# Synthesis of Cubane

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Introduction

Cubane is one of the five Platonic Hydrocarbons – a group of organic molecules whose carbon skeletons mirror that of the structure of the five Platonic Solids, which are a group of three-dimensional shapes Greek philosopher Plato thought were important enough to be named after himself.[1]


| Tetrahedron | Cube (Hexahedron) | Octahedron | Dodecahedron | Icosahedron |
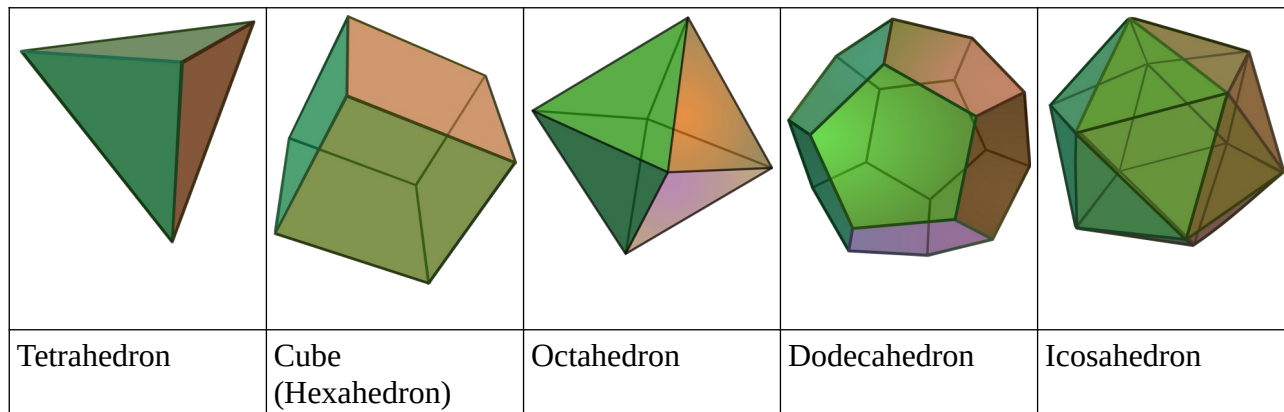
However, calling the Platonic Hydrocarbons a 'group' of molecules is a bit rich, as of the five Platonic Solids, only three of their counterparts are even physically possible, and we've only ever succeeded in making two of them.[3]
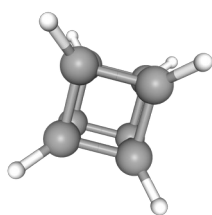
One of them is dodecahedrane (right), but anyone talking about dodecahedrane is a pretentious gump[4] who should be ignored, and the idea of a sphericallish carbon-based molecule is just stolen from Buckyballs anyway.
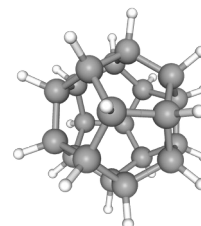
The other one is at the top of this page.

Cubane

Dodecahedrane

Left: © PubChem CID 136090, Right: © PubChem CID 123218

It's Cubane!

Cubane is a molecule with formula C_8H_8, which forms a white crystal[8, sect. 1], and which – now this next part is very complicated, so don't be ashamed if you have to reread it – is in the shape of a cube. This is an odd property for a hydrocarbon, which are usually filled with 120º bond angles, and it's what makes cubane such an interesting compound.
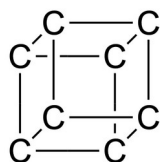
It has a melting point of about 130ºC[8, table 1], and isn't toxic so you could probably eat it if you want.[9] Someone once asked the IUPAC to come up with the systematic name for cubane, but they curled up in a thoroughly non-cubic ball and started crying.[5]

"But why should I care?" you ask, *"What's so special about cubane?"*

The 90º bond angles of cubane force the bonding electrons much closer together than they would prefer to be, which puts the molecule under strain[17] – in other words, cubane would be rather happy not to be cubane. What stops it decomposing is the fact that it has very little choice as to that *into which* it could decompose. Breaking one or even two of the C-C bonds still produces a very strained molecule,[8, sect. 1] so while cubane would love to decompose with all its heart, it has no route. In

many ways, it's like an organic chemistry student – highly unstable, but with no way out of its miserable existence.

What Does It Actually Do?

The way I interpret it, cubane is, for the most part, a vanity chemical. That is to say that the primary motivation for the development of its synthesis was simply the fact that it would be awfully pretty[26] – whoever heard of a cubic organic molecule?

Of course, there are *some* uses.[8] There are some boring ones[see 17], but where it really gets exciting is when you consider its *explosive* capabilities.

As mentioned before, the molecule is quite strained but cannot decompose at low temperatures – meaning that all that energy is stored up ready for a powerful release. Furthermore, the high density of cubane[8 sect. 1 again] and its derivatives means not-much-room, big-kaboom (yes, that's the technical term).

Cubane, when all its hydrogens are substituted for nitro groups, forms the below molecule – octanitrocubane (ONC) – which has a perfect oxygen balance – in other words, it contains all the oxygen atoms it needs to fully oxidise itself,[27] eliminating the need for a stoichiometric mix of fuel and oxidiser.
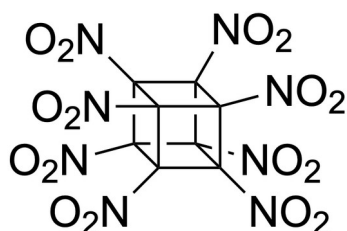
ONC explodes at an appreciable Mach ~30 (10 100ms^{-1}), however with the minute drawback that it is currently more expensive per gram than gold. We won't cover the synthesis of octanitrocubane, because its long and hard – only its parent, cubane. Speaking of which…

But How Do I Make It?

There are approximately a gajillion different routes for synthesising cubane. The route we'll be looking at uses ingredients which probably won't get you arrested! In fact, it's roughly the same route as that used by this chap (and this paper, if you're a nerd), but we'll be delving much further into the boring theoretical bits.

The first proper synthesis of cubane was published in 1964 in a famous paper by Philip Eaton and Thomas Cole[8, sect. 2.1]. And they said it was impossible! Their route involved around fifteen steps (not including purifications etc.) and has since been improved[16].
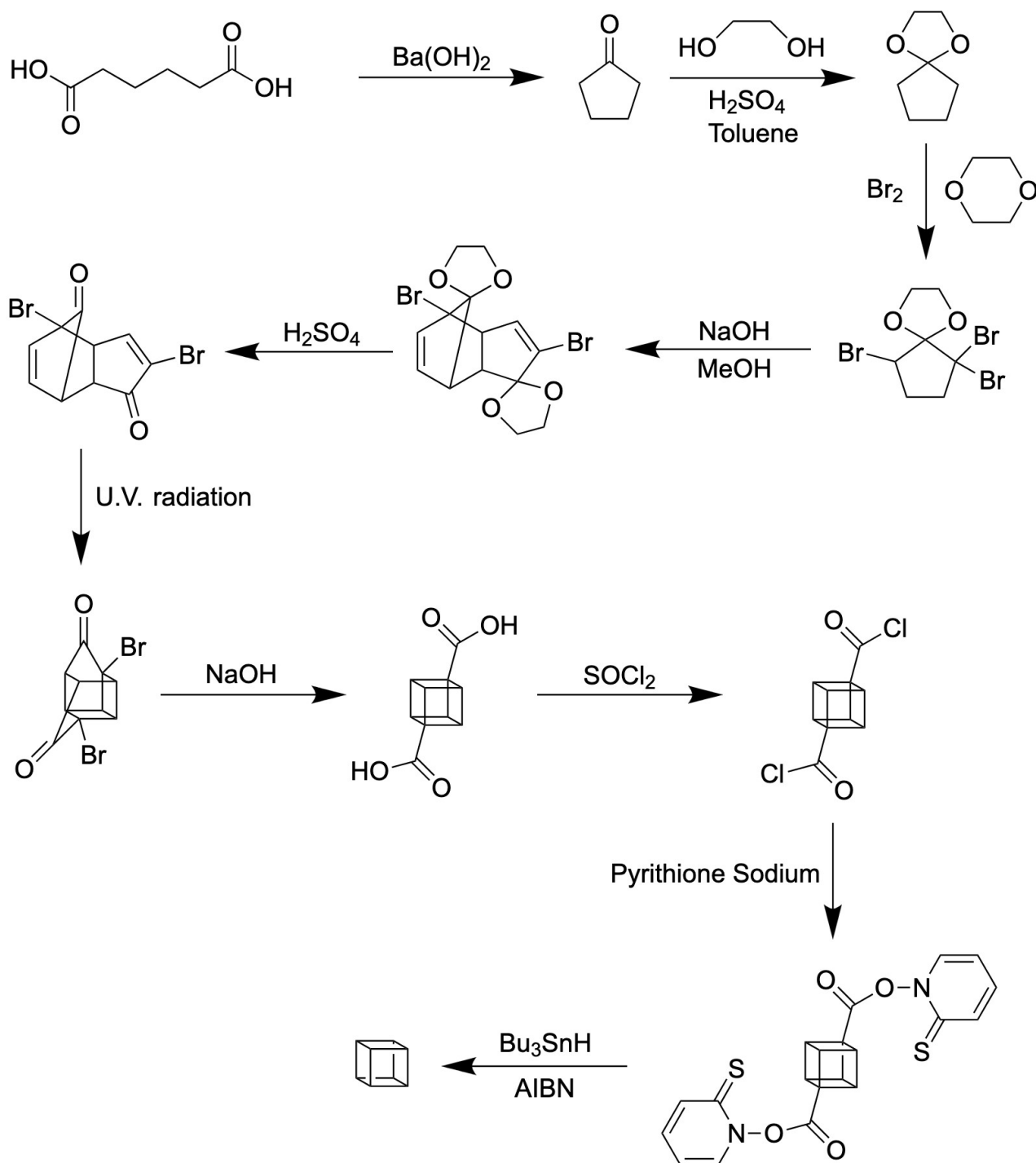
Overview

In general[15], all routes involve the following[8]:

- The creation of something that looks a bit like cyclopentanone
- A bromination

- A **Diels-Alder Reaction**
- A **Favorskii Rearrangement**, which usually generates cubane just with some sticky-outy bits
- The removal of these sticky-outy bits

Here's an overview of the route we'll be looking at:

Without any further ado, let's dive in.

Step One – Ketonic Decarboxylation of Adipic Acid

That's a lot of fancy words, isn't it? Adipic acid is the common name for hexane-1,6-dioic acid, which is an ingredient for – and which constitutes one of the '6's in – Nylon 6,6. In this step, we'll be making it into cyclopentanone.

It's a base-catalysed reaction, carried out at about ~290ºC in a nice simple solvent of water, for which the primary driving force is the increase in entropy due to the release of a CO_2 molecule. Let's take a peek at the mechanism.[7]

1. First of all, the OH- group from our base deprotonates the adipic acid, producing a monoadipate ion, with a by-product of water:
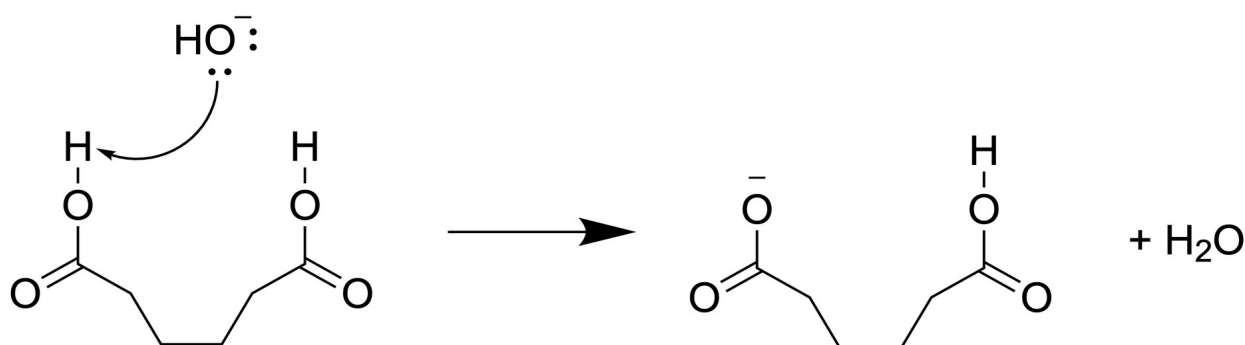

2. The adipate then gets its knickers in a twist, tangling up as shown above and allowing a hydrogen bond to form between the dissociated oxygen and the other hydrogen:
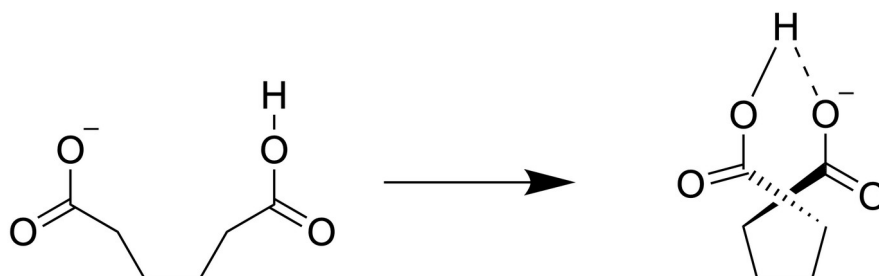

3. This next step is the most complex – this is a **concerted mechanism**[10], so there's a lot of stuff going on at once:

- Firstly, the additional electron pair on the charged oxygen is used to form a double bond with the attached carbon.

- This carbon then switches its bond between carbon 1 to carbon 5, forming a carbanion which instantly causes its double bond with the oxygen to break heterolytically, forming the intermediate pictured in the middle – you can now see the five-carbon ring emerge.
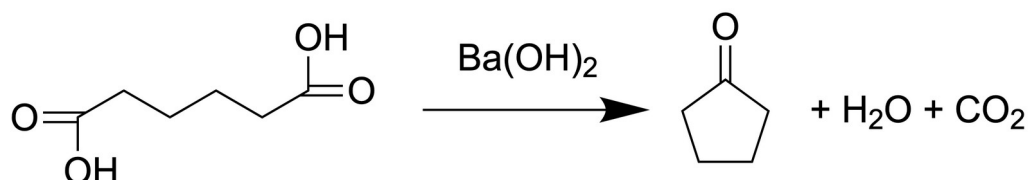
Thereafter, the weak hydrogen bond breaks, releasing carbon dioxide, another by-product:
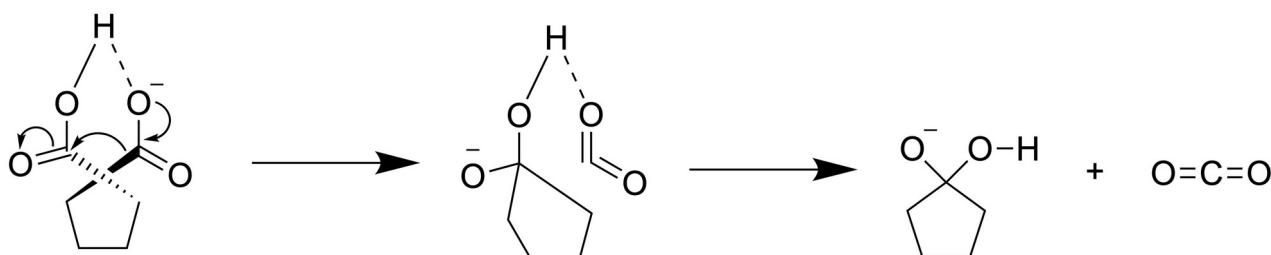
4. Last and probably least, the resultant anion decomposes into our dear cyclopentanone as shown, regenerating the -OH group in the process:
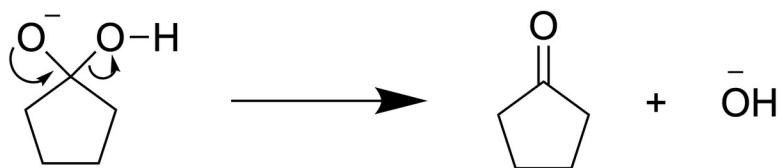
Our overall equation is therefore:

Exciting!

Before we're finished, we still need to extract and purify our cyclopentanone – currently it's mixed up with our water, catalyst, and unreacted adipic acid.

One of the best ways of doing this is **salting out**, which is when we add salt (in this case, something basic like a carbonate) to our mixture in order to decrease the solubility of the thing we want (cyclopentanone), causing it to separate.[6] Using a basic salt has the added advantage of neutralising any unreacted adipic acid:

adipic acid + carbonate salt → adipate salt + carbon dioxide + water

After that, it's the simple matter of a distillation to get our lovely liquid cyclopentanone!

Step Two – Protection of the Ketone

Ketones are an absolute pain in the bum. They react with themselves; they react with the bromine that we'll be adding later – it would be nice if we good just cut those carbonyl groups off and be done with it.

Unfortunately, we're going to need them later, so we shall perform a reaction called a **protection**. As the name would suggest, this is a way of 'shielding' our ketone from reacting, but in such a way that we can then easily 'un-shield' (deprotect) it later, as we need. It's like wearing a shower cap.[11]

A common way to protect a ketone is by turning it into a **ketal**[13], like so:
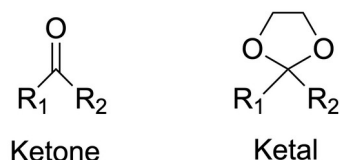
This oxygen-containing ring reacts with pretty much nothing except strong acid (see first article on right).

We'll be achieving this with ethylene glycol (IUPAC name: ethane-1,2-diol), in acidic conditions (more on this in a moment). The mechanism is surprisingly complex.
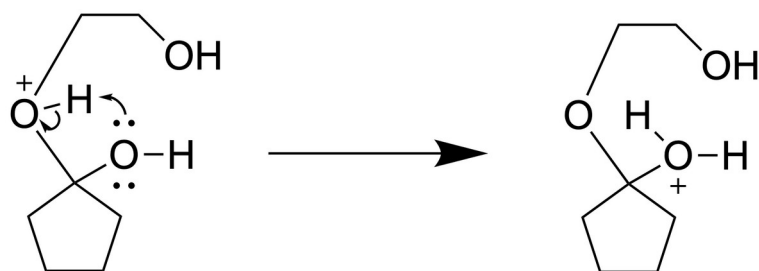
First, our carbonyl is protonated by our acid catalyst, generating a carbocation intermediate.
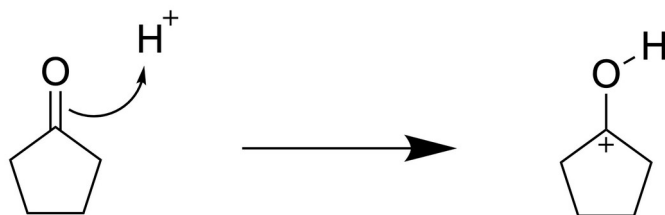
This is attacked by one of the nucleophilic oxygens on our ethylene glycol, generating this weird positively charged oxygen:
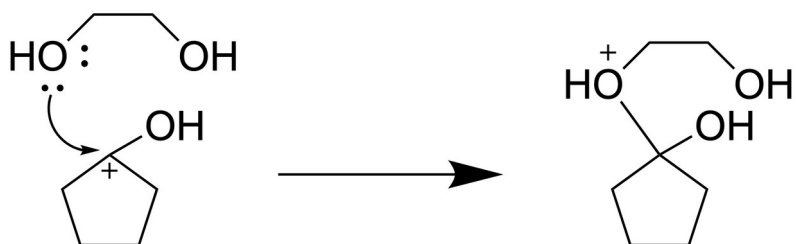
This species will quickly want to get rid of its extra proton, which is lucky as we have another oxygen brimming with lone pairs to accept it:

That's an example of proton transfer. An H_2O group is formed, which, much like someone reading this article, would much rather leave and be happy on its own. This leaves us with another carbocation:
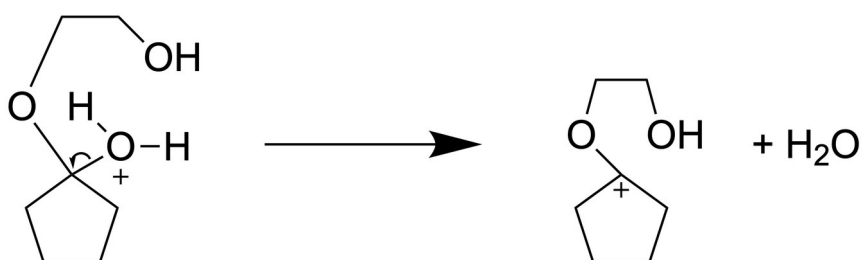
Finally, the carbocation is in very close proximity to the other oxygen of the diol, which makes it very easy for them to form a bond together – this creates another oxygen cation, which easily deprotonates to become nice and stable and regenerate the acidic proton:
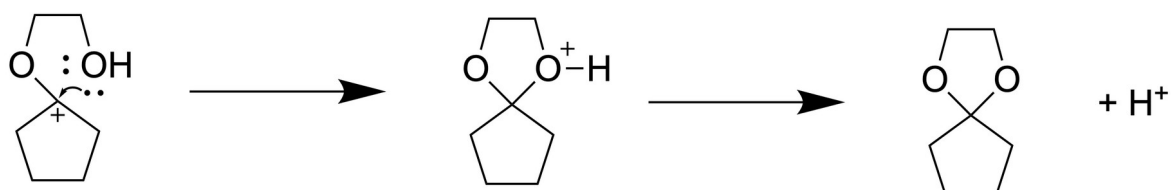
Now, this whole step in the synthesis presents a problem in that it is reversible, as we'll see below (see Step Five). To counteract this, we want to shift our equilibrium to the side of our products, and one way Le Chatelier tells us we can do this is by removing our products – in this case, our useless by-product of water.
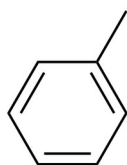
To make this more efficient, we remove our water by **azeotropic distillation**. This acts on a phenomenon whereby two liquids form a mixture, which, as far as distillation is concerned, acts as a single substance[14], and boils off as one fraction. This can alternatively be looked at as increasing the volatility of water, which by this method will be removed at ~84°[15]. The second liquid we add is toluene, A.K.A. methylbenzene (left).

Toluene

As it turns out, toluene here acts as a multi-purpose super-substance – not only is it a good solvent (remember that we can't use water), but actually has a use for providing our acidic catalyst. Toluene obviously isn't acidic itself, but in the presence of a weeny bit of sulphuric acid it forms something called 'para-toluenesulphonic acid'[18] (*p*-TSA) (below), which is acidic as balls.
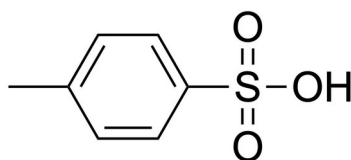
Once our reaction is completed, we separate our cyclopentanone ketal out with **vacuum distillation**, which is a distillation carried out a reduced pressure. By using a lower pressure, the boiling point is lowered and so we do not get any unwanted side reactions or decompositions that we would at higher temperatures.

Step Three – Bromination

For this next step, all we need to do is add three bromine atoms to our cyclopentanone ketal – two of them, we'll be removing again by dehydrohalogenation (to form alkenes), and the other we need for our Favorskii Rearrangement later on.

The precise mechanism of what's going on here is ambiguous, but likely involves the solvent we use[25] – dioxane, which forms a **complex** with bromine:
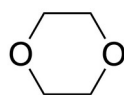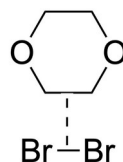
Dioxane   Dioxane Dibromide

It is hypothesised that the Br-Br bond length here is slightly longer than in Br$_2$, which means that there is a polarity between the two bromine atoms (see Figure 1). Maybe this enables the complex to pull off C-H hydrogens? Maybe the presence of the ketal group has something to do with it? God, I don't know *everything*.

At any rate, we can control the number of substitutions simply by stoichiometric mixing – that is to say, adding exactly three moles of bromine per mole of ketal. Even if some di- or tetra-bromos are

formed, the lack or addition of the massive bromine atom should alter the boiling point of such molecules enough that they will be prevented from coming over once we distill our product.

Step Four – Diels-Alder Reaction

Allow me to side-track for a quick history lesson.

Otto Diels and Kurt Alder were two big fans of sticking two things together. They loved sticking things together so much they stuck their own two names together, and discovered a chemical reaction involving sticking two things together.

In our case, the Diels-Alder reaction is an example of a **dimerisation**.[20] – which is a reaction to form a **dimer** – two of the *same* molecule stuck together. This word itself is also the product of sticking two things together, as it is a portmanteau of 'di' (meaning 'two'), and 'polymer'. Diels-Alder reactions take place between a **conjugated diene** (two double bonds separated by a single bond[21]), and a **dieneophile**, which is a substituted alkene or alkyne.

Here is the general mechanism:

Diene   Dieneophile   Cyclohexene
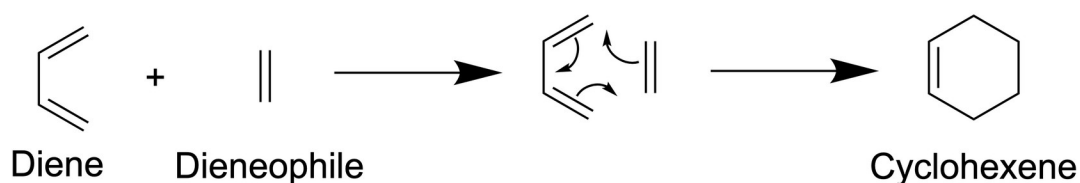
'But hang on a minute,' you say, 'There aren't any double bonds at all in our current precursor!'

Worry not! In basic conditions, haloalkanes undergo elimination to form alkenes. In this case, our 2,2,5-tribromocyclopentan-1-one ketal will form the intermediate (2-bromocyclopenta-2,4-dien-1-one ketal) below, which actually acts as both a diene *and a* dieneophile, and undergoes spontaneous dimerisation.
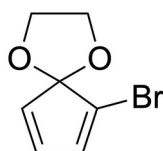
Because of this spontaneity, we are actually completing two steps in one – the dehydrohalogenation *and* the Diels-Alder.

Let's first look at the mechanism for the dehydrohalogenation. It's an elimination with a base - an AS-Level mechanism (see 3.3.3.2) – easy peasy. A hydrogen adjacent to the brominated carbon is pulled off, the electrons from this bond used to form a π-bond, and the bromine released as bromide.
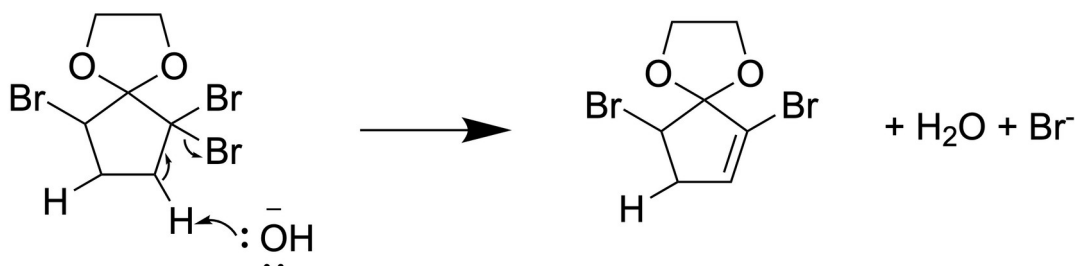
This then takes place a second time, exactly the same.
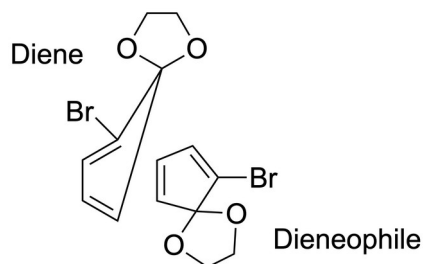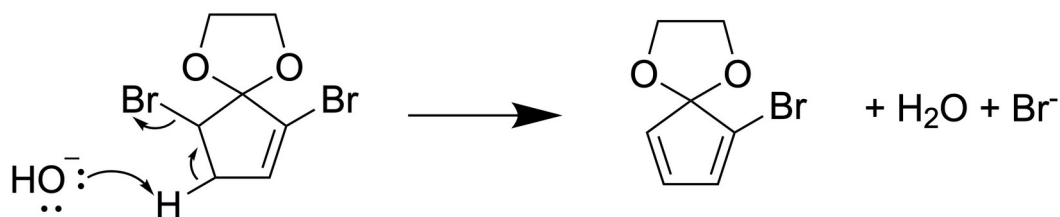
Now, the actual Diels-Alder Reaction. To make it more obvious what's happening, the two molecules of the diene have been redrawn (left). You should be able to see the same configuration of double bonds that is shown in the diagram of the general mechanism above.

The exact same concerted[10] mechanism occurs, and we are left with a six-membered ring:
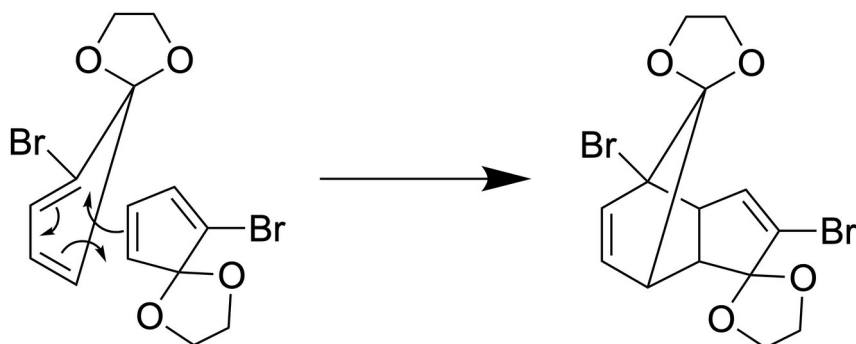

There we have it – the intermediate known as the bisethylene ketal. As mentioned above, the reaction takes place in basic conditions (usually NaOH). This is all in a solvent of methanol, at around 65ºC.

We can then separate our product by crystallisation. You may notice that at the moment this looks nothing like a cube, but not to worry! Trust the process.

Step Five – Deprotection

It's finally time to remove those cyclic ketals we added to protect our ketone – we'll be needing those groups again soon. Again, we'll be adding acid, but the reaction is much simpler to control[22] as we don't need to rigorously dry it of any water (it is, in fact, a hydrolysis). We're also allowed to use an inorganic acid this time: good old sulphuric.

To avoid using massively overcomplicated diagrams, I will henceforth be simplifying our current product to show only the important parts (in this case, the cyclic ketal group). We first see one of the oxygens protonated:
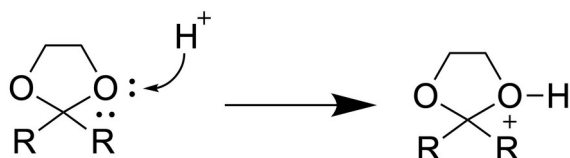
The oxygen isn't having any of that 'positive charge' nonsense, so yoinks the electrons from its bond with the carbon:
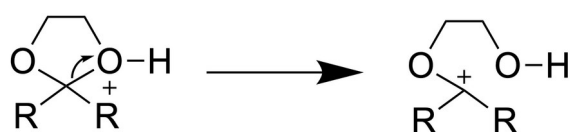
It is this carbocation that is then the target of the nucleophilic attack of our water:
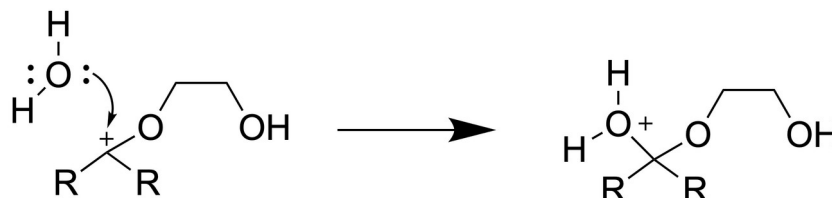
We then see a proton transfer to form a leaving group – the ethylene glycol we used those many moons ago to protect the ketone in the first place:
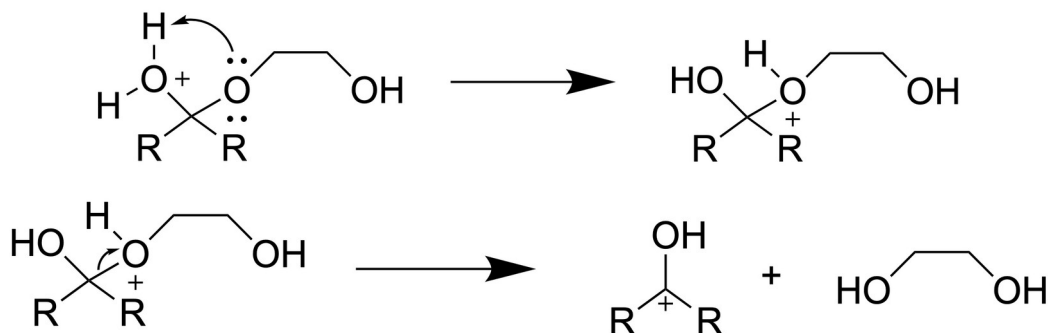
We're now left with a hydroxy group connected to a carbocation, which as you can imagine very quickly sheds its proton and forms the ketone:
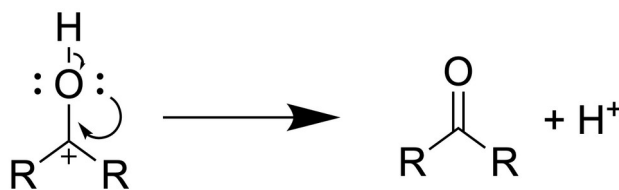
If we now bring back the rest of the molecule, we get the following overall formula:

The exact same thing occurs at each of the cyclic ketals. In some other syntheses – the Original, for example – the two deprotections are actually performed at different points. It shouldn't matter too much.

Guess what, though? No purification needed! We won't be purifying our product until right up near the end.

Step Six – [2+2]-Cycloaddition

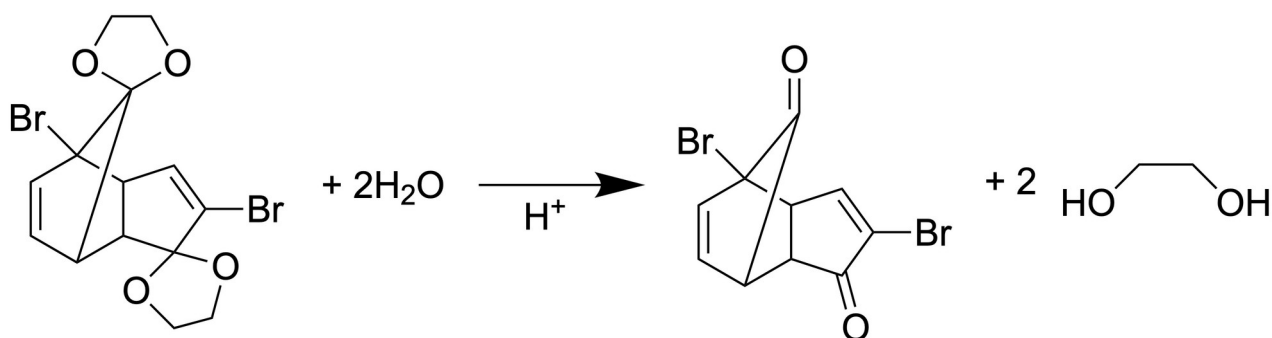Remember the Diels-Alder Reaction? It's actually one of a whole category of reactions called **cycloadditions**, which is when there is addition to make a cycle (And they say organic chemistry is hard).

The Diel-Alder Reaction is known as the [4+2]-cycloaddition, with the two numbers referring to the number of electrons from each reactant involved in the reaction. What this means is that for the Diels-Alder Reaction, four electrons from the diene move, and two electrons from the dieneophile.
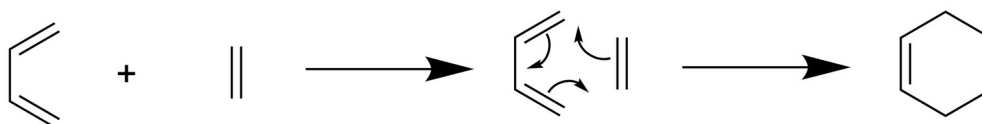
You can see that this is the case by counting the number of curly arrows, and, remembering that a full-headed arrow represents the movement of an electron *pair*, multiplying by two.

The next step in our cubane synthesis is the [2+2]-cycloaddition, which has this general form:
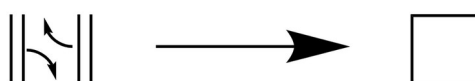
However, the reaction only takes place in the presence of ultraviolet light (see Abstract).
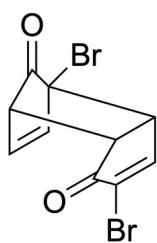
We can redraw are product yet again to make it look like this on the right. If it doesn't look like the same molecule to you, just keep staring. Also please note that the bond lengths are obviously not to scale.

In any case, you should be able to see the configuration of the two double bonds as shown above.

Like the Diels-Alder, the mechanism is pleasingly simple:
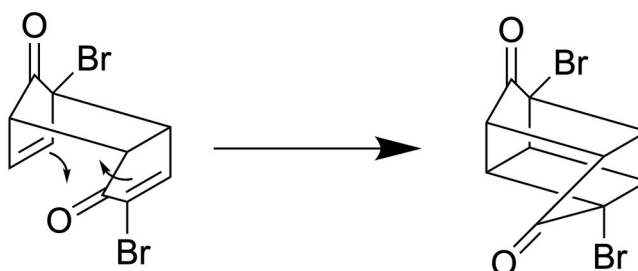
But what's that? A vaguely cuboid-looking thing[23]!? The end is within sight!

As mentioned above, the reaction takes place in the presence of U.V. – we also have to use a specific wavelength – approximately 325nm – as this is the wavelength required to activate one of the C=C double bonds. If the mistake is made of using light containing multiple other shorter wavelengths, the C-C bonds adjacent to the carboxyl groups are liable to break, which would result in a lot of unwanted nonsense.

Step Seven – Favorskii Rearrangement

The **Favorskii Rearrangement** is a way of making a big ring into a smaller ring. It needs a ketone and an α-halogen (halogenated carbon adjacent to the carboxyl group) – isn't that a coincidence? It's a base-catalysed reaction, carried out under reflux.

Again, the bulk of the current molecule has been excluded to put focus on the parts which are reacting – in this case, the two pentagonal sides, which undergo the same reaction. The mechanism[12] looks like this.
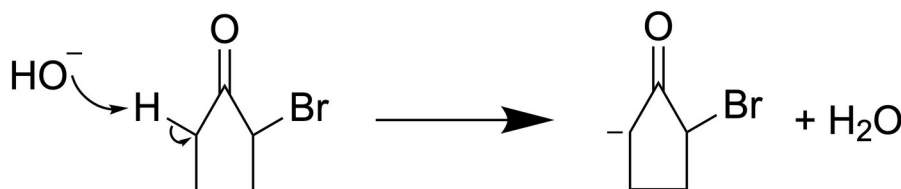
We first get an attack by the base, which scoops up the hydrogen opposite the bromine.

The carbanion, as you know, is not a massive fan of existing, so transfers its extra electrons to the first place it can find – the halogenated carbon (which has a slight $\delta+$ charge due to the electronegativity of the bromine). The bromine isn't a fan of that, so leaves. This forms an extremely strained cyclopropane intermediate that looks a bit like that bit in Squid Game:
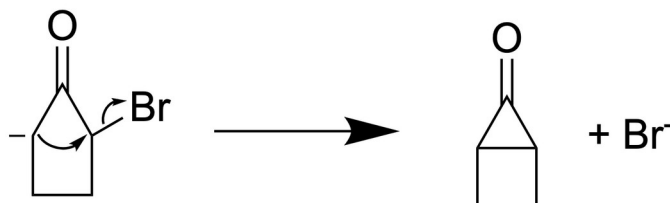
Another hydroxide ion comes along, but this times behaves as a nucleophile, and attacks the $\delta+$ carbon attached to the oxygen. The ketone becomes an oxide:
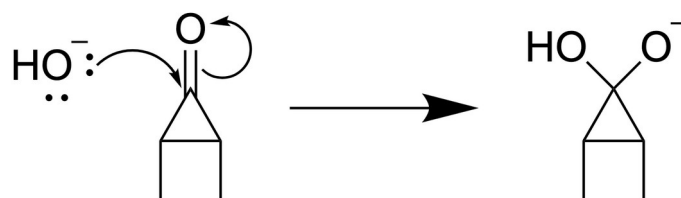
The oxygen decides it much preferred its old way of living – double-bonded to the carbon – so uses its extra electrons to reform it. This gives the system an excuse to break the strained cyclopropane ring, but forms another carbanion.
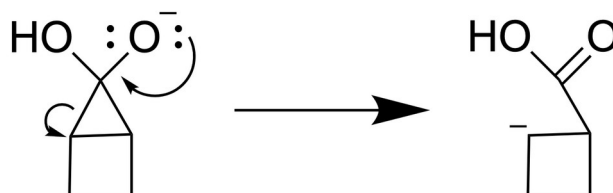
The carbanion essentially steals back the hydrogen it was separated from in the very first step of the mechanism, reforming a hydroxide ion:
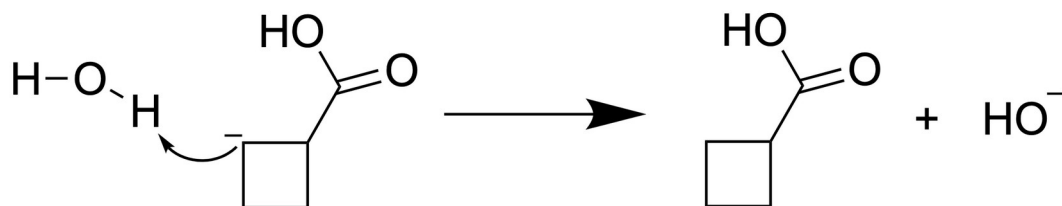
If we now put this in context of the whole molecule, this is the reaction:

Now that's a cube, if ever I saw one. This chemical – cubane-1,4-dioic acid – was the final stop on the cubane bus for Eaton and Cole's Original Synthesis, with the unsubstituted cubane coming in a later paper.

Step Eight – Barton Esterification

Some might be happy to stop here – the strained cubic skeleton has been achieved at last. However, we came here for cubane, and so cubane we shall get – not some hairy substitution. And so the final step is a decarboxylation, to get rid of those nasty additional groups.

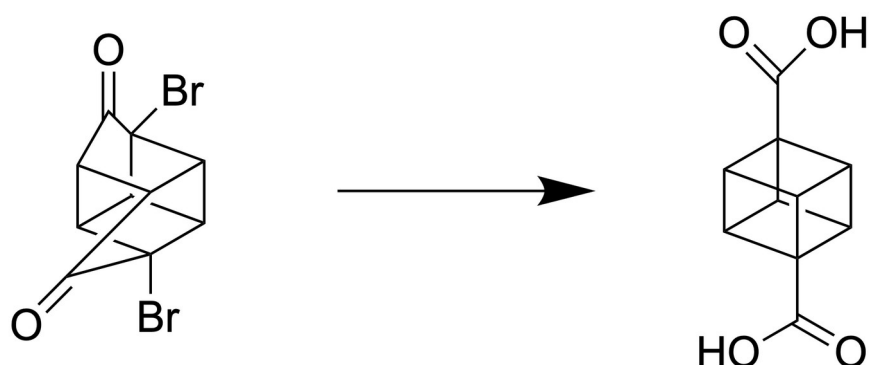Unfortunately, to go forward, we must first go a step back, and stick some stuff on top. What we want to perform is a reaction called a **Barton Decarboxylation**, which is a way of removing carboxylic acid groups via a free radical mechanism. Before we can do this, we need to convert it into a 'Barton Ester' – hold your nose, because things are about to get smelly.

The first step for this is converting our carboxylic acid into an acid chloride (ROCl). This is done by the addition of a chlorinating agent – in this case, thionyl chloride, $SOCl_2$. The mechanism[24] proceeds as follows.

The sulphur – with a $\delta+$ charge due to the electronegative oxygen and chlorines surrounding it – attacks the oxygen in the hydroxy group, severing its π-bond with the oxygen in the process:
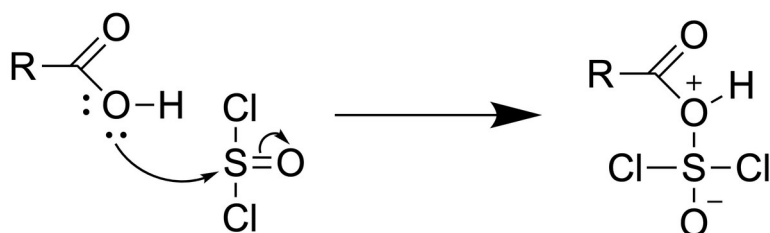
The oxygen was rather happy being double-bonded to the sulphur, so rudely kicks out the chlorine as an ion. As an act of revenge, the chlorine robs the hydrogen, forming hydrochloric acid (which, still being in solution, dissociates):
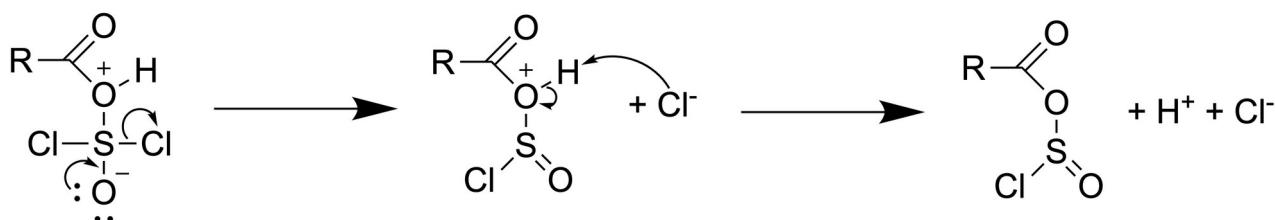
The chloride attacks the δ+ carbon in the centre of the former acid group, forming the acid chloride, but leaving an oxyanion.
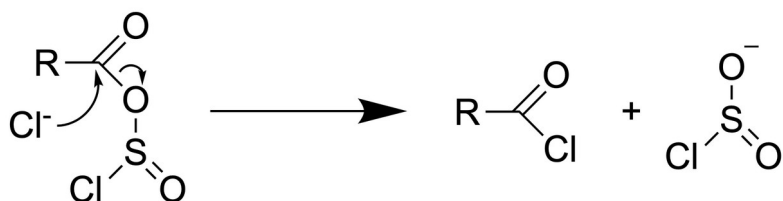
This is neutralised by the proton of the acid, which attacks the chlorine to produce sulphur dioxide and reform the acid[24]:
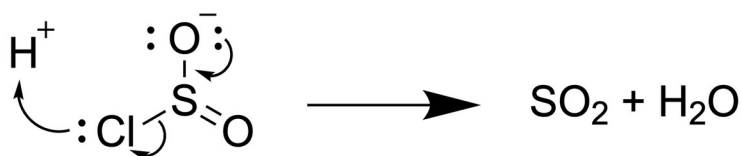
Once again recontextualising this in terms of the entire molecule, we get the following overall reaction:
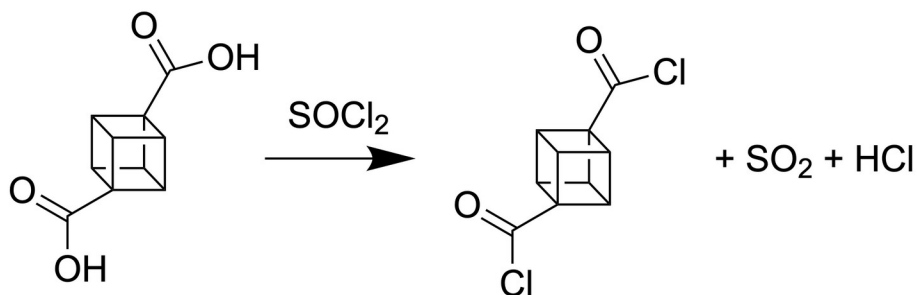
The purpose of replacing the hydroxy with a chlorine is to make something easily removable, as we are now going to replace it with our rather large Barton Ester.

We react **Pyrithione Sodium**, a sodium salt of which the anion is shown below. The mechanism constitutes a fairly mundane nucleophilic addition-elimination:
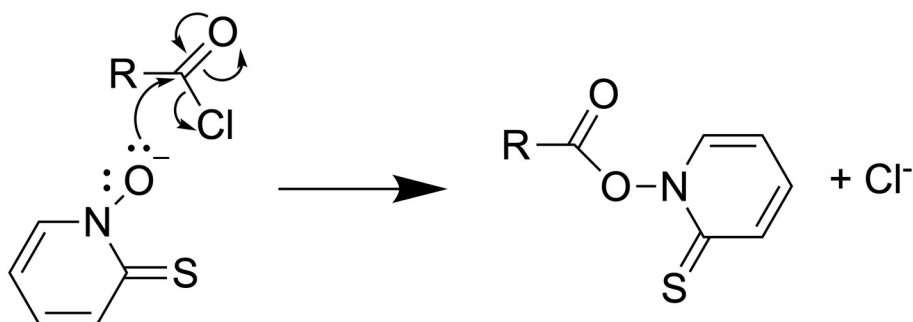
This may at this point seem like a fairly random thing to add, but the reason should become clear once the mechanism of the next step is revealed. Anyway, if we view this in terms of our larger molecule:
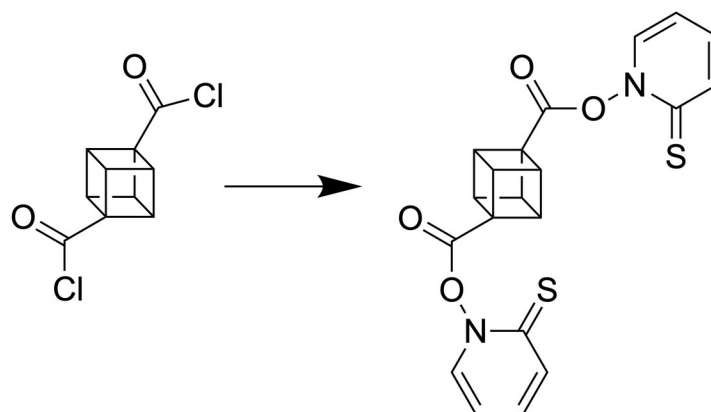
There's not far to go now.

Step Nine – Barton Decarboxylation

Free radical time! This isn't a U.V. reaction, so to introduce radicals into the mix we'll need a **radical initiator**. Our chemical of choice will be 'azobisisobutyronitrile', or AIBN if you're not a masochist. When heated, AIBN decomposes into two juicy radicals as shown, motivated by the entropic bonus of having two extra gaseous nitrogen molecules.
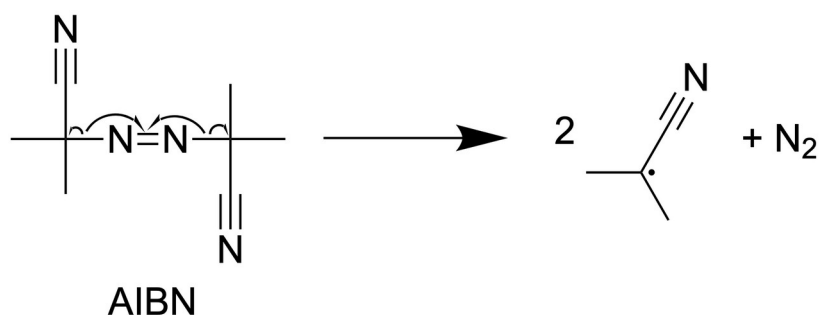
These radicals will then collide with our reagent, **Tributyltin Hydride** (a tin atom surrounded by three butyl groups and a hydrogen, $SnBu_3H$) to form •$SnBu_3$ radicals and hydrogen atoms.

The magic of the Barton Decarboxylation is in the stability of the S-Sn bond – this is what drives the reaction. As such, the mechanism involves the radical attack of the •$SnBu_3$ on the sulphur π-bond, which cleaves homolytically. The N-O bond also breaks, leaving this pyridine substitution, and a lone electron on a sort of carboxylate:
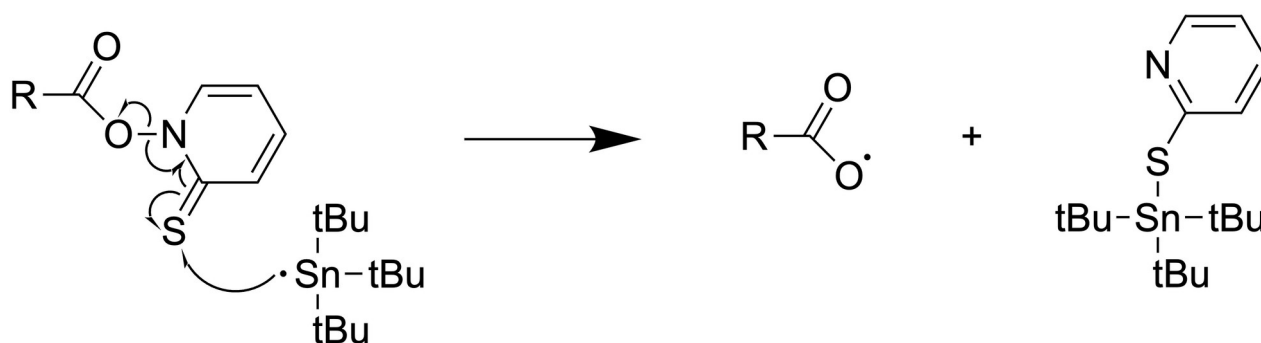
We then see this radical rearrangement of the 'carboxylate', which results in a molecule of carbon dioxide being released, and a carbon radical:

$$R \cdot \overset{O}{\underset{O \cdot}{C}} \longrightarrow \dot{R} + CO_2$$
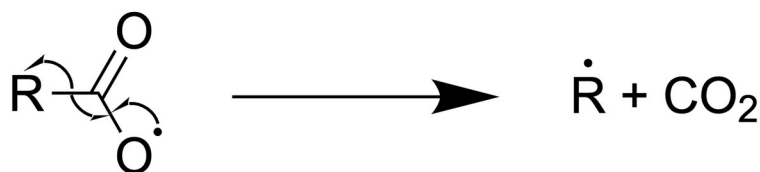
This carbon radical will then meet with the hydrogen radical liberated by the AIBN (see above), completing the removal of the carboxyl group.

Then – ta-da! – we have it. Cubane.
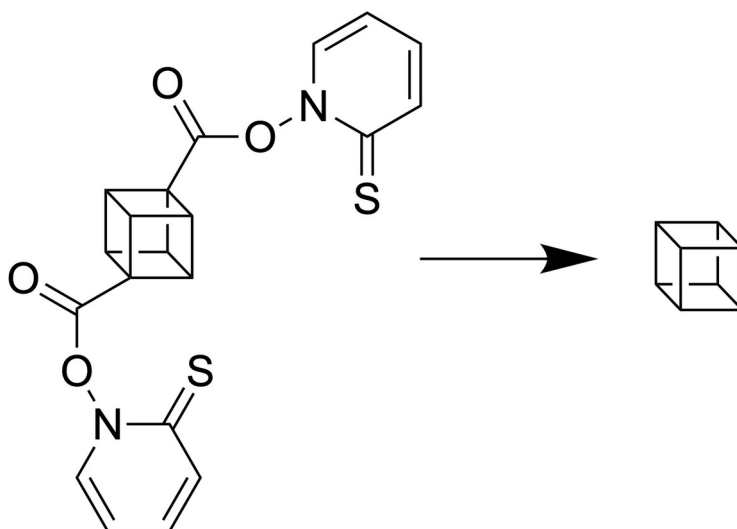
Endnotes

1.

Plato did not actually name them, but certainly had a thing or five to say about them[2], pairing each with the four elements of the Universe – Fire, Water, Earth and Air. He soon realised that the number of Elements (four) did not match the number of Solids (five), but fixed this glaring oversight by associating the dodecahedron with 'the Universe itself' – 'the Universe' of course, isn't an element, but then again neither are any of the other four so we'll give him a pass this time.

2.

In the dialogue 'Timaeus', or so I'm told. It's all Greek to me.

3.

Tetrahedrane, the smallest Platonic Hydrocarbon, is theoretically possible. 'Theoretically possible', if you ask me, means diddly-squat. It's 'theoretically possible' for me to press four-hundred, but that doesn't mean I have.

Still, the boffins have managed to make tetrahedrane with some sticky-outy bits, so bless them for trying.

The other two are octahedrane – which suffers from the same (although a more severe) sharp-bond-angle problem cubane was theorised to have – and icosahedrane, which can't exist simply because it would require carbon to form five bonds. Goodness, we chemists really have problems with the number five, don't we?

4.

Dodecahedrane was first synthesised by Leo Armand Paquette. The *second*-worst thing (besides making dodecahedrane) that Paquette ever did was plagiarise and then sabotage (see paragraph eight) a funding application he was meant to be reviewing, for his own personal gain. Twice.

5.

Not really. It's "Pentacyclo[$4.2.0.0^{2,5}.0^{3,8}.0^{4,7}$]octane". The abomination you see in the square brackets comes from the von Baeyer System, which is a way of describing polycyclic molecules (molecules with lots of rings). On account of the fact that this is a stupid name, we'll stick with cubane.

6.

This works due to something called the hydrophobic effect, which is what causes oil to be immiscible with water. This effect is commonly misattributed to the dissolution of hydrocarbons requiring the endothermic breaking of hydrogen bonds, but is more likely to be due to the fact that water forms cages around organic solutes, which are orderly (lack entropy). The good old Second Law of Thermodynamics is awfully critical of orderly, non-entropic things, and so would much rather that the formation of water-cages was kept to a minimum.

By forming in ginormous, non-dissolved clumps rather than tiny individual dissolved particles, organic molecules minimise their surface-area contact with water, which therefore reduces the formation of water-cages and makes the whole ordeal more entropically favourable.

When you add a salt to water, you add lots and lots of tiny particles with a large amount of charge stuffed inside them – water-cages formed with ions of a high density of charge are even more orderly, and so the system is even more willing to stop them forming (see sixth subheading). Hence, the addition of salt enhances the hydrophobic effect, which decreases the solubility of the organic molecule in the water.

7.

A *proposed* mechanism – nobody can quite agree on what it's actually meant to be.

8.

For a more in-depth paper on all things cubane, including approximately a mole of different synthesis routes, as well as some focus on nitrocubanes, see here. Scroll down to the biographies if you fancy a laugh.

9.

Disclaimer: do not eat the cubane. I searched far and wide on a paper which includes how it might taste, but came up unsuccessful, but as it's a plain old alkane with no functional groups – probably not very interesting. All the more reason to not eat it.

10.

'Concerted' comes from the phrase 'in concert', as it refers to a reaction in which all relevant bonds are made and broken at once. After seeing the abominations above, you probably agree that the word is not exactly music to one's ears.

11.

Or – to use this analogy of this clever-clogs – "the usage of painter's tape when painting a room". That article also goes into more depth on ketone protection.

12.

See this video by 'Professor' Dave. In that video, he actually touches on the 1964 Eaton Synthesis.

13.

Note that not all ketals are cyclic – a ketal refers to two oxygens bonded to any R group.
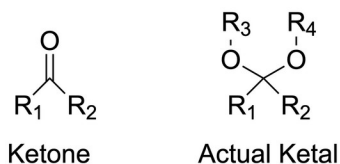
There is even, in fact, some debate over what this group is actually called – you may hear it referred to as a 'acetal', though strictly that is the umbrella term for carboxyl groups protected as diesters, and includes protected aldehydes (i.e. where R_1 or R_2 in the diagram above is instead a hydrogen).

14.

Azeotropes occur due to the two substances being in such a ratio that the intermolecular forces between molecules of the two different substances are stronger than the intermolecular forces between molecules of the same substance. Toluene actually forms a slight permanent dipole, so in the case of the water-toluene azeotrope it is presumably the case that the dipole forces between water and toluene outmatch the hydrogen bonds between water molecules, which are themselves weakened by all that nasty toluene getting in the way. See the second answer to this question for more on azeotropes. It doesn't cite any sources, but when has anybody ever lied on the internet?

15.

There is this weird one that starts with a cyclobutadiene derivative.

16.

Check out this blog post by this other guy who had the same idea as me (of writing an article about cubane). Granted, he happened to get to it eight years earlier, and has a so-called 'Ph.D.', whatever that is.

17.

This paper gives another overview of our dear cubane, but focuses a lot on its potential medical applications – apparently some chemicals have uses *outside* of explosives? The peculiar arrangement of the carbons in cubane allows for attached functional groups to be arranged in a yet unforeseen configuration in 3D space (see section three), which allows for unique interaction with active sites. The fact that cubane is non-toxic[9] also helps.

18.

The mechanism for the formation of *p*-TSA is actually very intriguing. It's called a **sulphonation** (which is a type of electrophilic aromatic substitution (see section three)), and adds a **sulpho** group. Recall that sulphuric acid can dissociate to form sulphur trioxide:

$$H_2SO_4 \rightleftharpoons H_2O + SO_3$$
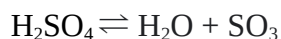
It is this sulphur trioxide that then reacts. Before we consider the formation of toluenesulphonic acid, let's look at benzenesulphonic acid. The electronegative oxygens of sulphur trioxide give a $\delta+$ charge to the sulphur, which attacks one of the electron-rich π-bonds of benzene to form a carbocation. To account for this extra bond, one of the S=O bonds breaks, leaving a negative oxygen:
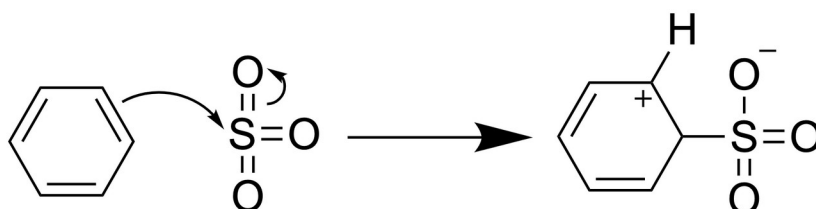
The hydrogen adjacent to the carbocation has been shown, as it is now stolen by the extremely nucleophilic oxide:
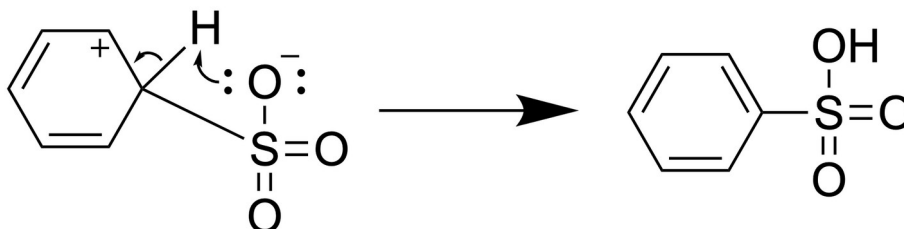
This alone isn't all that special, but becomes more interesting when you consider that it is toluene we are sulphonating (not benzene). The sulphonation of benzene results in only one product, but if you consider toluene there are three possible outcomes:
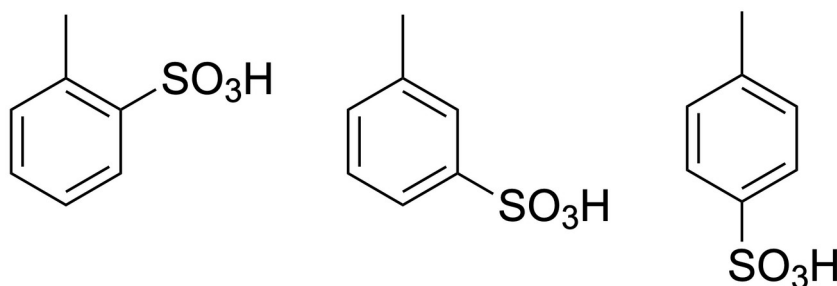
Left to right, they are ortho-toluenesulphonic acid (*o*-TSA), meta-toluenesulphonic acid (*m*-TSA) and *p*-TSA, with which we are familiar. You might expect all three isomers to be formed in roughly equal quantities, but remarkably our 'para-' isomer is by far the major product.

This is due to **resonance**[19]. If we now go back to look at benzene once more, recall that it has this resonance structure:

But now entertain the thought for but a moment that we have some sort of negatively charged group attached to our benzene as below. We find that the resonance structures look a bit like this (see section three):

You'll notice that the imaginary carbanions only appear on the carbons adjacent to the functional carbon (the 'ortho-' position), and the carbon opposite (the 'para-' position). Now, the methyl group on a m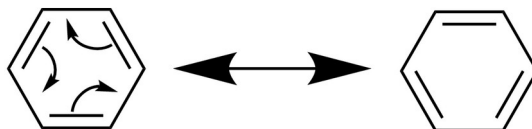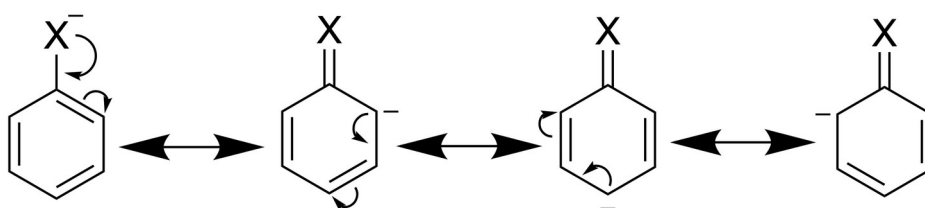olecule of toluene is not negatively charged, but it *is* electron-releasing, so we end up with a similar type of thing going on. Resonance is very quantum-mechanicsy, so we don't need to be shifting about actual particulate electrons – think of it more in terms of orbitals, or electron clouds. But in short, due to resonance, the ortho- and para- carbons average out to be more electronically dense.

Squish!
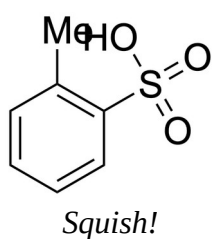
Remembering that the sulphur trioxide is electrophilic, this explains why substitution of the meta- carbons is less favourable. However, I did mention that it was the *para-* isomer which was the most abundant – why is *o*-TSA not also seen?

This is simply due to the fact that the sulpho group is large (left). It just doesn't physically fit next to the methyl group without having to bend around awkwardly.

19.

Resonance is our way of dealing with the fact that electrons aren't real. Classically, electrons are little balls and covalent bonds are two little balls suspended between two bigger balls, but we know of course that this isn't actually the case, and electrons have quantum physical behaviours.
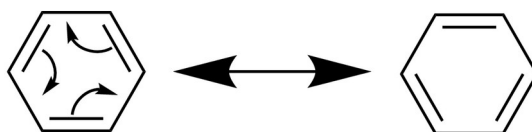
The most common example of a resonance structure is benzene (above) – picture this: it costs no energy for the electrons to move between the two configurations, so they do, a lot. And quickly.

What we actually observe when experimenting with benzene is the average of the two states, which explains why its bond lengths are all identical, and why it is so stable.

Picturing that? Good, because it's nothing like that at all. Neither of the two states *actually* exist – it's all quantum wibbly-wobbliness, and we invented resonance to rationalise this.

20.

Dimerisation technically refers to the addition of two identical monomers – Diels-Alder reactions do not always take place between two of the same molecule.

21.

As opposed to 'non-conjugated dienes' (more than one separating single bond) and 'cumulated dienes' (tee-hee), which are directly adjacent double bonds.

22.

The trickiest part the 1997 Synthesis references is the temperature control – the mixture must be maintained in a very tight range.

23.

Aside from the erroneously long bonds between the two pentagonal faces, the diagram of the current structure I have drawn is also wrong in that it does not contain any 90º bond angles at this point. Bonds in molecules will repel each other as far apart as possible, which has the symptom of pushing the molecule into the least strained position – in the case of the bis-ketal, you would expect to see distorted pentagons and squares rather than the perfect world I have imagined.

24.

I was unable to find a veritable source, so had to go off the word of this chap. In any case, it was better than this nonsense put out by Khan Academy (later rectified).

25.

The educated people of the internet concur that this reaction has an unusual feature in that it involves the breaking of C-H bonds. As such, it likely involves something involving free radicals. In a paper by the U.S. military, a number of different solvents were explored, but it was found that only dioxane does the job (which perhaps means it should be promoted from the role of 'solvent' to 'reagent'). Dioxane dibromide is a fairly common brominating agent, after all.

26.

Note: complete conjecture.

27.

'Oxygen balance' is explosives talk for the number of oxygen atoms a molecule *needs* (to be fully oxidised) in proportion to the number of oxygen atoms it *has*. For example, TNT (M_r = 227.1) combusts like so:

$$C_7H_5N_3O_6 + 5.25O_2 \rightarrow 7CO_2 + 2.5H_2O + 1.5N_2$$
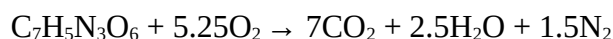
10.5 addition moles of oxygen atoms are needed to oxidise one mole of TNT, so the percentage by mass of excess oxygen is $(16.0 \times -10.5)/227.1 = -0.74 = -74\%$. The closer this number is to 0%, the better.[28]

For ONC.:

$$C_8N_8O_{16} \rightarrow 8CO_2 + 4N_2$$

As you can see, all the oxygen required for combustion is self-supplied, giving an oxygen balance of 0%.

28.

There are obviously other factors affecting the effectiveness of an explosive. Interestingly, heptanitrocubane (ONC with one 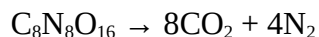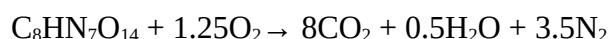less nitro group) – despite its inferior oxygen balance of -12%, has proved in practice to be a more 'effective' explosive.[29]

$$C_8HN_7O_{14} + 1.25O_2 \rightarrow 8CO_2 + 0.5H_2O + 3.5N_2$$

It is also possible to have a positive oxygen balance, which will occur when a molecule contains more than the number of strictly necessary oxygen atoms.

29.

An even more effective cubane-based explosive is octaazacubane, N_8, which in fact has nothing to do with cubane other than its shape (it is actually a nitrogen allotrope).
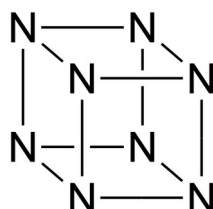
Octaazacubane is more than twice as powerful (measured by TNT equivalence) than ONC, making it by far the most powerful chemical explosive, and – oh, wait, it's entirely theoretical.[see 3]

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