p-v)

It is a standard lesson in organic chemistry texts that tertiary amines can be distinguished from primary or secondary by the fact that they do not react with nitrous acid. This is, as Smith and Loeppky²⁸ put it in their somewhat testy 1966 paper, "the most persistent myth in organic chemistry, notwithstanding a veritable parade of experimental refutations extending over an even century." For what good

it did (notwithstanding their paper, the myth persists half a century later), they proposed that the reaction proceeds by nitrosative cleavage (Fig 4.15):

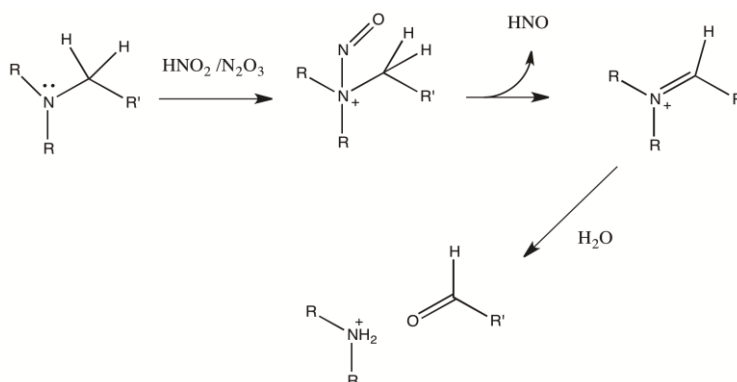


Fig 4.15: Smith and Loeppky's nitrosative cleavage of tertiary amines.

This is, admittedly, a slow reaction, taking many hours at the standard operating temperature of 0°C; in the paper mentioned, they proceeded at room temperature or above, allowing almost 3 hours for the reaction to come to completion.

It is on this count that organic trioxide solutions take their most radical divergence from the chemistry of nitrous acid: they react swiftly, and sometimes produce products never seen in a nitrous acid work-up.

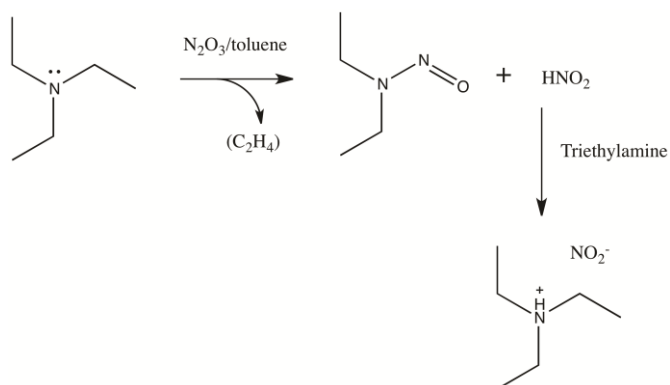


Fig 4.16: Products of rigorously dry triethylamine and dinitrogen trioxide.

The reaction of triethylamine in a trioxide solution (Fig. 4.16) occurs immediately upon addition. It will first produce a bloom of red colour that quickly fades (most tertiary amines will produce a coloured complex at first). This red species can be preserved in a reaction at -78°C , but all attempts to isolate it at room temperature failed, the only remnant being a deep red stain in some of the crystalline products. Smith and Loeppky also reported the formation of red coloured compounds with triethylamine at low temperature that vanish on warming; they credited it to the formation of a temporary tertiary nitroso compound. The solution turns green as white or pale yellow precipitate forms, accompanied by vigorous gas evolution. The primary product is triethylammonium nitrite $[(\text{C}_3\text{H}_5)_3\text{-NH}]^+[\text{NO}_2]^-$, stained yellow or red (as per normal, the salt will be nitrate when trioxide is in excess).

The production of protonated salts implies the presence of moisture, but these products form regardless of how rigorously the anhydrous conditions are enforced. The presence of moisture will lower the yield (the nitrite product is extremely hygroscopic) and cause greater colour variation, but under the best conditions the yield is around 50%. The source of the protons for this product appears to be the other 50% of the starting material, which undergoes nitrosative cleavage, as Smith and Loeppky proposed, the major product of this being diethylnitrosamine (from the subsequent reaction of the secondary amine with trioxide/nitrous acid). The other expected products of this cleavage would be ethanal or ethylene, but this was not detected in solution by NMR, nor in the vapour by GCMS; a modest increase was seen in the level of 28.04 a.u. fragment, which

could be ethylene, but also nitrogen gas. The gaseous products are otherwise found to be mostly nitric oxide (1 mL will produce 130 mL of nitric oxide gas) and some solvent vapour. This quantity of gas amounts to 74% of a 1:1 yield for amine/NO; alternatively, and more in keeping with the proposed mechanism, if half the triethylamine is undergoing nitrosative cleavage and producing HNO as a byproduct, this molecule can further react with N_2O_3 to produce HONO and two molecules of NO, arriving at the same stoichiometric yield. HNO dehydration to produce N_2O is reported to be extremely rapid²⁹, yet N_2O is nevertheless not detected among the reaction products.

In an attempt to better capture the breakdown products and understand the rapidity of the reaction, I made use of three other tertiary amines (Fig. 4.17). Rather than clarifying the nitrosative cleavage reaction, bulkier tertiary amines were instead discovered to engage in chemistry entirely their own.

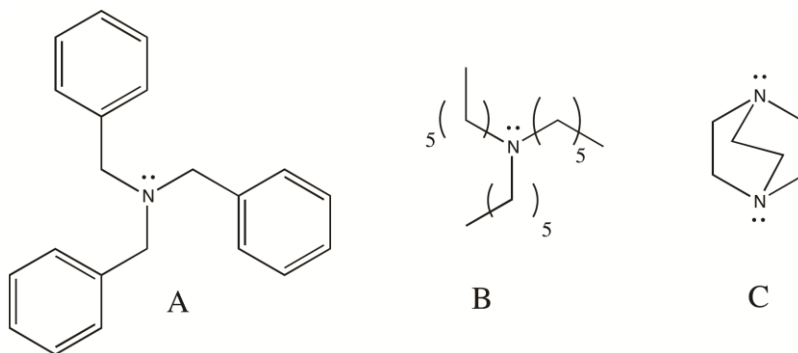


Fig 4.17: Tertiary amines used to probe the N_2O_3 reaction. A) Tribenzylamine. B) Trihexylamine. C) 1,4-diazabicyclo[2.2.2]octane (DABCO).

When tribenzylamine (also described in the Smith paper) is used, the reaction produces no colour, and the expected cleavage product, benzaldehyde, is

mostly found when trioxide is present in excess, and is never a major product. The main product, a waxy off white powder, is nevertheless altered from the starting material; when protected from air, it is seen in the IR to possess a number of small bands in the 1600-1750 region, and at least four strong bands from 1378 to 1297 cm^{-1} ; once it is exposed to air, these bands vanish (but 1297 remains), and this product recrystallizes as tribenzylammonium nitrate (strongest band at 1390 cm^{-1}). This product could be interpreted as nitrite, though nitrites typically have bands lower in the 1200 region, and nitrites are not known to easily or spontaneously oxidize to nitrates. This suggests that an air sensitive intermediate has formed from the union of trioxide and the amine.

Trihexylamine displays the same behaviour, but here the product forms a pale red-violet colour on reaction. When protected from the atmosphere it is isolated as a yellow oil, which nevertheless turns plum purple when diluted in dichloromethane. It too is found to have a series of strong bands in the 1300-1400 region of the IR, though without the weak bands around 1700, and exposure to moist air or water quickly eliminates them, creating instead a single sharp band at 1700 cm^{-1} , which later evolves into what appears to be trihexylamine n-oxide. Tellingly, the oil loses mass ($\sim 4\%$) during the first few minutes of air exposure (this does not continue afterwards), and the resulting oil is no longer purple when dilute. The NMR is not seen to change appreciably.

This curious chemistry is the most dramatic with DABCO: here, trioxide solutions in toluene become nearly black immediately upon the addition of the DABCO. Stoichiometric additions produce only a yellow gum, but higher ratios of

trioxide will dry the product, and above 2:1 the product will begin spontaneously precipitating. The best yield was found at an 8:1 ratio. This air-sensitive intermediate is a vividly orange powder, which is relatively stable under inert atmosphere (when sealed, it will develop an overpressure of nitric oxide gas over a period of days). The reaction is clearly due to the addition of trioxide or some component of trioxide, as shown by the marked increase in mass (by a factor of 1.875, which is 80% of what the addition of two molecules of trioxide would account for). The IR (which must be a mull, as it reacts in KBr pellets) displays two bands in the 1300-1400 region, but also a strong band at 1897 cm^{-1} (Fig 4.18). A new band is also found in the Raman, at 1908 cm^{-1} . When exposed to moist air, the powder will lose approximately 18% of its mass and bleach white, releasing nitric oxide gas in the process. This white product is the protonated nitrate salt of DABCO.

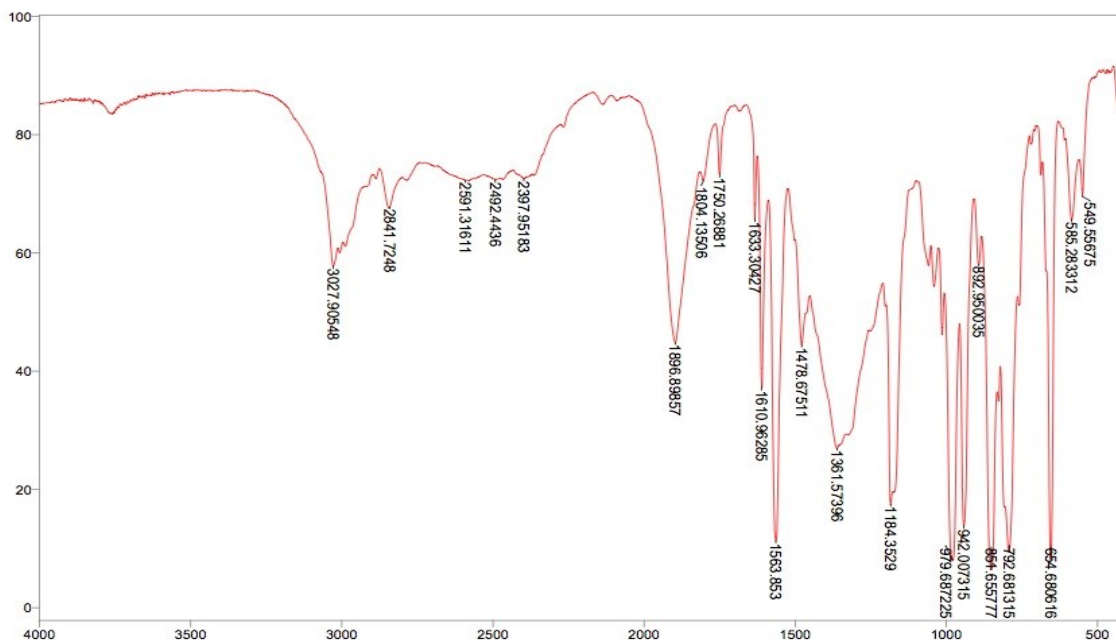


Fig 4.18: DABCO adduct with N_2O_3 (orange powder).

The orange product is somewhat soluble in warm dichloromethane or chloroform; DMSO will also dissolve it to make a blue-green solution (N_2O_3 itself is navy blue in DMSO), but this seems to entrain further reactions. Both the ^1H NMR and ^{13}C NMR show a single peak downshifted from the DABCO peak, proving that the cyclized structure has neither opened, nor is it mono-substituted. Addition of more DABCO to this mixture will not show a second peak, however, but will produce a blended average that broadens at lower temperature, demonstrating the labile nature of the interaction. The white salt is poorly soluble in organic solutions, but also shows one main peak.

This orange DABCO product acts as a nitroso donor: it reacts immediately with mercaptoethanol (also glutathione or benzyl mercaptan) to produce the nitrosothiol product, and was quantified in this way; the reported yield of 89% is based on the assumption that it has a similar reactivity with thiols as trioxide or any other nitrosating agent, and that it delivers two equivalents of NO^+ (a control was prepared in which preformed nitrosothiol was exposed to DABCO, and this did not lead to its break down or depress the concentration in any way). This establishes it as an active nitrosating agent, and the high yield justifies discounting an alternative explanation: solids treated with dinitrogen trioxide are sometimes found to have residual trioxide adhering to them (white powders remain green) for hours or days afterwards. It does not seem reasonable to propose that mere adhesion could account for so much trioxide being trapped. The trihexylamine and tribenzylamine/ N_2O_3 products were similarly tested; fresh trihexylamine/ N_2O_3 product will also react with either mercaptoethanol or benzyl mercaptan to give the nitrosothiol,

though in reduced yield compared to the DABCO: 30%, assuming that it delivers one equivalent. The tribenzylamine product also reacted in a manner not fully explored, but did not yield the nitrosothiol.

Taken together, this makes the case that in DABCO, at least, the reaction with dinitrogen trioxide forms an adduct of the form $[\text{N}_2\text{O}_3]\text{-N-(C}_2\text{H}_4)_3\text{-N-[N}_2\text{O}_3]$. The exact molecular structure remains, at this time, theoretical. DFT calculations of the ground state (B3LP/6-311++G**) find that the structures pictured in Fig 4.19, in which the lone pairs of the DABCO and the trioxide are associated, are in fact stable.

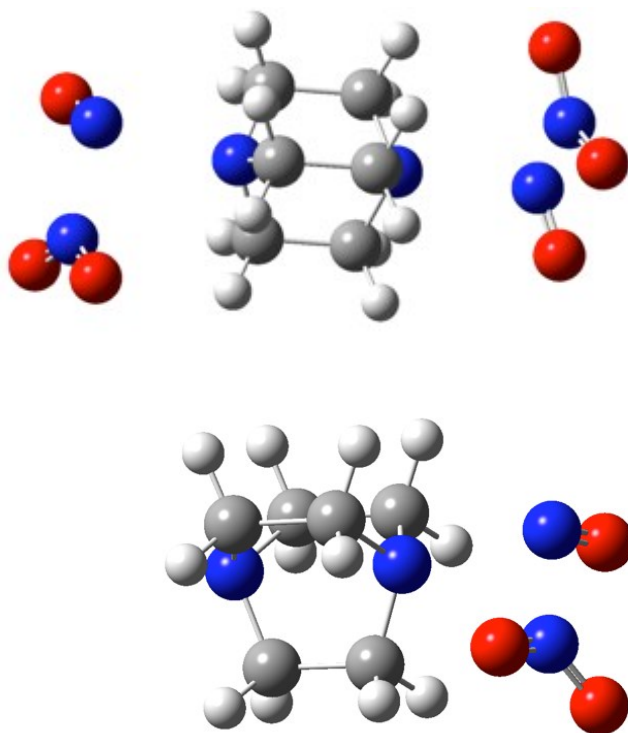


Fig 4.19: DFT calculated structure of the ground state of the trioxide/DABCO adduct (TOP-bis, BOTTOM-mono adduct).

In Table 4.1, we see the associated important bond lengths, as well as the calculated absorption wavelengths and oscillator strengths.

Table 4.1 DFT Calculated *Mono* and *bis* DABCO/Trioxide Adduct Data

	Bond Lengths (Å)			s1*		s2		s3	
	R ₃ -N	ON-NO ₂	O-NNO ₂	λ ₁	f ₁	λ ₂	f ₂	λ ₃	f ₃
<i>mono</i>	2.2931	1.8971	1.1449	528	0.0014	406	0.1463	332	0.0004
<i>bis</i>	2.3562	1.8896	1.1420	586	0.0013	536	0.0013	413	0.0701

*S_n denotes the excited state. Wavelengths given in nm. f_n denotes the oscillator strength.

This demonstrates that the N₂O₃ molecule is not altered much in the formation of the complex, with only a slight lengthening of the N-N bond. The intense oscillator strength predicted for the second excited state of the *mono* product fits with the observed initial reaction when a small amount of DABCO is added to a trioxide solution in excess: the solution becomes a dark red-brown liquid (the *bis*-adduct is insoluble in most solvents, but is bright orange). Attempts to study the dark solution are frustrated by its readiness to react with air, or to precipitate when the atmosphere changes, or to suddenly yield yellowed DABCO when warmed. Careful dilution and transfer into a short path length cell was able to net a UV-Vis spectrum, in which it could be seen that the colour stems from a broad peak that extends over the 300-400 nm range (essentially a shoulder of the intense <300 nm absorption of DABCO itself), and an extremely long tail that reaches throughout the visible range. This deviates from theory somewhat, but fits the general pattern of the *mono*-adduct absorbing strongly in the violet region (appearing red), where the *bis*-adduct red shifts into blue absorption, becoming more yellow-orange.

It is clear that reaction with water proceeds by the elimination of NO and the formation of HNO₃ (Fig 4.20). Stoichiometry demands that HNO be eliminated, but all attempts to detect the normal breakdown product of this reaction--nitrous oxide--showed no such species. It is possible that HNO forms but further reacts with the

N_2O_3 around it, producing nitrous acid and NO gas instead (the presence of some nitrite would be obscured by the nitrate), but again, this would require a nitroxyl/trioxide reaction that was extraordinarily rapid, and it seems more likely that HNO is not being formed as a discrete molecule in the first place. Dinitrogen tetroxide is also known to form adducts of this kind^{30,31,32}, but this is the first reported instance of such a product with the trioxide, to my knowledge.

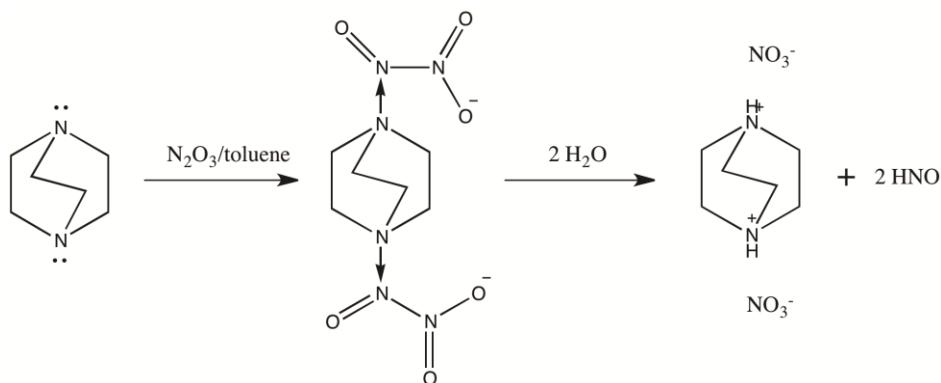


Fig 4.20: Formation and decay of the DABCO/ N_2O_3 adduct.

The behaviour of both the trihexyl and tribenzylamine suggests that a similar reaction is occurring, but that most of the unstable intermediate exists in a slightly different form. The 1897 peak in the DABCO IR suggests that the nitroso is formally $\text{N}=\text{O}$; in N_2O_3 itself, this peak is reported as 1840 cm^{-1} , whereas NO^+ is found nearer to 2300 cm^{-1} and NO^- is in the 1300s. The lack of nitrosylation with thiols shows that either the $\text{N}=\text{O}$ moiety is missing for the trihexyl and tribenzyl intermediates, or that it is more akin to NO^- .

This then provides an extra piece of the puzzle surrounding benzotriazole. The bright yellow product that forms when it is reacted with trioxide is likely an adduct of this form, through the exposed lone pair on the triazole ring, as shown by the sharp IR band at 1817 cm^{-1} which vanishes when exposed to air. This yellow

product also reacts with thiols to produce nitrosothiols, though gauging from the yield of nitrosothiol, only 16% of the benzotriazole product is capable of NO^+ donation. It is likely that this adduct is only a minor product amongst others; the nearby N-H proton no doubt makes formation of a proton-sensitive adduct unfavourable.

Finally, two tertiary basic molecules which do not form such adducts are triphenylamine and triphenylphosphine. As is perhaps obvious, in the case of triphenylamine the reaction proceeds entirely by the nitrosation of the rings, as with phenol and no adduct forms (Fig 4.21). Triphenylphosphine, on the other hand, reacts cleanly to form the triphenylphosphine oxide. When moisture is present during the reaction, an interesting side product results (Fig 4.22), a hydrogen bonded adduct between the oxide and nitric acid, first described by Tranter and Addison¹⁸. In the amine, reaction with the rings obviously out-competes adduct formation (or the adduct itself reacts with the rings), whereas in the phosphine, the drive to form the oxide protects it from further reaction.

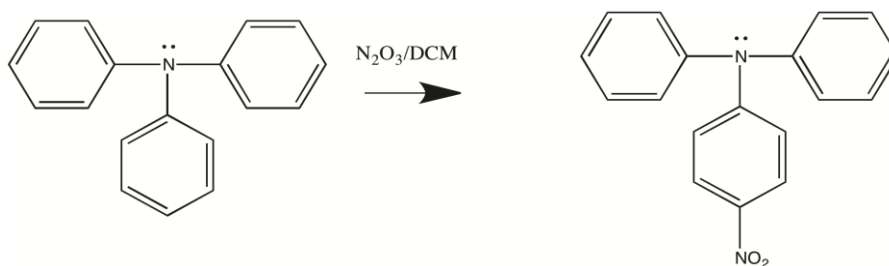


Fig 4.21: Mononitration of the triphenylamine ring.

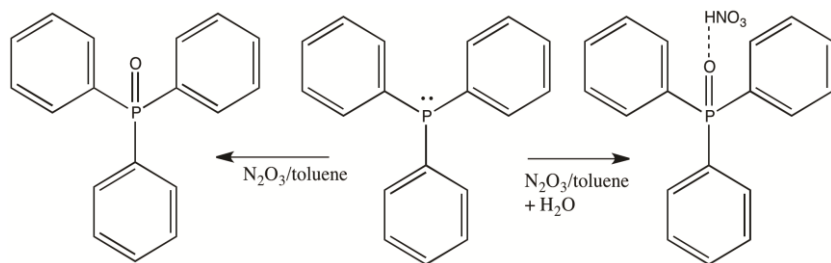


Fig 4.22: Triphenylphosphine to its oxide (left) and Tranter's adduct (right).

Other Nucleophilic/Electrophilic Reactions (4.1-w,x):

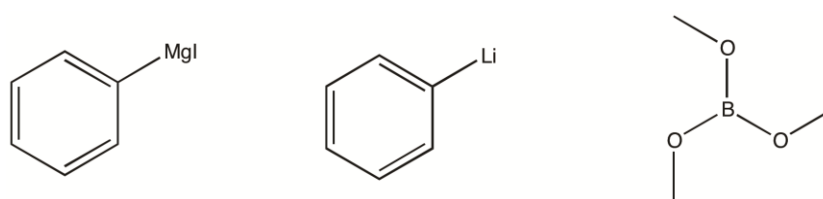


Fig 4.23: Miscellaneous nucleophilic and electrophilic targets for N_2O_3 . Left to right, phenylmagnesium iodide (Grignard reagent), phenyllithium, trimethyl borate.

In all the cases so far examined, dinitrogen trioxide has been the target of nucleophilic attack by the lone pair of various species, with NO^+ formally acting as the acceptor. It is worth exploring then what effects stronger nucleophiles would have, and also whether the trioxide will still behave as NO^+ if it is not explicitly treated as such, i.e. whether the lone pair of the trioxide can itself act as a nucleophile, to attack an electrophilic target such as trimethyl borate (Fig 4.23).

This first question can be explored using phenyl anions (Eq 4.6). This has been attempted in the past; during the heyday of Grignard experimentation,

chemists³³ attempted the mixing of gas phase nitrogen oxide species with standard Grignard reagents, but this only resulted in a complex array of products. In a similar vein, in the 1960s researchers³⁴ attempted to combine Grignard reagents with benzenediazonium salts as a way to produce azobenzenes in non-aqueous environments, but this too produced many products and required decades of refinement. It was hoped that organic trioxide solutions and Grignard reagents might combine the merits of both and provide a clean synthesis of nitrosobenzene.



Eq 4.6: Aryl anion attack on dinitrogen trioxide.

Sadly, initial experiments with phenylmagnesium iodide were not encouraging, and at least half a dozen brightly coloured compounds, from red to violet, were seen to form.

The somewhat simpler phenyllithium was also used, and this reacted cleanly in the sense that it quickly produces a lot of lithium nitrite and nitrate, but the organic product was once again at least half a dozen different darkly coloured products. Spectroscopically, nitrosobenzene was detected, demonstrating that the aryl ring is capable of making a nucleophilic attack on the NO⁺ of trioxide, but this could have been guessed from its behaviour with phenol. What this does suggest, however, is that when the nucleophile is particularly aggressive, it can react with the trioxide faster than the trioxide can oxidize the nitroso group, and thus presents a strategy for their preservation.

Lastly, trimethyl borate was introduced to a trioxide solution to test the trioxide's potential as a nucleophile. It was hoped that a boron-nitrogen bond might form through attack by the nitrogen lone pair, and perhaps that is how the reaction begins. What is found, however, is that trimethyl borate was a poor choice to test this assumption, as it readily offers up methoxide anions. Careful trap-to-trap distillation, yields a large amount of methyl nitrite ($\text{CH}_3\text{-ONO}$) and a second compound, which in the NMR appears downfield to the nitrite, and has been identified as methyl nitrate ($\text{CH}_3\text{-ONO}_2$). The mixture is a brilliant orange colour when solid, but melts to a colourless liquid at room temperature and decays quickly, releasing nitrogen dioxide. It is unclear which species attacks which in the formation of these oxygen bridged nitro compounds, but there is nothing in this to challenge the general view that dinitrogen trioxide behaves primarily as an electrophile.

4.3 Conclusions

Given these results, it is reasonable to think of dinitrogen trioxide as truly a 'nitrous anhydride', the aprotic form of nitrous acid. Furthermore, in the case of almost all of the reactants tested, the results can be interpreted in a manner consistent with the standard model, in which N_2O_3 is a donor of the nitrosonium ion (NO^+), producing nitrite as a byproduct along with whatever has been displaced by the nitrosonium (H^+ , in most cases). This must of course be taken with the understanding that the ionic species does not exist in any appreciable amount in the

organic solution, merely that this is how the molecule breaks down upon interaction with a Lewis base.

The key point is that the absence of water can make a profound difference in the chemistry of these solutions. In some cases, a lack of water or abundant HONO in solution prevents some products from forming, such as the nitrosophenol from the phenol reaction, which instead produces nitrophenol. The lack of protons can simplify the chemistry, such as in the breakdown process of primary amines; by cutting off more complicated pathways which otherwise tend towards a multitude of products, only two main products are made instead. Finally, the absence of water or free protons in the tertiary amines allows products to form that would otherwise be immediately destroyed.

In sum, dinitrogen trioxide solutions are potent nitrosating, nitrating, and oxidizing agents that nevertheless do not entrain extensive side chemistry, and can be relied upon to only attack specific functional groups. In the case of the DABCO adduct, they can be used to create a solid, water soluble nitrosating agent. A further advantage is the fact that so many reactions can be carried out in non-toxic toluene, in low solvent volumes, and with almost nothing in the way of side products or toxic residues, which makes these blue-green solutions of a poisonous gas unexpectedly 'green'.

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Chapter 5: Inorganic Chemistry of Solvated Dinitrogen Trioxide

In the previous chapter, dinitrogen trioxide solutions were used as one might expect them to be used--as a substitute for nitrous acid-- so as to understand them by virtue of their similarities. Important differences exist, however, and a more complete picture of this reactant can be gained by treating them as NOT nitrous acid. To that end, various reactions were conducted that are abnormal for nitrous acid chemistry, so as to probe the boundaries and possibilities of this system. Given the vast dimensions of the category 'abnormal', this can only be a brief foray, but it suggests future avenues of research.

Of particular interest was the redox behaviour of solvated dinitrogen trioxide. The reduced form of dinitrogen trioxide is unknown, presumably because it too easily cleaves into NO and nitrite. Only the dianion, $\text{Na}_2\text{N}_2\text{O}_3$ ¹ (also called oxyhyponitrite, trioxodinitrate, or Angeli's salt) can be made², and this is accomplished by oxidation of a form of nitrogen that is already reduced, hydroxylamine (Fig 5.1). Thus another curious feature of N_2O_3 is that although as a neutral molecule, it is held together by a long bond, and the addition of an electron (into the π^* orbital) causes this bond to break entirely, the addition of *two* electrons ends up stabilizing the molecule and strengthening this bond.

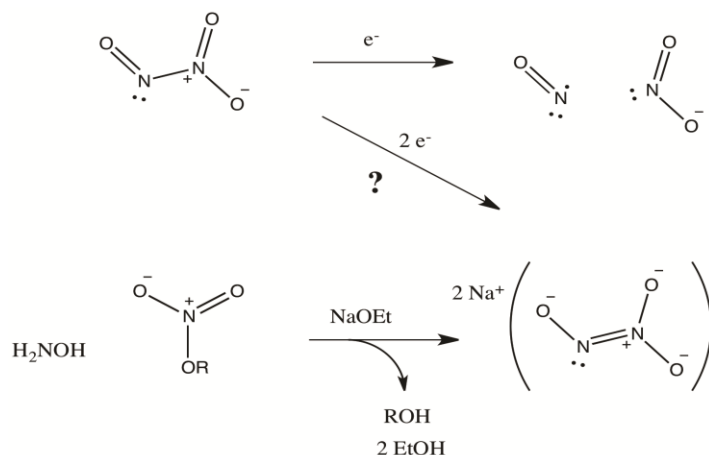


Fig 5.1: Top: Reduction of N_2O_3 , causing cleavage. Bottom: Oxidation of hydroxylamine to make Angeli's salt (dianion of N_2O_3).

Thus the fact that trioxide in solution is stabilized raises the tantalizing possibility that it could withstand a single electron reduction, at least long enough to make a second reduction, thus approaching trioxodinitrate from a novel direction. In general, there are a great many nitrogen oxide products which *could* exist, but for their tendency to collapse into the stable gases (NO , NO_2 , N_2O , N_2) or common anions (NO_2^- , NO_3^-), and having a means to bypass some of these decay pathways would be very useful.

Experimental

The experimental processes used here are in all aspects similar to that employed in the preceding chapter. Where unspecified the trioxide solutions were prepared in excess stoichiometry, $\sim 1 \text{ mol/L}$, at 0°C . 'Trioxygen' designates dinitrogen trioxide, and 'tetroxygen' is dinitrogen tetroxide. Tetroxide is prepared by the same

methods as trioxide, with appropriate changes to gas ratios. Yield is reported as the percent of recovered mass of the purified product, compared to a theoretical calculation. Products and IR absorptions of particular note are designated in **bold**.

5.1-a) Alkali metals (Na, K, Li): A trioxide solution is prepared in toluene at both 0°C and -79°C, and a small chip of the metal to be tested (freshly cut, washed in hexane, dried under nitrogen) is introduced. The reaction is sluggish at 0°C (proceeded over minutes) and seemingly non-existent at -78°C, but in both cases the metal chip glazes over after 3 hours with a white crust of powder, with evolution of nitric oxide. Analysis of the white powder by IR shows it to be **potassium/sodium/lithium nitrate**.

5.1-b) Alkali/Ammonia (Na, K, Li): The alkali metal is washed in hexane, dried under argon, and ~0.01 g is dissolved in liquid ammonia (condensed from the gas in an ethanol slurry cold trap) under an argon atmosphere to produce the brilliantly coloured solvated metal reducing agents. A cold solution of N₂O₃ in excess is added dropwise via a metal cannula (positive argon pressure must be maintained at all times, or a mixing of vapours from the two solutions in the cannula can cause it to plug). The reaction is instantaneous and releases abundant gas (CAUTION: perform only on a milligram scale), coating the inside of the vessel with fine white

powder. Analysis by IR shows it to be primarily **potassium/sodium/lithium nitrate**.

5.1-c) Potassium Hydroxide: Pure N_2O_3 is condensed at -79°C in excess over a bed of potassium hydroxide pellets. In less than an hour it is found to have rendered the pellets into a white powder, accompanied by the steady evolution of pure nitric oxide gas. The powder is identified by IR and UV-Vis as pure **potassium nitrate** (KNO_3) in quantitative yield.

The experiment is repeated with the trioxide as a toluene solution on ice, at a concentration of 1 mol/L. Potassium hydroxide pellets (1 g) are added and stirred for 1 hour, to produce a mixture of **potassium nitrite/nitrate** ($\text{KNO}_2/\text{KNO}_3$) in a 30:70 ratio in quantitative yield, as a white powder. Nitric oxide gas is slowly evolved in the process. Similar results are obtained for dichloromethane or chloroform solution, though chloroform reacts at a noticeably faster rate.

In a third experiment, the ratio of hydroxide to trioxide is raised to 1: 0.75, and the trioxide is introduced slowly, in quarters every half hour. This is accomplished by preparing the argon purged solvent over a bed of hydroxide under dynamic NO pressure, with stirring, then injecting the oxygen slowly. Prepared in this way, the yield is 86% nitrite, 14% nitrate. After the powder has been vacuum dried for 1 hour, it is returned to a trioxide solution and stirred for 1 hour, which transforms it entirely to pure white potassium nitrate.

In a fourth trial, trioxide and tetroxide (N_2O_4) are prepared separately in toluene solutions (1 M), and an equimolar amount of dry sodium nitrite is added. No reaction results. The addition of 1 mL of water to each causes the evolution of NO gas from the toluene/water interface; the toluene layer of the tetroxide solution becomes dark blue. After 1 hour of stirring both samples are recovered and dried and are found to be potassium nitrate in quantitative (99%) yield (trioxide product is pure white, tetroxide is bright yellow. Purity is checked by UV-Vis and IR).

The yield is determined by comparison of the absorption peaks in the UV region: in water, the ϵ_0 for nitrite is 28.59 L/(mol•cm) at 354 nm and 11.945 L/(mol•cm) for the faint minimum at 300 nm (determined from pure samples); for nitrate, it is 9.343 L/(mol•cm) at 300 nm. The quantity of nitrite is given by the absorption at 354 nm, and subtracting the appropriate amount from the 300 nm absorption gives the absorption due to nitrate; this result is compared to a calibration curve prepared from mixed samples of known composition.

The experiment was repeated with sodium hydroxide, with similar results.

5.1-d) Water: The reactant is titrated into 10 mL of a 1 mol/L trioxide solution in acetonitrile, and the level of trioxide is monitored by UV-Vis. When 10 mL of water have been added (a 50:50 mixture), the level of trioxide has fallen to 7.2 mmol/L (the level predicted for pure water is 2.96 mmol/L). The product is **nitrous acid** in quantitative yield. UV-Vis: Fine structure at 333, 347, 358, 371, 383 nm.

In water immiscible solvents (toluene, dichloromethane), the added water remains in a clear aqueous layer, while the organic layer remains blue. A 1 mol/L mixture of trioxide/toluene plus water is stirred for an extended period of time and the concentration of trioxide in the organic layer is measured by UV-Vis; after 1 hour the trioxide level has fallen to 21% of its starting concentration; losses beyond this point are consistent with a control prepared under the same conditions without water (~4% loss per hour) due to diffusion into the septum and/or slow leaks.

Reversing the process, a 10 mL sample of water is prepared with standard trioxide solution techniques (slow injection of O₂ into an NO saturated environment) to make a 1 mol/L solution of nitrous acid as a clear, faintly blue liquid. An equal volume of toluene is added and stirred for five minutes, during which a rich blue-green colour evolves in the toluene. Measurement by UV-Vis gives a concentration of 0.053 mol/L N₂O₃.

5.1-e) Nitric acid: Concentrated nitric acid (68% acid, 32% water) is titrated into 10 mL of a 1 mol/L solution of trioxide in toluene at 0°C. A separate red-brown aqueous layer forms underneath the blue-green toluene layer. When 6.1 mL of nitric acid has been added the blue-green colour in the toluene layer is judged to be gone (a murky brown colour remains). The product is a toluene solution of **dinitrogen tetroxide** above a mixture of nitrous acid in water. UV-Vis: 220, 343 nm in toluene. The tetroxide can be isolated by trap-to-trap distillation as a colourless liquid. The product forms nitrate and nitrous acid when added to pure water.

The experiment is repeated in acetonitrile, and a green solution results after the addition of 10 mL nitric acid. Analysis by UV-Vis shows that the solution contains 9.7% of its starting dinitrogen trioxide level.

5.1-f) Hydrochloric acid: One mL of concentrated aqueous hydrochloric acid (36.5%) is added to an equimolar trioxide solution. In water immiscible solvents, 20 minutes of stirring allows for the formation of a cloudy yellow-brown solution; in acetonitrile, the solution immediately becomes a clear red-orange. In either solution the product is seen to be the same. Bubbling nitrogen gas through the solution for 20 minutes and collecting the stream in a liquid nitrogen cold trap gives **nitrosyl chloride** as a brilliant orange solid. It evaporates quickly at room temperature, and was identified by the UV spectrum³ of its vapour. UV-Vis: ϵ_{max} at ca. 220 nm, 341 nm, smaller peaks at 435 nm, 474 nm.

5.1-g) Sulfuric acid: The acid is introduced to excess trioxide in a non-aromatic solvent (dichloromethane or acetonitrile) to yield a white product; in dichloromethane this will be an oily paste, whereas in acetonitrile, the product forms as dry granules. The product will spontaneously decay to nitric oxide and sulfuric acid if removed from the solvent. The product is instead washed three times with cold dry acetonitrile, then dried under vacuum to yield **nitrosylsulfuric acid**⁴ (chamber crystals) in 78% yield as a fluffy white powder. Alternatively,

washing with acetonitrile then stirring with dry dichloromethane for 24 hours will yield dense white chunks of dry precipitate, in similar yield. The product decays in air with release of nitric oxide; reacts violently with water and alcohol, again releasing nitric oxide. IR: 3470 (br), 1656 (w), 1438, 1383, 1363, 1268, 1156 (str), 831 cm^{-1} . Confirmed by comparison with product prepared by literature techniques⁵ (absorption of NO gas into sulfuric acid).

Nitrosylsulfuric acid can be prepared in aromatic solvents, but this produces intensely coloured side products (red and orange) from reaction with the solvent. In benzene the reaction is relatively clean and this solvent may be used for the synthesis if necessary, though the level of purity has not been ascertained.

CAUTION: Use of mesitylene as a solvent will produce a violent chain reaction, and should be avoided.

5.1-h) Copper (I) Chloride (CuCl): Green commercial CuCl is purified by dissolving in concentrated hydrochloric acid, precipitating with water, then washing with ethanol/ether and drying, yielding a pale grey powder. One gram is mixed into acetonitrile and added to 10 mL of an equimolar N_2O_3 /acetonitrile solution. A nearly black solution results almost immediately; purging the remaining N_2O_3 with argon reveals the product as an intense emerald green. This can be dried to a deep green solid, identified by IR as pure **copper (II) nitrate**. Yield of crude powder: 95%. IR (nujol): 3375, 1787, 1589, 1450, 1355, 1288, 835.

5.1-i) Mg/Anthracene: Magnesium-anthracene was prepared by heating magnesium metal in a tetrahydrofuran solution of 0.5 mol/L anthracene under inert atmosphere conditions⁶. Solvent was distilled and kept in a dry box before use. No reaction was observed when the magnesium/anthracene was added to a trioxide/toluene solution.

5.1-j) Ferrocene: A drop of trioxide solution mixed with a solution of ferrocene (1 mmol/L) will produce the distinct dark blue/green (violet in natural light) colour of **ferrocenium**.

5.1-k) Mercury: A drop of mercury is added to a solution of trioxide in toluene, in a sealed vial with minimal headspace, at room temperature. After an induction period of ~1 min a stream of colourless gas begins to evolve, consisting mostly of nitric oxide. This continues for several hours to days, during which time a white to yellow powder will begin to form as a crust around the mercury droplet. The gas evolution ceases when the green colour of the solution has faded. The product was collected and dried from one vial; other vials were prepared and left undisturbed for two weeks, during which long white to yellow-umber crystals will radiate from the mercury droplet. IR of both shows that the powder and crystal have the same composition. Powder and crystals are air and moisture stable, sparingly

soluble in aromatic solvents, and otherwise insoluble. The product is identified as a previously unreported compound, **Hg₄N₄O₉**, a nitrate salt of a mercury nitride. IR: 1458, 1384, **1291**, 1252, 1002, 862, 795, 711. Elemental analysis: Calculated for Hg₄N₄O₉: N-5.59%. Found-4.31% (error 0.3%). DSC: Crystal: exotherms at 143°C (7.523 J/g), 164°C (12.55 J/g). Powder: Exotherms at 136 °C (14.76 J/g), 163 (2.5 J/g) 180 (3.76 J/g). XPS: Two Hg binding energies ~ 105.5 eV and 101 eV, two nitrogen binding energies ~ 406 eV and 399.5 eV. See Discussion for X-ray crystallographic data.

Hg₄N₄O₉ is insoluble in most solvents, but is sparingly soluble in hot toluene. In acid, the Hg₄N₄O₉ will yellow and dissolve slowly; this may take hours in 36.5% HCl, but it will dissolve in a few minutes in HNO₃. In aqueous base it breaks down into black-green powder (believed to be mercury (I) oxide).

Treating mercury with trioxide in other solvents (benzene, xylene, chlorobenzene, 1,1',2,2'-tetrachloroethane) produces a similar result to a lesser extent, but it does not occur at all in acetonitrile. This solution remains blue for one week with no evolution of gas or precipitate. After two months resting undisturbed a very fine powder is recovered, which is different from the Hg₄N₄O₉ product, but was not satisfactorily identified. IR: 1655, **1584** (vs), 1422, 1384 (w), **1295** (vs), 1108, 1085, 945, 805, 704.

5.1-l) Mercuric nitrate/chloride: Samples of mercury (II) nitrate and chloride are each prepared under the conditions described in 5.1-k. After three days the mercury (II) chloride has not reacted in any way. The mercury (II) nitrate is attacked within moments, dissolving over hours into a black oil under a red supernatant (unidentified).

5.1-m) Sulfur: A solution of trioxide in toluene prepared over a bed of powdered sulfur results in no chemical reaction. Over the course of a week, crystals of pure sulfur form. A control with only toluene produces similar results.

5.1-n) Potassium Chloride: Four 10 mL solutions are prepared, of 1 M trioxide/toluene, trioxide/acetonitrile, tetroxide/toluene, and tetroxide/acetonitrile, all at 0°C. An equimolar amount of KCl (s) is added to each and stirred for 1 hour. No reaction is observed.

In a second trial, 2.6 mL of KCl (aq) (saturated) is added to both toluene solutions. The mixtures are stirred for 1 hour, and NO gas bubbles out slowly. A white precipitate forms in the aqueous layer and is found to be **potassium nitrate**, contaminated with nitrous acid.

In a third trial, the KCl (s) is added to the acetonitrile solutions, with the addition of a single drop of water. The mixtures are stirred for 2 hours; the blue

trioxide solution becomes muddy green a few minutes after addition, where the colourless tetroxide becomes pale yellow. Qualitative analysis of the powder after 1 hour shows it to be mostly KCl with some KNO_3 . The tetroxide solution is purged with argon gas for 20 minutes into a dry ice/ethanol cooled trap to recover a minute amount of NOCl gas in acetonitrile (as a yellow solution, off-gas measured by UV-Vis, as in 5.1-f). The trioxide solution is similarly purged, but the trap must be replaced after 5 minutes to remove the N_2O_3 --the solution at this time is a bright yellow-- and purging is continued for 20 more minutes. A bright yellow solution is recovered, also of NOCl. Measuring the off-gas of 100 μL of each solution after 10 minutes gives an estimate of the NOCl concentration; the trioxide solution is found to have ~ 2 -3 times more NOCl than the tetroxide solution.

5.1-o) Graphite: One gram of graphite powder, kept in a 130°C oven for a period of two years (not strictly necessary), is added to a concentrated (0.5 mol/L) trioxide solution in toluene, and stirred. Solutions are prepared and stirred at: -78°C for 8 hours, 0°C for 8 hours, 0°C for 24 hours, and 23°C for 24 hours. The solutions are also prepared in a Fisher-Porter high pressure apparatus, heated to 40°C and stirred for 24 hours, and to 60°C for 24 hours. Trioxide/toluene solutions at these latter temperatures remain green, but with a visible component of NO_2 gas.

After exposure to trioxide, the graphite samples are dried under vacuum for 24 hours and examined by TGA, DSC, and IR. No change is detected in the -78°C or 0°C graphite samples. TGA of the other samples to 900°C shows, beginning at

~600°C, the following mass losses: Control- 2%, 23°C- 19%, 40°C-15%, 60°C- 17%.

The IR of each contains a strong peak at 1384 cm⁻¹ prior to TGA treatment, which disappears after heating. No significant changes occur in the DSC in the temperature regime 25°C-250°C. Elemental analysis of the 23°C product: Calculated for 19% mass as N₂O₃: C-81, N-7%. Found: C-95%.

Discussion of Results

Solvated dinitrogen trioxide was tested with an array of conditions that are common in inorganic chemistry. It was reacted with bases (treating it as a Lewis acid), with acids (treating it as a Lewis base), with metals and reductants (treating it as a one-electron acceptor), with inorganic salts (assuming that it is a salt), and with known intercalation media (treating it as a neutral planar molecule). Though most of these classes overlap, it is still a testament to the versatility of this molecule that it was found to assume all of these roles to some extent.

Reactions with Base:

In the previous chapter dinitrogen trioxide was repeatedly used as a target for nucleophiles, primarily by amines, which may attack through the lone pair of their nitrogen. In such a reaction (Fig 5.2), the initial step involves the trioxide accepting a lone pair from the amine; that is, it acts as a Lewis acid.

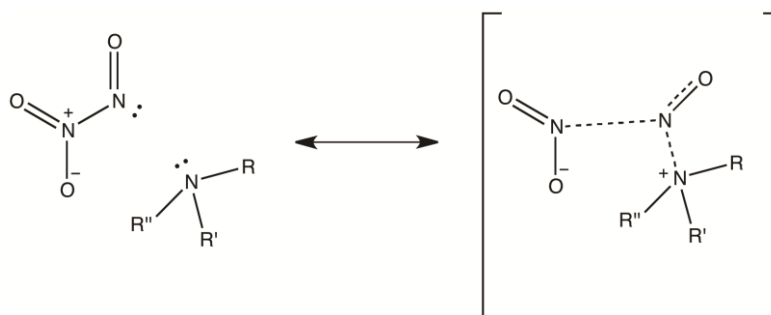


Fig 5.2: N_2O_3 as a Lewis acid in amine reactions.

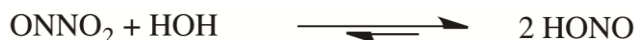
Whether this intermediate breaks down heterolytically, to yield nitrite and a nitroso species, or remains intact to form the adduct, or cleaves off one of the R groups depends on the circumstance. This reactivity was initially clarified by treating trioxide with simpler bases, such as hydroxide.

Although sodium and potassium hydroxide are not soluble in organic solvents, adding them as solid pellets to organic trioxide solutions still enables them to react by surface chemistry with the solvated trioxide. The trioxide is attacked by the hydroxide in a standard Lewis-acid-base reaction, yielding nitrous acid and nitrite; that is, a strong Lewis base plus what must be considered a moderately strong Lewis acid (as it reacts to completion with amine, a weak base) yields a salt and a weak Lewis acid (Eq 5.1):



Eq. 5.1: Dinitrogen trioxide and sodium hydroxide.

We must consider this reaction as in principle reversible, as most of the dinitrogen trioxide ever used in chemistry is formed by the analogous equilibrium, which we've seen before (Eq 5.2):



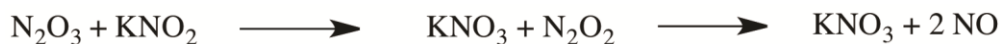
Eq. 5.2: Dinitrogen trioxide and water.

The relative position of these equilibria is controlled by the electronegativity of hydrogen versus sodium, and by the relative insolubility of sodium nitrite in organic solvent, as compared to nitrous acid, which stays in solution.

In the reactions here under consideration the alkali nitrate is found in place of the nitrite, for the reasons alluded to in the last chapter: dinitrogen trioxide quite readily oxidizes nitrite to nitrate. In fact, in a 1:1 mixture of potassium hydroxide and trioxide, both will be entirely consumed, yet the product will be found to be 70% nitrate and only 30% nitrite.

This naturally raises the question of how this can happen, if the trioxide is being consumed by the hydroxide; the answer was mentioned elsewhere in the last chapter, in that the HONO product of the reaction can further combine to make more N_2O_3 (one trioxide can, in effect, act twice). The follow-up question becomes whether this is truly the trioxide performing the oxidation, or the nitrous acid itself. While two species in equilibrium can make definitive answers to such questions misleading, it is certainly the trioxide that is responsible, given two observations. First, the transformation from nitrite to nitrate does not proceed to 100%, which

would be expected if HONO itself were capable of the needed oxidation. Second, addition of sodium nitrite to a concentrated solution of nitrous acid has never been shown to produce large amounts of nitrate (here the low N_2O_3 concentration and presence of water evidently impede the process).



Eq 5.3: Oxidation of nitrite to nitrate.

If nitrite is being oxidized by N_2O_3 , by the stoichiometry of this reaction (Eq 5.3), the transformation of nitrite to nitrate must involve the production of N_2O_2 , which, being unstable at these temperatures, dissociates into two NO, as evidenced by the slow evolution of gas that accompanies these reactions, which is also seen any time nitrite is produced. This last point is worth noting, as reactions with trioxide that do not produce appreciable NO gas almost certainly do not proceed by the formation of nitrite. Trioxide solutions typically leak small amounts of NO at all times, but in rapid reactions, the formation of bubbles is a telltale sign that nitrite ion is being produced, then subsequently oxidized. Examples from the previous chapter include triethylamine, which produces large amounts of NO gas, as compared to trihexylamine, which produces almost none.

This secondary oxidation, as it relies on N_2O_3 , is obviously faster when the trioxide is already present rather than requiring it to form by HONO dissociation, and as such adding hydroxide as a solid to a trioxide solution necessarily exposes the nitrite as it forms to some N_2O_3 . Limiting this exposure, by first restricting the amount of trioxide used (to a ratio of 1 hydroxide to 0.75 trioxide) and by

introducing it slowly, will therefore limit the nitrate formation. By taking these steps I was thus able to shift the yield of the salt to 86% nitrite and 14% nitrate; even greater care could undoubtedly improve this yield further.

A noteworthy detail is that pure sodium nitrite, taken dry from a bottle, will be more or less inert under a bath of trioxide solution, whereas nitrite formed from a previous reaction oxidizes easily. This appears to be a question of lattice energy strength, i.e. dinitrogen trioxide by itself is unable to solvate the ions. Nitrite formed in a previous reaction, though dried under vacuum, undoubtedly contains some hydrate (due to HONO being trapped out in the precipitate), and this allows its subsequent reaction with an otherwise dry trioxide solution. Dry nitrite will react with a toluene trioxide solution if a few drops of water are added to the mixture; this partially solvates the nitrite, and in moments bubbles of nitric oxide gas will form, streaming from the surface of the water/toluene interface (water and toluene together, without nitrite, do not produce this response, nor do other aqueous salts such as NaCl or NaNO₃).

The transformation of nitrite to nitrate was noted by Shaw and Vosper when they studied these solvated trioxide systems⁷, but they ascribed this action to the presence of N₂O₄, as this is a more powerful oxidizing agent. They also reported that N₂O₄ would only oxidize nitrites of less strongly ionic metals (Ag, Tl, Ni, perhaps due to weaker lattice energies), but would not perform this action on alkali nitrites. This assertion is not backed by any citation or mechanism, but perhaps refers to the work of Addison and Lewis^{8,9}, who reported that oxidation of nitrites by tetroxide

only occurs to a significant degree above 100°C. Oza and Oza¹⁰ confirmed this, though they added that in the case of calcium nitrite, the presence of a hydrate would allow oxidation at lower temperature; dehydrating the nitrite prior to reaction greatly limited the oxidation. Since tetroxide reacts with water to produce nitric and nitrous acid, this raises the specter of trioxide being the true active agent at room temperature or below.

To gauge this assertion, I prepared a toluene/tetroxide solution under the standard reaction conditions, and added sodium nitrite. If tetroxide does react, this should be evident by the formation of both nitrate and dinitrogen trioxide:



Eq 5.4: Proposed oxidation of nitrite by dinitrogen tetroxide.

Neither product was detected. Naturally, as with trioxide there is the issue of lattice energies to overcome; however, adding a small amount of water to the tetroxide solution immediately causes the formation of nitrous acid, and the tetroxide solution becomes the rich blue of trioxide. The nitrite oxidizes entirely to nitrate, but the mechanism can no longer be distinguished. Two observations can be made: first, in both cases, the oxidation proceeds by the formation of bubbles of nitric oxide, which is predicted to form by the trioxide mechanism but not by tetroxide, and second, the nitrate formed by trioxide is a pure snow white where the tetroxide product is stained yellow, due to the formation of trace side products or adsorption of N₂O₄. If the trioxide oxidation were proceeding, in truth, by the tetroxide

mechanism, it is unclear why it would not also be yellowed in this way. It is possible that either mechanism may be viable, but provisionally, I conclude that nitrite is oxidized at low temperatures by trioxide in solution, rather than by tetroxide.

Reactions with Acid:

We do not commonly think about species that are described as acids as reacting with acids, but the fact that every acid has its conjugate base pair and acid strengths differ means that acid-acid chemistry is an often quite important part of a particular species' chemistry.

First, we must reconsider Equation 5.2, the reaction with water. In aqueous solutions this equilibrium lies far to the right, due to the high concentration of a species on the left side (H_2O), and the greater stability that a hydrogen bonding species will have in a protic environment. The fact that organic solutions work to exclude water alters this relationship. This can be seen when water is added to trioxide solutions: in water miscible solutions such as acetonitrile, the N_2O_3 is immediately consumed as the equilibrium shifts to nitrous acid. But in immiscible organics such as toluene or dichloromethane, the water layer separates, and the two layers effectively compete to hold onto the nitrogen species in its hydrous and anhydrous forms. This has been described in some detail in model biological systems, in terms of water-organic partition coefficients^{11,12}. Squadrito and Postlethwait noted that while the conditions of a cell, "will not favor the formation

of either N_2O_3 or N_2O_4 ," nevertheless, " N_2O_3 will generally be more likely to form than N_2O_4 "; this was thought to be because NO was less reactive under these conditions.

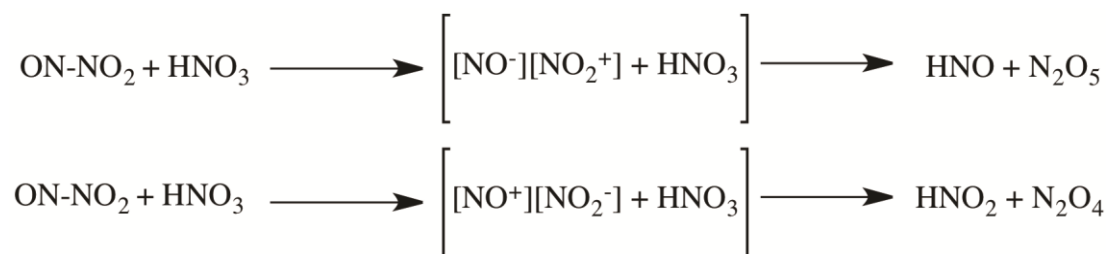
Performing reactions in solvents in which nitrous acid is a byproduct eventually causes a water layer to form, evidence that the nitrous acid is recombining to make more N_2O_3 and water. On occasion, a reaction in which the initial trioxide has been stoichiometrically consumed, leaving only nitrous acid (such as secondary nitrosamine formation), will be seen to become blue again upon sitting, demonstrating a preference for the anhydrous form even when water is present. The ready oxidation of nitrite to nitrate just discussed is another such case: if the K_{eq} between HONO and N_2O_3 in an organic solution was small, and N_2O_3 is responsible for the oxidation of nitrate, then this reaction would not occur so quickly.

The literature value given for the $K_{\text{eq}} = \text{N}_2\text{O}_3 / [\text{HONO}]^2$ in aqueous solutions is, as DLH Williams¹³ noted as recently as 2004, highly variable, but he goes on to note that by 'general agreement' the value of $3 \times 10^{-3} \text{ M}^{-1}$ is 'probably the most reliable¹⁴'. Thus in a 1 mol/L nitrous acid solution one will find 2.96 mmol/L of trioxide. Toluene solutions of trioxide in 1 mol/L concentration stirred with water will gradually lose trioxide to the water layer, but after 1 hour, measurement by UV-Vis will still show a concentration of 0.22 mol/L of trioxide, seventy-three times the ratio that normally exists in water alone. It is difficult to accurately determine a K_{eq} from more extended stirring, as losses to water compete with other means of N_2O_3 destruction (that is, NO escape), but approaching the question from the other

direction gives a better idea: a faintly blue 1 mol/L solution of nitrous acid stirred with toluene will, in a matter of minutes, produce a rich blue organic layer. The dinitrogen trioxide shows a strong preference for the organic layer, and by measurement of the visible spectrum and using the formula $K_{eq} = [N_2O_{3(toluene)}] / [HONO]^2$, one can calculate $K_{eq} = 0.0666 \text{ M}^{-1}$. That is, the trioxide concentration in mixed toluene/water is 22 times higher than in water alone.

In water miscible solvents, a modest increase of K_{eq} seems to occur. A small amount of water added to an acetonitrile/trioxide solution quickly reduces the level of trioxide to a mere trace, but even when the level of water reaches 50:50, the trioxide concentration exceeds that expected in pure water. Assuming that the extinction coefficient of trioxide has not varied much (as the spectrum has not changed from that of pure acetonitrile), one can approximate a new K_{eq} to be $7 \times 10^{-3} \text{ M}^{-1}$, or roughly twice that of pure water.

When it comes to the reactivity of dinitrogen trioxide with strong acids, the molecule begins acting more like a salt of nitrosonium and nitrite, and its reactions resemble the classic double substitution reactions. Though we consider N_2O_3 to be sensitive to the presence of H^+ , in fact this cannot be considered in isolation; the counter-ion is an important factor in how the molecule breaks down. In water, the OH^- counter-ion allows the formation of nitrous acid. Reaction with nitric acid, by contrast, entails two different possible pathways (Eq 5.5):



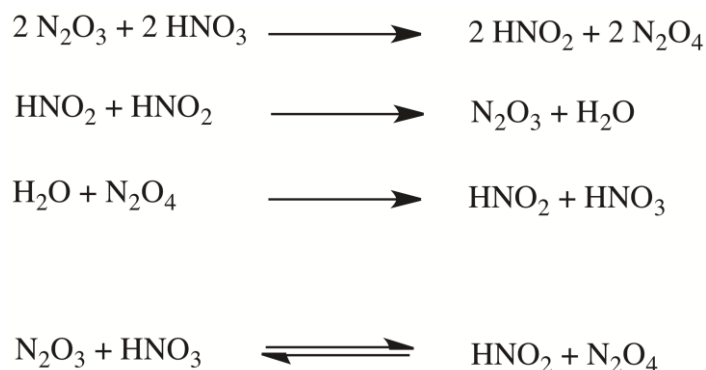
Equation 5.5: Possible products of nitric acid/ dinitrogen trioxide reaction.

The first product may rearrange to form dinitrogen pentoxide, and the second may become dinitrogen tetroxide. The formation of pentoxide in this way is unlikely, both because it requires the trioxide to behave as a nitrosyl anion and nitronium cation (putting a positive charge on the more electronegative fragment), and because the pentoxide can be considered the anhydride of nitric oxide; it forms nitric oxide spontaneously when mixed with water, and water is present in the mixture already.

In fact, on addition of nitric acid to a toluene solution we see the second pathway being followed: red-brown dinitrogen tetroxide settles out as a separate layer, mixed with nitrous acid and water. The colour may suggest the formation of NO₂ gas, but in fact this is the expected colour for aromatic solvents of dinitrogen tetroxide¹⁵, due to π donation from the solvent. This product can be separated by distillation, but the reaction does not proceed readily: a 1 mol/L solution was titrated with almost 10 equivalents of nitric acid before the blue of trioxide was judged to have been fully consumed.

This may seem to be an issue of immiscibility, and indeed it is: immiscibility is what allows the reaction to go to near completion. When this experiment is

repeated in acetonitrile, an addition of 10 mL concentrated nitric acid to 10 mL of trioxide solution (16 HNO₃: 1 N₂O₃) leaves a green solution, with 9.7% of the initial trioxide concentration still intact, an equilibrium point having been reached. Equation 5.5 above must be appreciated as merely one half of this equilibrium process; the full process is seen below (Fig 5.6):



Eq. 5.6: Equilibrium between nitric acid and dinitrogen tetroxide.

Thus addition of nitric acid establishes an equilibrium between trioxide and tetroxide, rather than simply consuming the trioxide completely. Given that the chemistry of nitrogen oxides frequently produces nitric acid as one of many byproducts, this explains why such formation is not terribly detrimental to dinitrogen trioxide formation.

Hydrochloric acid, on the other hand, reacts on contact with a trioxide solution and appears to go to completion. It will turn a blue toluene solution a sickly yellow-green after a few minutes of stirring (the product forms slowly due to immiscibility), whereas in acetonitrile, it will turn a clear, red-orange colour within seconds. Regardless of the solvent, the product of this reaction is nitrosyl chloride¹⁶

and nitrous acid. The nitrosyl chloride is stable in solution and can be used as such in further reactions; otherwise, it can be isolated by bubbling a stream of nitrogen through the solvent and collecting the gas in a dry-ice/ethanol cold trap. The yellow gas condenses to a clear red-orange liquid, which boils at room temperature. The reaction is a textbook double substitution (Eq 5.7).



Eq 5.7: Hydrochloric acid and dinitrogen trioxide.

It is at this point that I can return to the question raised in Chapter 1, regarding the possible alternative to the reaction scheme described by Yost and Russel¹⁷ for the production of NOCl from NO₂ (Chapter 1, Fig 1.6). In it we saw how the reaction scheme could proceed with the same stoichiometry, but with N₂O₃ as an intermediate, explaining the necessity of a catalytic amount of water. If this is the true pathway, then presumably it should proceed even more quickly in a trioxide solution; Eq 5.6 compares the two, and where the tetroxide pathway (or tetroxide by way of a trioxide intermediate) produces nitrate, the trioxide alone should produce nitrite. To test this hypothesis, I treated KCl salt with both tetroxide and trioxide solutions in both toluene and acetonitrile. No reaction was seen for either one of them. Here, as in the case of dry nitrite, a small amount of water to overcome the lattice energy of the salt is necessary, liberating K⁺ and Cl⁻ in association with H₂O to react with the trioxide.

However, the desired product (NOCl) is destroyed by contact with water, making solution based synthesis less practical. Delivering the KCl to solution by the

use of a brine allows the reaction to proceed to completion, producing KNO_3 in quantitative yield, with NO gas evolution, but no NOCl could be recovered. In acetonitrile solutions to which a single drop of water has been added, the reaction will proceed slowly, and traces of KNO_3 are found in the precipitate, while minute quantities of NOCl can be recovered from the solution.

Clearly, this reaction is not as favourable in a solution phase as on a solid surface (the original reaction is carried out on damp crystals). However, in both cases the KCl is consumed and some NOCl is made; furthermore, though the NOCl concentration is small, UV-Vis of the vapour obtained from 100 μL of reaction mixture shows that the trioxide mixture obtains NOCl in almost three times the quantity that the tetroxide mixture does. This result would make little sense unless trioxide were in some way involved in the reaction scheme. Furthermore, where trioxide solutions exist in an equilibrium with water (which destroys NOCl), tetroxide consumes water, and should be a more suitable environment for forming water sensitive products, and yet less NOCl is found. On the basis of this experiment, I can make no firm conclusions, but it casts serious doubt on the proposal that tetroxide alone is responsible for this reaction.

Last in my series of acid reactions, I considered sulfuric acid. Research into the chemistry of sulfuric acid and nitrogen oxides is extensive¹⁸, extending over a century, due to the role of nitric oxide in the lead chamber process for the synthesis of sulfuric acid¹⁹. A byproduct of this process is nitrosylsulfuric acid (NOHSO_4), aka

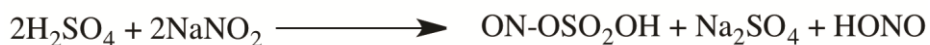
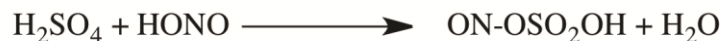
chamber crystals, which is an important industrial chemical even today²⁰ (used mostly, as it happens, as a means to generate NOCl, by reacting it with HCl).

In the laboratory, chamber crystals can be made from fuming nitric acid and sulfur dioxide (Eq 5.8). This form of the reaction produces no side products that could otherwise decay the product.



Eq 5.8: Chamber crystals from nitric acid.

The alternative path, and the one more commonly available to chemists, is by the reaction of sulfuric acid with various sources of nitrosyl cation, those being aqueous nitrous acid, solid sodium nitrite, or dinitrogen trioxide (Eq 5.9):



Eq 5.9: Standard laboratory preparations for chamber crystals from sulfuric acid.

It is easily appreciated that these are all merely variations on a theme. Very old literature states that sulfuric acid will simply absorb nitric oxide, but it has been demonstrated that some contamination with oxygen/nitrogen dioxide is always

necessary for the nitrosylsulfuric acid to be produced¹⁸; that is, this reaction proceeds largely through a nitrous acid/nitrous anhydride (N_2O_3) pathway.

This method has some drawbacks, however, as it creates a final product that is both wet and impure. Water is a product in all these reactions and can react with the nitrosylsulfuric acid, though in the case of the sodium nitrite reaction the sodium sulfate product is a stable desiccant, and it helps to stabilize the resulting acid. Separating the two tends to lead to destruction of the product, however. Even direct reaction of dry sulfuric acid with dry gas yields enough water that the product is a gooey paste that can easily break down back to sulfuric acid. Furthermore, where nitrosylsulfuric acid precipitates nicely out of fuming nitric acid (from the sulfur dioxide method), sulfuric acid dissolves nitrosylsulfuric acid, and at high concentrations it becomes so viscous that complete reaction becomes unfeasible. Thus nitrosylsulfuric acid prepared in this way will always contain significant amounts of sulfuric acid (commercially, it is sold as a mixture of the two).

Here, organic trioxide solutions prove to be different not by virtue of unique chemistry, but for the more pragmatic reasons of work-up. Sulfuric acid added to a trioxide solution immediately produces nitrosylsulfuric acid as a white precipitate. When prepared in acetonitrile, the product settles out as a white precipitate, while the water and HONO stay associated with the solvent (dichloromethane will also produce a solid precipitate, though less finely separated). Drying this directly will destroy the product, as this will free the trapped water, but repeated washing with cold dry acetonitrile gives the pure nitrosylsulfuric, which may be dried and stored

in a dessicator. Thus when sulfur dioxide and fuming nitric acid are not available, an alternative laboratory synthesis of pure, dry nitrosylsulfuric acid can instead be achieved with sulfuric acid, dry solvent, and a nitric oxide source.

Unfortunately, this does not work in all solvents. Since the side product of the reaction is still HONO, water immiscible solvents will produce a separate water phase that will combine with the sulfuric acid and nitrosylsulfuric acid as an oil that crashes out of solution. Attempting to remove the solvent will destroy the product. Furthermore, aromatic solvents, though excellent for forming trioxide solutions, react with nitrosylsulfuric acid over time, more rapidly the more donation there is from ring substituents (benzene will slowly yellow, toluene will go red, mesitylene will violently erupt). Chemically speaking, this oil still behaves as nitrosylsulfuric acid and can be used as such, but it loses potency as it reacts with the solvent.

Reactions with Reducing Agents

Early work with these solutions was an attempt to form stable N_2O_3 salts as a simple direct means of approaching Angeli's salt, $[\text{M}^+][\text{N}_2\text{O}_3^{2-}]$, in the hope that the stabilizing effects of solvent could help bypass the cleavage of the molecule from one electron reduction (Eq 5.10):



Eq 5.10: Decay of dinitrogen trioxide from one electron reduction.

Unfortunately, the alkali metals all proved reactive with the trioxide solutions, even at -78°C , although slower than one might expect, developing a white crust over a matter of hours. The product was only nitrate salt with the evolution of nitric oxide gas, and it was evident that the trioxide was simply breaking down upon reduction.

A more rapid electron delivery system was attempted by dissolving the metals first in liquid ammonia. This did indeed rapidly reduce the trioxide in solution, which rapidly breaks down, producing nitrate and gas in a single explosive burst, even at -78°C .

In response to that, less reductive methods were tested, using ferrocene and a magnesium-anthracene system. Ferrocene was found to reduce the trioxide easily, to nitrate with the accompanying gas evolution, while magnesium-anthracene produced no reaction.

From this it was concluded that while solvent polarity and π -cloud interactions may stabilize the trioxide molecule (as discussed in Chapter 3), full reduction still leads to its destruction; the reaction pathway that leads to NO gas formation is the preferred pathway, even in solution.

This one-electron oxidation pathway is standard for its reaction with metals. When copper (I) chloride is mixed into a solution of trioxide, it quickly forms a copper (II) salt; since the one electron oxidation of the trioxide evolves nitric oxide and leaves nitrite, and this nitrite is further oxidized to nitrate, the product of this reaction is simply the deep green copper (II) nitrate.

It would be misleading to think of the trioxide as a particularly powerful one-electron oxidant, however. Other metals were exposed to trioxide solutions in their pure form, and in most cases they remain inert. Zinc, magnesium, and gold are unaffected by exposure. This contradicts some earlier research²¹ that suggests that zinc should react with N_2O_3 to produce nitrites, but those studies were based on the pure trioxide, or else on tetroxide with some trioxide added to accelerate the tetroxide chemistry²². Iron, copper, and cobalt will all eventually react (forming red oxide, green oxide, and an unidentified magenta product), but as this is only seen weeks after the trioxide itself has faded it cannot be considered a true product of trioxide.

The exception in these trials is mercury, which reacts readily with trioxide: after an induction period of less than a minute, a stream of clear gas is seen pouring off the surface of the mercury, and a crust of white powder has collected around it. This product (dubbed 'mercury blue'), if left undisturbed for a week or longer in its reaction vessel, crystallizes in long yellow to amber needles. The crystals grown in toluene have nearly identical IR signatures to the raw powder. X-Ray crystallography reveals them to be $\text{Hg}_4\text{N}_4\text{O}_9$, in which three mercury are arrayed as the base of a shallow triangular prism with a nitride at the apex (Fig 5.4). The fourth mercury is bound directly to one of the points of this triangle. Three nitrates form the necessary counter-ions; by charge, we suspect a mixed valent species, in which two mercury are mercury (I), and two are mercury (II). Other possible redox forms were considered (Table 5.1), but two Hg^{+2} and an Hg_2^{+2} (the dication form common

to Hg⁺) fits best with the arrangement of the nitrate and the two different Hg bonding pairs.

Table 5.1: Possible redox forms of 'mercury blue' salt.

Formula	Hg	Bridge atom	Anions	
Hg ₄ N ₄ O ₉	2Hg(I) 2Hg(II)	N ³⁻	3 NO ₃ ⁻	
Hg ₄ N ₄ O ₉	4Hg(I)	N ¹⁻	3 NO ₃ ⁻	
Hg ₄ N ₄ O ₉	4 Hg(II)	O ²⁻	2 NO ₃ ⁻	NNO ₂ ⁻²
Hg ₄ N ₅ O ₈	Hg(II) 3Hg(I)	N ¹⁻	2 NO ₃ ⁻	NNO ₂ ⁻²
Hg ₄ N ₆ O ₇	2Hg(II) 2Hg(I)	N ¹⁻	1 NO ₃ ⁻	2NNO ₂ ⁻²
Hg ₄ N ₇ O ₆	3Hg(II) Hg(I)	N ¹⁻	0 NO ₃ ⁻	3NNO ₂ ⁻²

XPS scans support the assignment of the nitrogen, showing two unique oxidation states (Fig 5.3): the stronger signal is at 406 eV (nitrate is typically >405 eV), while the weaker is at ~398 eV (nitride is found at ~397)²³. The scans taken thus far were not able to differentiate between the oxidation states of the mercury.

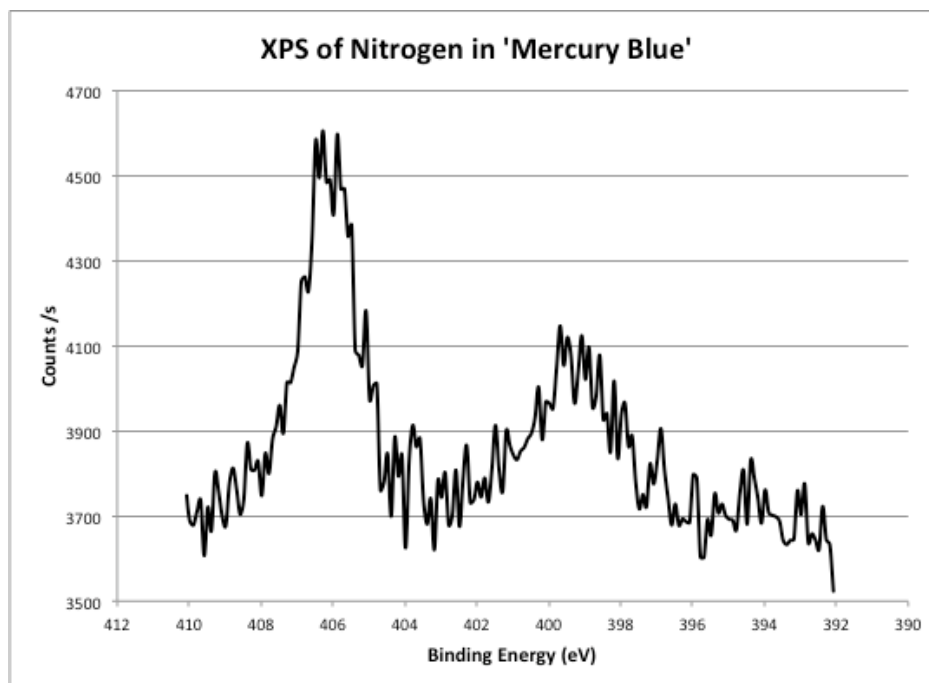


Fig 5.3: XPS of nitrogen in Hg₄N₄O₉ 'mercury blue' crystal.

The bonds of the central mercury nitride cation are all fairly standard for mercury, given the large size of the atom (Fig 5.5). We see two classes of bonds: two Hg-N bonds ~ 2.2 Å, in which the mercury point towards two symmetry equivalent mercury ~ 2.5 Å distant (thus the repeating pattern is Hg1b---Hg1-N-Hg2---Hg2b), and two terminal mercury, which are separated by bonds 2.3 Å and 2.5 Å, which do not subsequently point at another mercury but are instead directly associated with two nitrates (giving the pattern N--Hg3---Hg4---(NO₃⁻)₂). Given the similarity in lengths of the Hg-Hg bonds (both the nitride-Hg1-Hg2-nitride bridges and the terminal Hg3-Hg4 chains are approximately 2.5 Å), it is likely that each mercury pair is a Hg(II)-Hg(I) mixed valent species.

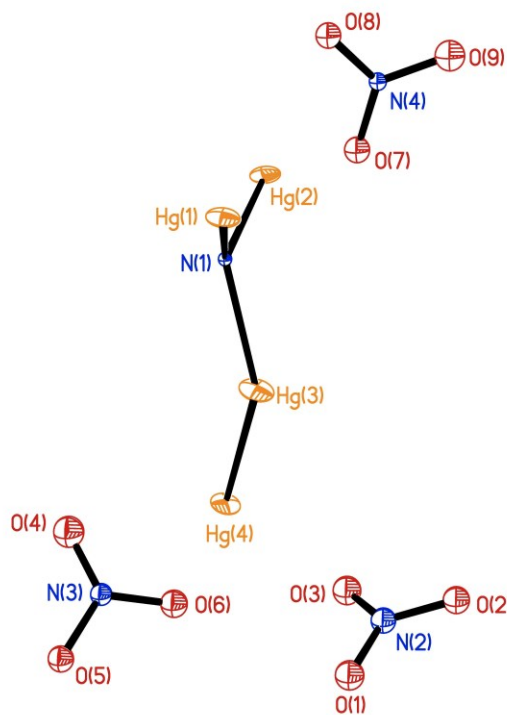


Fig 5.4: Crystal structure of the Hg₄N₄O₉ molecule.

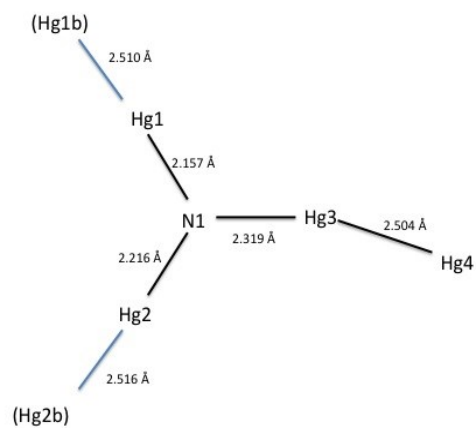


Fig 5.5: Bond lengths of the central mercury cation. Intermolecular bonds in blue.

Figure 5.6 illustrates how these mercury nitride linkages form an extended network, in which Hg1 and Hg2 form the chain, while Hg3 and Hg4 form the terminal branches (most nitrates omitted for clarity):

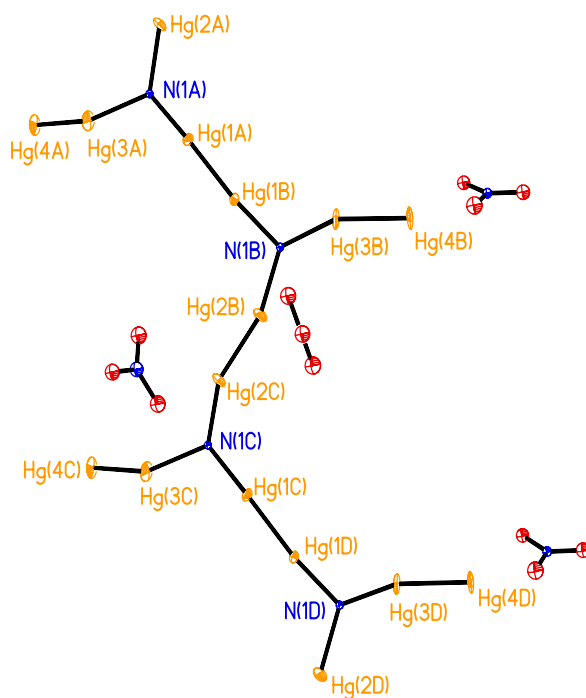


Fig 5.6: Mercury-nitride chain created by $\text{Hg}_4\text{N}_4\text{O}_9$ cation.

Finally, we see how these branches mesh with each other, through a layer of the nitrate counter-ions (Fig 5.7):

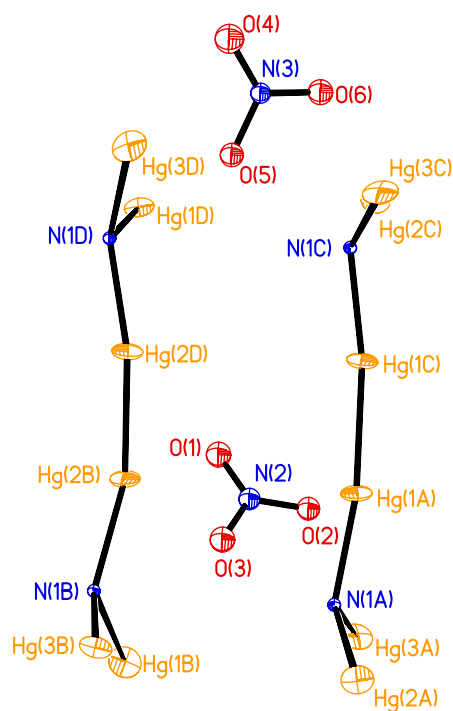
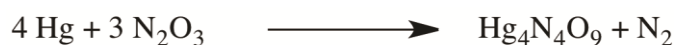


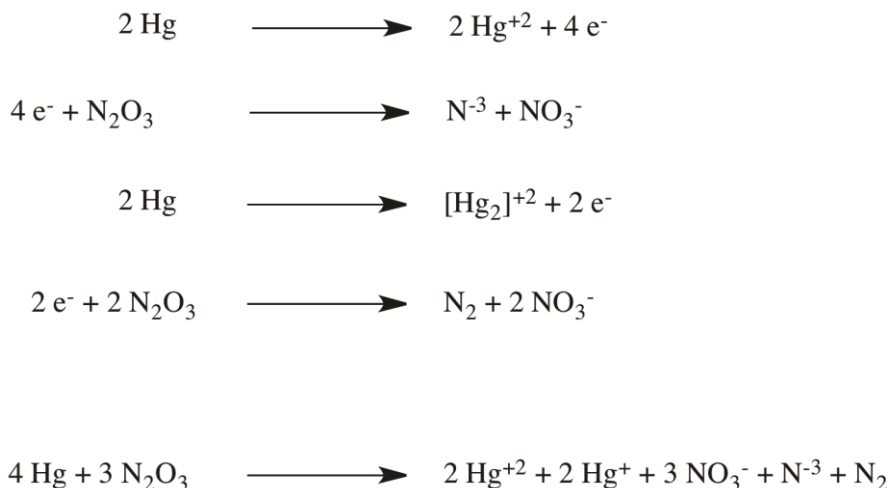
Fig 5.7: Two parallel mercury chains, layered with nitrate anions.

The stoichiometry of this reaction suggests that nitrogen gas should be the major byproduct (Eq 5.11):



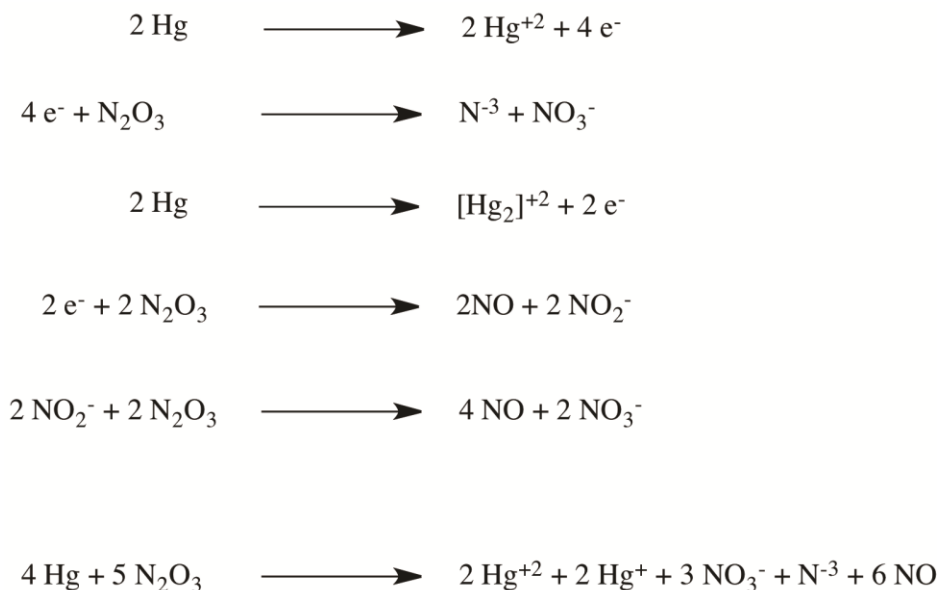
Eq. 5.11: Formation of the 'mercury blue' nitride.

This can be rationalized as the reduction of two trioxide to form nitrogen and nitrate, combined with a third trioxide undergoing what amounts to an unusual electronic disproportionation into nitride and nitrate, with the extra electrons furnished by the mercury (Eq 5.12).



Eq 5.12: Mercury product formation with nitrogen as the side product.

However, the gas product appears to be mostly nitric oxide, as in previous metal reduction reactions. What must be borne in mind is that these reactions occur in a large excess of N_2O_3 , and the apparent stoichiometry is probably misleading. A separate pathway presents itself, more in keeping with what has been seen before (Eq 5.13). The formation of nitride is the same, but the formation of nitrate can be seen to not necessarily involve nitrogen formation:



Eq 5.13: Mercury product formation with NO as the side product.

It is not outside the realm of possibility that both processes may be in operation, and that nitrogen formed may have escaped detection.

The fact that this product does not form in acetonitrile suggests that either polar solvents (or contaminant water) inhibits the process which forms the nitride, or that the aromatic rings are necessary to stabilize an intermediate of this process. However, a droplet of mercury in liquid N_2O_3 will upon warming form a small amount of white product before the trioxide boils away completely; this product appears by IR to be the same $\text{Hg}_4\text{N}_4\text{O}_9$, in lesser yield; the reaction is not seen to proceed at lower temperatures, and must be extremely slow.

Differentiating between the nitride product and mercuric nitrate is difficult by IR, but is simplified by the chemistry of the two. The nitride product is largely insensitive to the trioxide solution itself, whereas pure mercuric nitrate is quickly attacked, and dissolves into a black oil. This is likely the source of the black or brown tint sometimes seen on the crystals.

Performing the same experiment in a large vessel, with abundant headspace, fails to produce the reaction. Since a large headspace allows NO to diffuse out of solution, causing the production of N_2O_4 , we can rule out tetroxide as the active component. This is confirmed by separately preparing a toluene/dinitrogen tetroxide solution, which also fails to react with the mercury, as will toluene saturated with only NO . Each of these will produce a very fine dusting of semi-crystalline material over the surface of the mercury, but not the abundant product seen otherwise. It is possible that dinitrogen tetroxide is involved in a secondary

reaction, as the reaction occurs over a long period and tetroxide will evolve with time.

A rationale for the dinitrogen trioxide being the necessary component of the nitride formation could simply be the number of N-O bonds that must be broken, and the means by which oxygen is eliminated. In tetroxide the oxygen migrate easily from one nitrogen to another (tetroxide is $\text{O}_2\text{N}-\text{N}_2\text{O}$, but often behaves as $\text{ON}-\text{NO}_3$)²⁴, but this necessarily leaves one oxygen on the nitrogen. In trioxide, only one nitrogen-oxygen bond needs to be broken, and there is a stable destination for it on hand (the $-\text{NO}_2$, which can then form $-\text{NO}_3$) as the reduction of the other nitrogen proceeds.

Reaction with Graphite

The stabilization of dinitrogen trioxide in aromatic solvents naturally raises the question of how the trioxide interacts with other ring systems, such as in surface or solid state interactions. In fact, the author has frequently observed that solid powders treated with trioxide, such as the solid triphenylphosphine products discussed above, will acquire a light green colour that will persist for months, even when the compound is left in the open air. Dinitrogen trioxide can be removed easily from a reaction mixture while it is still in solution by simple argon bubbling, the last traces fleeing when the solvent is dried, but in solid powders that have been exposed to it, this supposedly unstable molecule can become a downright stubborn

contaminant. At times, a powder left to dry overnight under vacuum will, once bottled, be found to still be off-gassing small amounts of NO and NO₂ gas.

To explore this interaction a bit more rigorously, we opted to expose graphite to trioxide solutions. The intercalation of other species in the layers of graphite is a rich field of chemistry^{25,26,27}, and one seldom discussed intercalator is dinitrogen pentoxide²⁸. As dinitrogen trioxide is chemically and morphologically very similar to the pentoxide, both being planar N-O complexes, it made sense that a similar interaction would occur between graphite and the trioxide. In addition, the stabilization of trioxide by ring systems, possibly in clathrate-like formations, made for a distinct possibility that this could also occur in solid systems.

For powdered graphite treated with pure trioxide at -78°C, no change is seen (by IR, DSC, TGA), but since intercalation usually proceeds at elevated temperatures (when the sheets of graphene are able to move freely relative to each other), this experiment was repeated at 0°C, 25°C, and 60°C, using toluene as a stabilizing solvent. After 24 hours soaking in these solutions, the graphite was dried under ambient conditions and examined.

By simple observation, nothing had changed in colour or consistency or even odour. Off-gassing at room temperature is difficult to detect, but sealing the graphite samples in an airtight container for 24 hours produced an atmosphere that, while clear, had a pronounced nitric bite to the human nose. An IR spectrum in a KBr pellet shows the appearance of the telltale peak of a nitrate, at 1384 cm⁻¹. TGA analysis shows that for samples exposed to trioxide in solution at room

temperature, up to 16% of its mass (above the baseline) will volatilize when the sample is heated to 600°C (Table 5.2). This is a considerable amount of substance for the graphite to have taken up, though it is possible that this represents not a weight gain, but merely a chemical change and increased volatility of the carbon fragments. However, the fact that this maximum is achieved at 25°C (when the solutions are warm but trioxide is still mostly intact), but begins to decrease above this (when trioxide begins to break up substantially) suggests that trioxide specifically is responsible for the mass change.

Table 5.2: Mass loss in TGA analysis of graphite treated in trioxide solutions.

Preparation Temperature	-78°C	0°C	25°C	40°C	Control
% Mass loss at 600°C	3%	5%	19%	15%	3%

X-ray powder diffraction of the treated graphite reveals a subtle but distinct change in the two most intense diffraction peaks. Both peaks narrow and shift to slightly higher 2θ values after being treated with the dinitrogen trioxide. The 2θ value of a graphite peak, which in our starting compound was found sharply at $\sim 26.48(\pm 1)^\circ$, corresponds with the repeat distance of the layers, by the Bragg formula (Eq 5.14):

$$l\lambda = 2 l_c \sin \theta_l$$

Eq 5.14: The Bragg formula.

Where λ is the wavelength along the symmetry axis of interest, l_c is the repeat distance, and θ_i is the diffraction angle from the axis under measurement. As intercalation causes dilation along the c-axis (that is, causes the layers to swell), a change in peak position is an enormously sensitive method for detecting intercalation.

In this case, the shift of the peaks to the right (to greater 2θ , from $26.48(\pm 1)$ to $26.53(\pm 1)$, changing the d-spacing by 3.36 to 3.35 Å) is slight but measurable. Furthermore, we see a reduction in the FWHM (full width, half maximum) of the peak and a subtle change in shape, without the development of new peaks, which suggests that rather than simply intercalating as an alkali metal might do, or as nitrogen pentoxide is presumed to do, the dinitrogen trioxide is interacting with the ring system more.

Alternatively, the trioxide could be rendering the graphite more volatile by attacking the ring system directly, perhaps breaking up the fused rings. Elemental analysis of the room temperature treated graphite showed it to be 95% percent carbon, with only a trace of nitrogen (0.2%, less than the 0.3% error). It is odd, however, that the level of the carbon is depressed below 100%, and suggests substantial oxidation. If this analysis is not an artifact or sampling error, it could be that N_2O_3 is oxidizing the graphite rings in some way so as to render them more volatile (by up to 19% of the total mass of the powder).

Iranpoor et al.²⁹ have recently reported using dinitrogen tetroxide adsorbed onto activated charcoal as a selective nitrosation species; I attempted a similar

procedure to what they describe by refluxing the N₂O₃ treated graphite with aniline in dichloromethane. No reaction was observed.

5.3 Conclusions

Notwithstanding the existing body of research that shows that dinitrogen trioxide in solution is formally a neutral molecule, in most of the experiments performed it was found to act in a strongly ionic fashion; in a sense a hard salt that is readily soluble in organic and even non-polar media. The key to this capacity is the fragility of the molecule; it is a neutral species held together by an exceptionally long (1.864 Å)³⁰ N-N covalent bond, which will cleave readily in either a homolytic or heterolytic fashion. It responds to nucleophilic attack by eliminating nitrite anion, and to one electron reduction by eliminating nitric oxide. Nevertheless, the fact that this long, fragile, labile bond forms at all shows that it exists right on the cusp of stability, and is thus very sensitive to the surrounding conditions.

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Final Conclusions, Original Contributions to Knowledge, and Future Work

The aim of this work has been to illuminate an obscure side of the characters of two nitrogen oxides. These species, nitric oxide and dinitrogen trioxide, appear to be unstable and short-lived intermediates under the conditions of everyday chemistry, but in fact are akin to any air or moisture sensitive compounds that require special handling. To fully appreciate their capabilities, they were studied in environments that enabled their other characteristics to emerge, as studying deep sea fish in the deep sea yields different results from scooping them up dead from the surface. The concern, then, has been to properly describe what's always been there, below the surface, and so forms a significant addition to the groundwork of basic chemistry.

Nitric oxide was found to catalyze the *cis-trans* isomerizations of diazo compounds, a formerly unreported result. This reaction did not proceed with detectable intermediates, but appears to stem from NO's capacity to act as a spin catalyst, enabling associated molecules to access spin forbidden pathways. Thus this is one of a very few spin catalytic systems described, in what is yet a sparsely studied field of chemistry.

Under the conditions studied, NO requires a nitrogen lone pair in order to interact; nevertheless, the fact that this occurs in the solution phase raises questions about what effects a flux of nitric oxide in a biological system may have, particularly in enzymatic transformations that involve a triplet intermediate. The impact of NO on such reactions, as well as on related isomerizations involving nitrogen (oximes and imines) should be studied. The increased use of diazenes in chemical designs

also recommends an examination of how low levels of NO, either in solution or in the gas phase, may impact these designs. Lastly, any reactions in which the spin state of the intermediates is significant, such as carbene and nitrene chemistry, or cyclization reactions, may be impacted by NO spin catalysis.

Dinitrogen trioxide was seen to be stabilized by organic solvents to the degree that it can be handled and used at ambient temperatures. Although this phenomenon has been reported before, this line of research has largely passed unnoticed, without being properly explored or its potential fully realized. The existing body of knowledge has been expanded upon by paramagnetic NMR studies, confirming the low dissociation levels of solvent stabilized dinitrogen trioxide. It has also been shown that high-grade solutions can be prepared at 0°C and effectively used at temperatures above this, expanding the temperature regime at which N₂O₃ chemistry is feasible. The thermochromism of these solutions was also demonstrated, in contradiction to past research, and new extinction coefficients were calculated for room temperature work.

The reactions of solutions of dinitrogen trioxide were studied. The reactions with tertiary amines, thiols, aldehydes, triphenylphosphine, trimethyl borate, phenyllithium, mineral acids, alkali salts, and graphite are described for the first time. A novel mercury nitride salt, Hg₄N₄O₉ was synthesized and the crystal structure was obtained. An adduct of N₂O₃ was found to form with DABCO and potentially other tertiary amines, the first report of an N₂O₃ adduct that is stable at room temperature. A novel method for the preparation of nitrosylsulfuric acid was developed which can provide a product of superior purity to some existing

preparations, as well as a novel method for the synthesis of nitrosyl chloride that is quite simple to execute.

Solutions of dinitrogen trioxide remain an almost untrammelled field of research, and future work is wide open. The mechanism of the solvent stabilization remains to be quantitatively described, as well as a full accounting of their deviations from Beer's law, the effects of high concentration, and the nature of thermochromic effects. The significance of the alternate C_{2v} form for N_2O_3 in solution is an interesting possible avenue of research. The reactions of the solutions of dinitrogen trioxide are likewise open to wider exploration, with the field of transition metal reactions in particular lying fallow, and metals more generally offering further research potential. The redox chemistry of $Hg_4N_4O_9$ in particular needs to be described, while the tertiary amine adducts such as $DABCO-(N_2O_3)_2$ would benefit from a more thorough characterization.

The versatility of these solutions has yet to be fully realized, in that different solvents may yield different results in sensitive reactions. Finally, the chief advantage of stabilizing dinitrogen trioxide in solution has been that it allows chemistry to proceed at room temperature or above, but this aspect remains to be explored.

APPENDIX: X-Ray Data

Table A1: 'Mercury Blue' Compound

Empirical Formula	Hg ₄ N ₄ O ₉
Temp. of acquisition (K)	100(2)
fw (g/mol)	1002.40
crystal system	orthorhombic
space group	A b a 2
a (Å)	11.2233(9)
b (Å)	20.1924(17)
c (Å)	9.3653 (8)
α (deg)	90
β (deg)	90
γ (deg)	90
V (Å ³)	2122.4(3)
Z	8
density (g/cm ³)	6.274
abs coeff (mm ⁻¹)	57.735
No. of reflections collected	11114
No. of independent reflections	2491
Data/restraints/parameters	2491/1/89
Final R indices [<i>I</i> > 2σ(<i>I</i>)] R1	0.0539
w R2	0.1327
R indices (all data) R1	0.0569
wR2	0.1351
Goodness of Fit on F ²	1.081

Table A2: Benzoquinone-Diphenol Adduct

Empirical Formula	C ₉ H ₈ O ₂
Temp. of acquisition (K)	100(2)
fw (g/mol)	148.15
crystal system	monoclinic
space group	P 1 21/c 1
a (Å)	10.900(6)
b (Å)	5.898(3)
c (Å)	11.414(6)
α (deg)	90
β (deg)	100.126(6)
γ (deg)	90
V (Å ³)	722.4(7)
Z	4
density (g/cm ³)	1.362
abs coeff (mm ⁻¹)	0.096
No. of reflections collected	8195
No. of independent reflections	1746
Data/restraints/parameters	1746/0/100
Final R indices [<i>I</i> > 2σ(<i>I</i>)] R1	0.0648
w R2	0.2080
R indices (all data) R1	0.0802
wR2	0.2136
Goodness of Fit on F ²	1.181