

Appendix I

Miscellaneous Anecdotal Information

You've probably heard the old saying, "Experience is a hard teacher, but some will have none other." It is not necessary that you experience every risky situation. There is a lot of anecdotal information that circulates because others have had "experiences." Here are some musings from our chemist covering friction sensitive compounds, acid neutralization, peroxide formers, cyanogen bromide and nitrocellulose decomposition which you might find interesting.

I.1 Things that go Bump in the Lab

People responsible for laboratory operations are constantly advised to keep incompatible chemicals separated. This usually amounts to keeping oxidizing and reducing organic chemicals on different shelves or cabinets. However, some of the chemicals used in a lab have an oxidizing and reducing agent either in the same molecule, as ions in a salt or as a mixture of the two. These compounds are incompatible with themselves. They are oxidizers and incompatible with the organics, and they're partly reducing and will react with the oxidizers. Because of this, they should get their own location, one that is sheltered from heat, shock and other chemicals so that fire or explosion of these is less likely. In labs where a variety of chemicals are used, knowing the kinds of chemicals that fall into this category is crucial.

The presence of oxygen in the laboratory air poses an incompatibility with the reducing materials; however, this is generally only a problem if there is a fire in the room. Oxygen in the lab can slowly invade a chemical container either by leakage or from the residual left each time the container is opened and can then form an in-molecule incompatibility, i.e., an organic peroxide. It is important to know what chemicals are susceptible to this action. This scenario happens to a wide variety of chemicals that can react with oxygen. In many cases the problem is ruined material and poses no hazard and, in many other cases, a material's normal use requires this to happen, (e.g., the drying of varnishes and paints). There are four distinct types of oxidation:

1. Molecule of oxygen attaches to an atom or bond.
2. Molecule of oxygen initiates a polymerization reaction of unsaturated bonds.
3. Oxygen initiates polymerization and co-polymerizes with the monomer, forming a poly-peroxide.
4. Oxygen is inserted into a carbon to hydrogen bond by a chain reaction, forming a hydroperoxide.

Oxygen is normally a diatomic molecule (O_2) which is made less reactive than it could be because it is also diradical with a "triplet" configuration of its electrons. In O_2 , unpaired, non-bonding electrons on each of the oxygen atoms, spin in the same direction. Same direction electron spins won't form a bond. If one electron on this oxygen forms a bond to another electron pair, whether itself a bond or unshared pair on an atom, the new diradical will always be with same direction spins. This configuration limits what oxygen at normal temperature and pressure will spontaneously react with; obviously a good thing! The molecule can attach and stick to reactive metal surfaces, low valent transition metal ions of salts or oxides, unbonded pairs of electrons on iodide, phosphines, sulfides, sulfites, amide ions or carbanions. Oxygen will react with a carbon-to-carbon unsaturated bond or a double bond of a monomer which produces an initially unstable diradical adduct that will become stable if another double bond reacts with either the other oxygen end or the carbon end of the adduct. This event is likely to happen because the oxygen molecule is surrounded by monomer molecules. The reaction can also proceed by adding-on other oxygen molecules alternating with the monomer, if the dissolved oxygen concentration is high and the polymerization of carbon species is relatively slow, as with more stable carbon radicals being generated.

The fourth type of oxygen reaction is more difficult and the oxygen needs assistance or an initiator. One way to initiate it is to use a radical generator such as those used in polymerization reactions. A

radical generator would do the hydrogen abstraction; this is the required first step as oxygen alone can't do this. Another way is to add a sensitizing dye, which in combination with light will reverse an electron spin on an oxygen molecule, making it a singlet type and more reactive for hydrogen abstraction. The resulting superoxide can directly combine with the nearby organic radical as the spins are now opposed. However, peroxides form without additives and in the dark if there is enough oxygen in the liquid and headspace. The rate of formation will accelerate over time, from a slow, long beginning to rapid accumulation years later. The additive that no one intends to add is probably (cf., *Advanced Inorganic Chemistry*, 6th ed) an iron, manganese or copper containing dust particle commonly found in the air. A metal oxide in the dust binds oxygen as a peroxy radical that can abstract a hydrogen from the liquid organic, forming a metal hydroperoxide and an organic radical that can adduct another oxygen in the solution. It is observed (cf., *Bretherick*, pg. 579 in 5th ed) that salts that bind tightly to transition metal ions, dithiocarbamates, can inhibit peroxide formation.

- (1) $M. + \cdot O-O. \rightarrow M-O-O.$ initiator metal superoxide
 (2) $M-O-O. + R-H \rightarrow M-O-O-H + R.$ initiator metal hydroperoxide and organic radical
 (3) $R. + \cdot O-O. \rightarrow R-O-O.$ hydroperoxy radical
 (4) $R-O-O. + R-H \rightarrow R-O-O-H + R.$ hydroperoxide and new organic radical, and:
 (1a) $M-O-O-H \rightarrow M. + O_2 + H_2O$ regeneration of initiator metal by superoxide dismutase and catalase type reactions

From the above, two ways to prevent oxidation are evident: (1) keep out oxygen and (2) disable the initiator. For oxidation types 2 and 3, the initiator is not needed. For these, one needs something that will attach to a radical that would otherwise perpetuate the chain of polymerization growth. Hydroquinone, which will sacrifice itself and become quinone by donating its hydroxy hydrogens, stepwise, nips the polymerization process in the bud. Each oxygen molecule consumes a hydroquinone though, but, more to the point, each hydroquinone defeats what each oxygen has started, and one oxygen can capture a great amount of monomer. However, in a true chain reaction process like the hydroperoxide formation, an inhibitor can recycle itself by reversing two of the chain steps. It can put a hydrogen on a carbon radical that is waiting for an oxygen to attach, and it can remove a hydrogen from an organic hydroperoxide or the initiator metal hydroperoxide, thus regenerating itself. This action essentially reverses reaction (4), reducing organic radical concentration and thus slows reaction (3), which is the oxygen consuming step. Abstraction from the metal peroxide is even more effective. Common inhibitors of this type are hydroquinones, phenothiazines or phenyl naphthylamines. These have hydrogens that are easily removed in a radical mechanism by being relatively stable radicals themselves.

The hydroperoxide formation occurs with many types of substances: liquids, gases stored under pressure as liquids and solids that are dissolved in a liquid. A liquid phase is essential for the oxidation types 2, 3, and 4 reactions to occur. The carbon atom with the abstractable hydrogens can have a variety of different neighboring atoms or functional groups, which determine its reactivity. The essential feature required is an orbital of the attached atom or functional group as a non-bonding pair, on oxygen or nitrogen, or a "pi" system double bond or aromatic group which have orbitals parallel to the carbon-to-hydrogen bond that gets broken. The neighboring atoms or functional groups on this carbon also can determine what the product peroxide can do. The possibilities are: hydrolysis to form hydrogen peroxide which slowly and spontaneously decomposes; slow and spontaneous decomposition of the hydroperoxide to a ketone or carboxylic acid; or accumulate and even protect itself by polymerizing or further crystallizing out of solution. Something this energetic, that concentrates and becomes hard to detect, is worrisome.

Detection of peroxide formation the reaction can be visual, odor detection or by using a chemical method. Usually, an indicating substance is oxidized by the oxygen-to-oxygen bond to something that has color. The color intensity will be proportional to the amount of peroxide. The questions to be asked

when using chemical methods are: what is being detected and what can be missed? Even when using the visual method, one must ask: what can one see, and where? When using the odor detection method, the container either must be opened or is leaking. There must be a substantial amount of peroxide present for an odor to be detectable.

The visual method can look for unusual viscosity, crystals suspended in liquid, precipitation of solid or crystal residues in the area of the cap. The latter indicator can be hidden and may react when a lab worker turns a screw cap or ground glass stopper. The odor smelled is generally similar to an organic acid, and may well be, for the most part, a decomposition product that could only be from an oxidation of the material. For chemical methods to work, the peroxide must be in solution and the color reagent must be oxidized by the peroxide bond. A small portion of the liquid is added to an iodide salt in acetic acid and, in more extreme cases, hydrochloric acid, where heating for some time is included, has been the most common chemical method. Another popular method uses test spots on plastic strips that are commercially available. These utilize catalase enzymes and a dye that becomes visible on being oxidized. These are scaled to measure up to 100 ppm (mg H₂O₂ per liter) and using dilution with a (known to be) clean solvent (e.g., from unopened container), it will read higher ranges. Other methods involve oxidation of iron(II) to iron(III) in the presence of thiocyanate which complexes to form a red color. This can be done as a quantitative test and is readable up to 400 ppm peroxide as hydrogen peroxide. The hardest peroxides to detect are the dialkyl peroxides that form from copolymerization with alkenes. Unfortunately, these can also be the most reactive, and are easily detonated.

Methods of detection and methods of chemical treatment are similar: reduce the O – O bond. Other methods can involve:

1. absorption of peroxides on an alumina column,
2. hydrolysis of the peroxide to hydrogen peroxide by base catalysis,
3. disproportionation of hydroperoxide to oxygen and alcohol using a metal based catalyst, and
4. forcing a controlled peroxide rearrangement where the organic portion of the molecule is the reducing agent (i.e., just like the explosion, only controlled, hopefully).

Another common method of treatment is distillation of the unoxidized liquid from the peroxide. This can be done in one of two ways. If the material is known to be free of water, non-alcohol / non-carbonyl, and low level in peroxides, then sodium metal (i.e., a reducer) can be added to the distillation pot along with benzophenone to serve as an indicator of active sodium remaining; a blue color of sodium diphenylketyl radical indicates that excess sodium remains to scavenge any remaining peroxide. A second method is to add mineral oil in equal volume to the material to be distilled. The mineral oil serves a dual purpose. It prevents peroxides from being concentrated at the end and may, for some peroxides, allow them to decompose steadily as they are heated. The actions to take with an oxidized material is dependent on a complex of factors including:

- ♦ the amount of material being dealt with
- ♦ the value of the material
- ♦ the concentration of peroxide, accurately and completely detected
- ♦ the type of peroxide that is formed
- ♦ water miscibility or solubility of the material
- ♦ the hazard of undissolved peroxide residues

Given a reasonable lab quantity of material where the peroxide is not precipitated or crystallized, the concentration of peroxide detected will set the course. If one liter of liquid with 100 ppm peroxides (as mg H₂O₂ per liter) is distilled down to dryness and the residue explodes, the energy is roughly equivalent to good firecracker or a .22 caliber bullet charge (i.e., one kiloJoule). This is the same energy as a 280 pound weight falling from a 30-inch height onto the floor or a change of two degrees Fahrenheit in a cup of water. This serves as a level at which one needs to know that peroxides are present. With a chemical

reduction, the amount of heat generated and the ability of the liquid to absorb the heat with a limited temperature increase needs to be determined beforehand. A reducing agent or disproportionation catalyst that generates the least amount of heat on being oxidized and is used as a water solution is the best way because water is a good absorber of heat. Using aqueous ferrous sulfate on diethyl ether, 1:4 in volumes, one can treat 1200 ppm peroxides with a 5 °C rise in temperature of the total mixture. Iodide salt is even lower in heat generated, but is slower and requires acidic medium and higher temperatures. However, it is good for the detection technique.

The chemical type of peroxide formed is also an important factor as to what will work practically (i.e., whether to save the material or discard it safely). There are four distinct types based on its being a hydroperoxide vs. dialkylperoxide and hydrolysible vs. not hydrolysible. Hydrolysis is possible if there is a chlorine, ether, hydroxy, oxide, amide or amine on the same carbon as the peroxide. The first three (i.e., chlorine, ether, hydroxy) come from oxidation of ethers, alcohols and oxygen copolymerizations with chloroalkenes like vinylidene chloride or chloroprene. The ethers and alcohols produce hydroperoxides initially, which then can form polyalkylidene or cyclic peroxides. These peroxides are also hydrolysible due to the oxygen atom's presence on the same carbon as the peroxide, even though it's a peroxide itself. Non-hydrolysible hydroperoxides form from allylic and benzylic oxidations. The good news is that they remain as hydroperoxides which are easier to reduce and in many cases will rearrange to non-peroxide products following formation or on distillation from mineral oil. Non-hydrolysible dialkyl peroxides are the most dangerous; they form by copolymerization of alkenes, usually dienes or ene-yne, with oxygen. They tend to come out of solution, are hard to detect and reduce if in solution, and the molecular weight per O – O bond is usually low; higher energy per mass.

A material that is water soluble simplifies disposal options. If it is in a state of advanced oxidation, dilute it, reduce it and put it down the drain.

Regardless of statements in Chapter 4, the time it takes to accumulate a potentially hazardous quantity is too widely variable and dependent on nuances of the situation and the nature of the material. A radical chain reaction that is truly autocatalytic, will generate the means to increase its rate as it generates its product. In the case of hydroperoxide formation that requires hydrogen abstraction and the chain reaction, a constant concentration of organic radicals will give a constant rate of accumulation of hydroperoxide as long as there is sufficient oxygen in solution. The concentration of radicals will only increase if the initiator catalyst, metal containing dust, is active and oxygen is supplied. The rate of radical concentration growth will be constant with time and determined by the initiator catalyst activity and amount, given that oxygen availability is not rate limiting. With a constant amount and activity of catalyst, the peroxide accumulation rate will be quadratic and could be cubic if the amount of catalyst dust also steadily accumulates. Early on this is true, but limitations such as the rate at which oxygen can invade the container, the solubility of oxygen in the liquid and catalytic species concentration, can level the rate to a constant, dependent on the rate of oxygen invasion. Effective inhibitors can delay the onset of normal radical growth rate and chain reaction rate by a year or maybe two. Observed times to produce a ten-fold increase can vary from two months to two years in the low level stages and the time to reach a measurable level of 1 ppm may be days or months. This translates to what is observed with the most common material, diethyl ether; it takes years to be potentially dangerous if it is kept closed tightly. Therefore, it is important that you keep track of your potential peroxide formers and periodically check the condition of the containers and their contents.

This is just a sketchy overview of the factors and issues in a huge and important aspect of chemistry. Many fundamental lessons of chemistry come to bear here. Knowledge gained from synthetic techniques is applicable to this concern. Examples include ozonolysis with safe recovery of the desired product and the use of peroxide compounds and formation and rearrangement of peroxides in the course of a synthesis plan. Peroxide formation and dealing with it has a considerable body of useful literature to peruse.

Bretherick's *Handbook of Reactive Chemical Hazards*, 5th edition is now current.

Handbook of Laboratory Safety, 4th edition, CRC Press

Handbook of Chemistry and Physics, latest editions have good coverage.

Review of Safety Guidelines for Peroxidizable Organic Chemicals; Richard J. Kelly in *Chemical Health and Safety*, Sept/Oct 1996, p.28

Organic Peroxides (a series of volumes) Daniel Swern, Wiley-Interscience

Advanced Inorganic Chemistry, 6th edition, Cotton, Wilkinson, Murillo, Bochmann; Wiley. p.460 (superoxides)

Illustrative topics in Bretherick's are:

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|--------------------------------|---------------------------|-------------------|
| ♦ Poly(1,3-butadiene peroxide) | ♦ Tetrahydrofuran | ♦ Ethyl acetate |
| ♦ 1-allyloxy-2,3-epoxypropane | ♦ Diisopropyl ether | ♦ Methyl acrylate |
| ♦ 2-propanol | ♦ 4-methyl-2-pentanone | ♦ Dimethyl ketene |
| ♦ 2-butanol | ♦ Peroxides in Solvents | ♦ Divinyl ether |
| ♦ Diethyl ether | ♦ Peroxidizable Compounds | ♦ Vinyl acetate |

I.2 Why Water Splatters on Sulfuric Acid (and Not When Sulfuric Acid is Added to Water)

You have all heard the advice, "Don't add water to acids, add acids to water!" Obviously, bad things may happen if you fail to follow sound advice. To find out why this is good advice, first consider some relevant factors in the reaction:

- ✓ Density of sulfuric to water: 1.84
- ✓ Viscosity of sulfuric to water: 24.2 vs. 0.89 mPa sec
- ✓ Heat capacity of sulfuric to water: 138.9 J/mole °K vs. 75.3 J/mole °K
- ✓ Heat of dilution of sulfuric neat to infinite: 95.0 kJ/mole
- ✓ Heat of first water of hydration (using perchloric acid as model)
 - $\text{HClO}_4 + \text{H}_2\text{O} \rightarrow \text{ClO}_4^{(-)} \text{H}_3\text{O}^{(+)} \quad 55.8 \text{ kJ/mole}$
 - $\text{ClO}_4^{(-)} \text{H}_3\text{O}^{(+)} + x\text{H}_2\text{O} \rightarrow \text{H}^{(+)} \text{aq} + \text{ClO}_4^{(-)} \text{aq} \quad 32.95 \text{ kJ/mole}$
- ✓ Addition of subsequent waters produces less heat than that of the first.
- ✓ Molarity of sulfuric to water: 18.4 mole/liter vs. 55.6 mole/liter
- ✓ Boiling point of sulfuric to water: ~290 °C vs. 100 °C

Putting this together:

A stream of sulfuric acid poured into water penetrates it more readily than water into sulfuric due to density of sulfuric being greater than water and due to viscosity of sulfuric being higher than that of water; more momentum of sulfuric and less resistance of water vs. less momentum of water and greater resistance of sulfuric. Thus, water is more retained at sulfuric acid surface.

The lower viscosity of water allows a faster distribution of the heat generated, by convection; sulfuric poured into water will have heat removed into bulk of water more readily than it would through the bulk of sulfuric acid when water is poured onto it. The water will take the heat of reaction.

Sulfuric acid can take 1.8-times the amount of heat that water takes per molecule and per temperature rise. However, there's more water molecules on the surface of contact: 2.1 : 1 [ratio of molarities to the $\frac{2}{3}$ rd power]. Water takes more heat at the surface of contact. Water boils at a far lower temperature, though.

Order of mixing in a reaction can influence its initial outcome in terms of composition. Sulfuric acid being dispersed into water will take water molecules in a succession to full hydration as there is more water available to it as it progresses into solution. Water onto sulfuric will initially bind with one sulfuric acid molecule, forming mono-hydrates as water penetrates into sulfuric acid bulk. In a successive hydration, the first water bound, $\text{H}_3\text{O}^{(+)} \text{HSO}_4^{(-)}$, produces the majority of the whole heat of hydration of

sulfuric acid. The temperature rise of a sulfuric acid hexa-hydrate (not a definite structure) is the whole heat added divided by the heat capacity of the whole complex, $\sim 590 \text{ J/mole } ^\circ\text{K}$, where the mono hydrate formation may produce only 60% of the full heat of hydration, it has a heat capacity of $\sim 220 \text{ J/mole } ^\circ\text{K}$ or 37% that of full hydrate; the temperature rise could be ~ 1.6 that of the hexa-hydrate formation taking the heat.

Water slowly poured onto a sulfuric acid surface will form a shallow pool that has as a liquid-liquid contact, a layer of sulfuric acid mono-hydrate, that realizes a higher temperature and a bulk that readily distributes the heat formed, having only to achieve a lower boiling point -- that of water. Thus, water splatters on sulfuric acid and not the other way around.

What about bases???

I found via calculation, and had observed approximately by doing, that a temperature increase of $\sim 10 \text{ }^\circ\text{C}$ occurs in an aqueous solution for each added normality for both sulfuric acid and sodium hydroxide when either is added to water as 100% sulfuric or pure sodium hydroxide. Thus, trying to make 8 N solutions of either will result in a $100 \text{ }^\circ\text{C}$ solution starting from room temperature. The hydrogen ion associated with sulfuric and the hydroxide associated with sodium are so loosely bound that on associating with a water molecule, or several really, there is heat released (interestingly, a similar amount per mole for both proton and hydroxide). Only really strong acids like trifluoromethanesulfonic or "triflic acid", perchloric, the 100% stuff, not the 72% dihydrate that we see commonly, and really strong bases like the hydroxides of sodium, potassium, rubidium and cesium (tetraalkylammonium ions should be the case also) will do this.

We couldn't resist testing the "wrong way" addition of water to sulfuric to see just how bad it can be. On a scale of 25 ml sulfuric in a 250 ml beaker (I was even wearing long gloves!) slow addition of water behaved as I had suggested, but the amount of splattering was less than I had predicted. I would still suggest that adding water to a bottle of sulfuric is a bad idea (you can get away with that with hydrochloric and even nitric). Adding water to sodium hydroxide pellets, enough to cover the pellets, will give a slow buildup of heat rather than immediate reaction -- lower surface area to mass with pellets -- but this has been observed to explode ultimately due to the steam produced (somebody else's observation, not my goof!).

1.3. Peroxide Crystals found in isopropanol

A storage room, that has for decades held surplus lab chemicals from a number of research groups in a medical sciences building on campus, is finally emptied of its contents. It's mostly familiar chemicals that are used in quantity, solvents, salts, indicators and stains, biochemicals and chromatography materials. All taken to the facility where they are sorted by type, stored for pick-up by a commercial disposal company or disposed of by sewer, neutralization or bulking of flammables. A chemist sorts the approximately 100 gallons of solvent surplus in bottles ranging in sizes 100 ml to 5 gal. cans; mostly glass gallon bottles. The goal is mundane, separate the chlorinated solvents for separate bulking from the fuel-blending solvents. The cardboard boxes of four one gallon bottles seem very old, easily from the Upper Disconian Era of the late '70's. Diethyl ether, notorious for auto-oxidation over years, shows no overt signs of crystallization from peroxide formation, but a cautious whiff of the bottle cap indicates the sour, acetic acid odor that can only be peroxidation, at this point, extensive. Unopened boxes of dioxane and tetrahydrofuran bottles, some are sour as well.

The best is yet to come; a box with two brown bottles, labels long gone, but each with white tape on which "isopropanol" is written. One bottle nearly full, sniff says isopropanol, as expected, and no more. The other, about a fifth full -- hold on-- what's that crystalline mass, nearly as much as the liquid, laying there? No crystals at the neck, the cap turns easily, (no cushion or liner under it) so give it a sniff too. Sour and no distinct isopropanol odor at all. Sometimes experiments that don't give expected results are collected in a bottle for scrutiny later and the bottle is not re-labeled. It is deemed best to assume

peroxide crystals, in awesome proportions, no less, and be careful. Label this “isopropanol, crystalline residue, PEROXIDES?” and find a safe place for it -- the “reactives” shelf.

The liquid is mobile enough, similar to water, and a sample is carefully pipetted out. Two tests are done on the liquid. The obvious is a titration for peroxides using thiosulfate as titrant on a 0.1 ml sample of liquid allowed to react one hour with acetic acid, hydrochloric acid solution with excess iodide, lots of iodine produced. The result is 8.5% as hydrogen peroxide equivalent, about as much as is ever seen, probably a solubility limit of the peroxide. The other test is using a gas chromatograph, two columns, to see what familiar things are there. Approximately 16% isopropanol and 10% acetone, both logical to be there, but also a signal pair that may be isopropyl acetate, indicating that methyl acetate from a peroxide rearrangement is trans-esterified with isopropanol. Then one more late arriving one, 17.5 min. and 19.5 min. on each column respectively, about where adamantane appears.

A few days after the peroxide discovery, the commercial disposal company arrives to take the stored items. The lead worker, shown the crystalline peroxide prize, adds water to fill the bottle, the hope here is that the peroxide dissolves or decomposes by hydrolysis and hydrogen peroxide decomposition. The latter happens, but way too slowly. Oxygen bubbles slowly grow on the crystals and lift some smaller ones to the top of the liquid. The crystals are square plates that collect in what seem to be masses of overlapping plates. The plate size range is 1 to 5 mm square and 0.1 to 1 mm thick. These floating ones are now safely obtained crystals, no chipping away at the mass needed (people get injured doing that!). With the object of interest in hand, three tests are done. Two are obvious; put a small (1 mm sq.) grain on a metal spatula into a flame and strike another (2 x 2 x 0.1 mm) with a hammer. In the first, the crystal melts, then flames rather spectacularly, like “special effects” flame. In the second, one blow shatters the crystal and the next detonates it with a sharp report as loud as the “cap” used in the toy gun. The third test is head-space GC, sampled at 55 °C, on the two columns normally used for solvents. A crystal of size similar to the previous tests gives a large signal pair: 17.5 min. and 19.5 min. So, that was the actual peroxide detected before.

Decomposition with water is too slow, even though, being surrounded with water it is at least safe. To be taken by the company, it must dissolve in something and be shipped as a peroxide solution. Dimethyl phthalate is what is used to dissolve butanone peroxide as a 50% solution. It should work similarly in every respect with this. When some was obtained, as someone’s surplus, luckily, the water was mostly, and carefully, poured off and about 1.5 liter was added. Dissolution takes days, (but who’s going to push it?) and occurs smoothly.

Google searches on “acetone peroxide” give some timely results. There are many web-sites that tell one how to make acetone peroxide (and, of course, tell you NOT to do it!), the detonator explosive that in combination with other explosives, shrapnel and an igniter is the suicide bomb of the middle-east wars. A point that is well made in many discussions is that in mixing acetone, 30% hydrogen peroxide and a catalytic amount of concentrated sulfuric acid, keeping the temperature of the mix at near freezing, <10 °C, produces the less sensitive form, the trimeric peroxide. At higher temperatures, the more sensitive and volatile dimeric is formed preferentially. Also, trimeric, if allowed some time at ambient temperatures, will sublime slowly and reform as dimeric peroxide. So, dimer it is in this case, certainly, even though the formation chemistry is very different.

The initial monomer, 2-hydroperoxy-2-propanol, can be formed in two ways. The above description is of acidified acetone, protonated at the ketone oxygen, taking hydrogen peroxide at the carbonyl carbon. The auto-oxidation formation involves diatomic oxygen being inserted between hydrogen and the middle carbon of isopropanol or isopropyl ether in a chain reaction involving catalytic activation of oxygen. In dimer or trimer formation, the initial monomer loses water to become a true monomer, acetone O-oxide, acetone with another oxygen stuck to the carbonyl oxygen. This is transient and will dimerize by attaching the end oxygen to a neighboring molecule’s carbonyl carbon. Another monomer can be added and the ring closed or the ring closes at the dimer stage.

There are two different references to peroxide decomposition above. One involves aqueous hydrolysis of acetone ketal, essentially replacing a hydroperoxide with hydroxide, via a transient ring opening that has a negative charge on a peroxide oxygen and positive charge on the ketal carbon. Water relieves the positive charge by adding to the carbon, forming a hemi-ketal, and protonating the peroxide as well. This same cleavage and addition of water continues stepwise and ultimately sets hydrogen peroxide free, leaving acetone. The other, involving acetate, mentioned above in GC analysis, is an energy producing decomposition with bond rearrangement. This is the decomposition that can make peroxide compounds dangerous. It can occur slowly and smoothly, or it can be initiated with heat or shock to occur all-at-once with the crystal mass of peroxide. With the slow reaction, energy produced is dissipated in the surrounding solvent without contributing to further reaction initiation. The initial bond cleavage is heterolytic oxygen to oxygen, leaving one oxygen with a high energy deficit of electrons, which is immediately relieved with the adjacent methyl group migrating, with its bond's electrons, to that oxygen. This leaves the electron deficiency on the acetone carbonyl carbon, similar to the hydrolysis mechanism, and this being in isopropanol solvent, the alcohol oxygen can add to that carbon and give its proton to the other oxygen. Now there is a hemi-ketal on one end of a peroxide and an ortho-ester of acetic acid on the other end. That ortho-ester could be hydrolysed to isopropyl acetate by any water in the solvent. With the rapid decomposition, of essentially isolated peroxide crystal, the initial rearrangement contracts the six-member ring of the dimeric peroxide to a five-member ring ortho-lactone, cyclic-ketal peroxide. That could decompose concertedly to two molecules of methyl acetate in an immediately following step. The calculated energy of one mole of peroxide, as monomer, rearrangement to ester is about 320 kJ.

The major concern of peroxide forming solvents is with isopropyl ether, while peroxide formation in isopropanol is well documented but much lesser known in the current chemical knowledge. This observer has never seen peroxide formation in the isopropyl ether (not even a 25 year-old one gallon bottle) but will never be a skeptic in the matter, either. Diethyl ether peroxides have always been observed to be in the ether solution which on evaporation of a small sample are as a varnish rather than crystalline. This has been the case with old, smelly, viscous diethyl ether in a 5 gallon can. Whether crystal or not, a buildup of this plastic form of peroxide, observed with p-dioxane and tetrahydrofuran also, hiding under a plastic screw-cap has the potential for friction sensitivity to detonation if the stuck cap is forced. The "fire-cracker amount" in the threads could break the neck of the bottle and possibly ignite the volatile solvent contained. The documented peroxide explosions in lab situations have been ones involving distillation, heating and concentration of peroxide residuals, and impact or friction with attempts to remove crystals from a container.

More peroxide accounts of similar nature come from ozonolysis reaction work-up. The peroxide compound is the molozonide or 1,2,4-trioxolane (acetone peroxide dimer is a 1,2,4,5-tetraoxane) that sometimes is not fully reduced at its oxygen to oxygen bond. The remaining peroxide has detonated on scraping out collected product on a sintered glass filter funnel. Others have occurred in use of dimethyldioxirane, an acetone peroxide nonomer, which becomes the dimer crystals mentioned above if allowed some time.

1.4. Cyanogen Bromide

Reference books like the Merck Index, Sax's Dangerous Properties of Industrial Materials and the multitudinous MSDS's give the chemical, physical and toxicological information on this material. Text books and biochemical research literature indicate its uses in biochemical techniques and chemical literature reviews its synthesis and uses in chemical synthesis.

By appearance it is a clear, colorless, crystalline (but soft, waxy) solid that is volatile with pungent, acidic and irritating vapor. It has a low melting point of 51 °C and vapor pressure is one atmosphere at 61 °C. It is slowly soluble in water and very soluble in acetonitrile, a 50% solution is often used, and can

be purchased as such. Its solution in water is stable for some time and pH is near neutral. It will hydrolyse and neutralize base if it is added to solution.

It is made by bromine oxidation of cyanide salt in aqueous solution, whether dilute or concentrated, and can be distilled into a receiver as a pure compound or kept as an aqueous solution if to be used soon. The molecule is linear, three atoms in the order, Br-C≡N. Triple bonds of small atoms are generally reactive towards polymerization or cyclic trimerization and this molecule is endothermic, its elements are more stable than the compound is in the gas phase. The MSDS accounts list an extreme temperature reaction as producing cyanogen gas and bromine as decomposition products, this seems to be energetically a slightly favored occurrence. A concern in Bretherick's Handbook of Reactive Hazards is that preparations of this have exploded on storage at room temperature years after being prepared. The reaction may be an oligomerization or polymerization, possibly caused by a trace of cyanide salt in the crystalline solid. If so, the cyanide, being basic (nucleophilic) starts the reaction by bonding its "C" end to the carbon of cyanogen bromide and the charge now shifted to the "N" end will bond to another carbon, and so it repeats. There is much extra energy to be had, particularly in energy per heat capacity that translates to a great rise in temperature.

A slower decomposition hazard that can result in eventual bursting is when the container closure allows atmospheric humidity to enter. Hydrolysis of cyanogen bromide then occurs, first to isocyanic acid, and then with trimerization to cyanuric acid, a white, opaque, water insoluble solid, and hydrogen bromide, which will exist as a pressurizing gas (it is not trapped by anything basic, condensed or released, unless the cap is too loose) that can make the container a danger on being opened. Viewing the material through the glass and observing the contents to be opaque, as opposed to being clear, will have to do as a warning that hydrolysis has occurred here.

The two most common uses of this material are in biochemical work; protein or peptide cleavage at methionine's carboxyl end and activation of sepharose to a cyclic iminocarbonate for binding proteins or peptides at their amino ends for affinity chromatography. Cyanogen bromide acts like a halogen where the C≡N part bonds to the nucleophile, sulfur or oxygen, producing hydrogen bromide and cyanate, R-O-C≡N, in the reaction with hydroxyl of sepharose and S-cyanomethiononium bromide from attachment to the thioether of methionine in a peptide. Methylthiocyanate is released when the carbonyl oxygen of methionine displaces it, forming an iminolactone five member ring with the four carbon atoms of methionine, which then hydrolyses to cleave the peptide. Amines are derivitized in similar manner, a cyanamide, RR`N-C≡N and hydrogen bromide or alkyl bromide are formed from secondary or tertiary amines, respectively. Cyanide is not observed in these cases to be released as such, it takes the nucleophile, bromide takes the electrophile.

In the case of water hydrolysis, hastened by addition of hydroxide, the observation will be consistent with the observed reactions in its use as a reagent; cyanide takes the nucleophile and bromide is freed to solution as such. In a balanced reaction of water hydrolysis of cyanogen bromide, Br-C≡N + H-O-H → three outcomes are possible:

- (1) H-Br + H-C≡N + ½O₂;
- (2) HO-Br + H-C≡N or
- (3) H-Br + HO-C≡N

Both in electropotentials, free energy and equilibrium position, and heat of formation differences, will greatly disfavor cyanide and oxygen (1), and cyanide and hypobromite (2), (can disproportionate into hydrogen bromide and bromic acid with a small gain in likelihood). Oxygen, if formed could throw the equilibrium by just leaving the scene, an end reaction. Cyanide, in (2), will be in contact with bromine, bromate or hypobromite, any of which will oxidize it to cyanate or back to cyanogen bromide, which is how it's formed anyway.

In stating that cyanide and bromide are products of alkaline hydrolysis, as in the Merck's entry and subsequently quoted by everything else as a result, is simply wrong. It's easy to demonstrate that cyanide is not a product; one gram of cyanogen bromide (in good condition) added to about 30 milliliters of water (takes a long time to dissolve) will give strong odor of same as it is pushed to dissolve. Add universal indicator and observe that pH is about neutral. Add 2 N base as though titrating and observe that violet basic color will slowly give way to neutral color as more cyanogen bromide dissolves. Repeat the portionwise addition until the crystal is gone and violet color persists. Give the solution some time and notice that cyanogen bromide odor is nearly vanished (be careful in any event). On being satisfied that the reaction has occurred reasonably, it's time for the ACID TEST (!) Add 30% phosphoric acid solution until indicator color is just red, cautiously sniff or use cyanide gas indicator paper or test for hydrogen cyanide with Prussian Blue test. The results will be weak if anything at all. If cyanide were the result of hydrolysis, the test, however done would be strongly indicating.

Just because cyanide is not being generated, doesn't make it safe as a result; cyanogen bromide is about as toxic and nearly as volatile as hydrogen cyanide. It is even more mobile in aqueous solution because it's less soluble than hydrogen cyanide and its Henry's Law constant (vapor pressure over solution per concentration in solution) is higher.

There is more information available on the toxicity of cyanogen chloride than there is for the bromide. Cyanogen bromide was developed to be a safer and easier to use form of the chemical in chemical synthesis and some biochemical applications. The chloride form, which is a gas, was used in chemical warfare as well. Being in high volume production and having a lethal history, the chemical was studied. Research in the late forties and early fifties demonstrated that cyanogen chloride reacts as expected with a mercaptan function in glutathione, forming a thiocyanate and hydrogen chloride as products. A second glutathione mercaptan then displaces the cyanide of the thiocyanate, forming a disulfide between two glutathiones and hydrogen cyanide is released. Thus it takes a reducing agent to make cyanide of what is essentially a cyanate. The oxidized glutathione can be regenerated on glutathione reductase, which consumes NADPH as the near ultimate source of reducing power. Cyanide blocks the electron transport chain of proteins and cofactors at the end of the line; just before electrons are donated to respired oxygen, rendering it unusable and stopping the electron current. With electron transport blocked, ATP is not made and the means to power muscles (diaphragm for breathing) is lost very soon. Having the electron chain backed up at least makes NADPH abundant enough. The toxicity of cyanogen chloride, bromide and iodide is thus the same as cyanide. There is a difference in that hydrogen cyanide is more lethal in high concentrations for short times than it is with lower concentrations and longer times, where concentration times time is equal in both cases. Cyanogen chloride or bromide, because of its mechanism being slower, will build its dose over time, in lower concentrations than cyanide can act.

Cyanide antidote kits are another matter though. It's not some "no-brainer" that one just takes the antidote when they see that they're poisoned. Some of the components must be taken intravenously, which is tricky, especially when time is tight. The usual strategy is to get hemoglobin to be a superior sequesterer of cyanide by oxidizing its iron to +3, methemoglobin, using a nitrite ester inhalation or sodium nitrite injection. This then gathers cyanide from the cytochrome iron and allows it to resume transporting electrons. Excess cyanide then can be oxidized using thiosulfate (thought of that as more a reducing agent, yes?), injected again, which converts cyanide to thiocyanate and leaves sulfite. Sodium bicarbonate must be administered to neutralize the lactic acid that is excess when the metabolism goes so reducing. There are alternatives for gathering cyanide, using vitamin B₁₂ or cobalt carbonyl. With a poisoning that requires this type of treatment, there is little time to be effective with it and if the poisoning is of lesser magnitude, just getting oxygen for the person will be suitable. Working in a fume hood, planning the work and the small amounts that are used in bench scale work, will make cyanogen bromide procedures safe.

I.5 Nitrocellulose Decomposition Progression

Commercial nitrocellulose preparations used as lacquers in biological specimen preservation are generally flakes or cotton with two of the three hydroxyls on glucose in the cellulose sugar chain derivatized as nitro esters, referred to as 12.5% nitrogen content. This is in a plastic bag, in a steel, paint-type can and wetted with water and alcohol to reduce static electricity that could cause ignition. This is reactively flammable, but not as much as the propellant called “gun cotton” which is tri-nitro cellulose. If this is kept at a warm room temperature over years, the alcohol can slowly evaporate out through the bag and the can, leaving only water with the plastic. Along with this, a slow hydrolysis of the nitro ester can produce nitric acid, which in turn, can accelerate hydrolysis of the ester to produce more nitric acid; an autocatalysis. The acid can slowly hydrolyse the cellulose to glucose, nitroglucoses and various other polysugar polynitro esters. The acid can also dehydrate sugars to form furans, which are part of the discoloration observed, from white to yellow-orange, commonly. An advanced degraded material can have enough nitric acid present to allow the material to fully hydrolyse to glucose and nitric acid when it is added to water.

An old and unopened can may show no material discoloration, and still have alcohol present, but start to show acid corrosion of the inside of the can. A yellowed sample can have a distinct “acid” odor that is of nitric and “acetic-like” character. A sour sample such as this is a candidate for disposal by hydrolysis, neutralization and sewer. In a more advanced state of decomposition, acid catalysed rearrangement of pyranose to the furanose isomer of glucose and acid-induced dehydration of this to furan derivatives occur. The furan is more susceptible to oxidation by nitric acid than is a sugar. Such oxidative action can form gases such as nitrogen oxides and carbon dioxide, along with carbon in a complex pathway. The gases can dissolve in the gummy furan mixture and build-up pressure that ultimately bulges the can, expands as a foam, that leaks out of seams or holes, and finally blows off the can lid and spray some gummy liquid all over the surroundings.

Such is the explanation for the finding of a bent lid, bulged can, plastic foam extruded out the cracks and stained, varnished wood in a locker for chemicals in a room that was usually at ~35 °C. In the open can was a foam-like charcoal formation. No indication anywhere that a very high temperature (the paper label was not browned), explosion or flame (no soot above the can) had been present. The bulging of the can could have been rapid and the contents could have been fairly warm, even hot to the touch as indicated by the partial melting of the plastic liner bag. There were no reports of sounds from the locker area, it’s remote in the building and most of the time no one is near anyway.

Three packages of nitrocellulose in three different stages of decomposition in the same locker; a lesson patiently waiting to be learned by someone.

