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The pyrolysis of chlorinated hydrocarbons

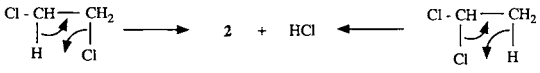
I was admitted to Imperial College in October 1938 when I was 20 years old. Because of the good marks I had obtained in the entrance examinations I was allowed to proceed directly into the second year. I completed the BSc with First Class Honors in 1940. Because of what turned out to be a minor problem with my heart, I had earlier been called to the Army and rejected. In any case, I was in a reserved profession and expected to work on a subject of national importance.

So, in 1940 I began my PhD work which mainly involved the synthesis of economically important vinyl chloride. The project was financed by the Distillers Company and I worked in association with a German refugee chemist, Dr M. Mugdan. We started off by studying heterogeneous catalysts for the addition of hydrogen chloride to acetylene.[1] At that time this was the preferred industrial process for vinyl chloride. Then, early in 1941, I began to study the homogeneous, non-catalysed

$$\underset{\mathbf{1}}{Cl\text{-}CH_2\text{-}CH_2\text{-}Cl} \xrightarrow{\Delta} \underset{\mathbf{2}}{CH_2{=}CHCl} + HCl$$

pyrolysis of ethylene dichloride **1** into vinyl chloride **2** and hydrogen chloride, the method almost universally used at the present time. This deceptively simple reaction turned out to be unusually complex.[2–4] It provides a good example of radical chemistry and eventually led to a correlation between structure and mechanism.

Many organic molecules decompose in the gas phase by the



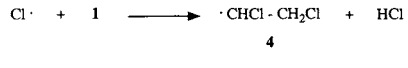
1 **Scheme 1** **3**

so-called 'unimolecular' mechanism. The transition state is depicted in Scheme 1, and such a mechanism should also be available to 1,1-dichloroethane **3**.

The gas phase pyrolysis of 1,1- and 1,2-dichloroethane affords nearly quantitatively HCl and **2**. For my PhD work in 1940–1942 I studied these two reactions in a glass tubular-flow reactor. When the glass is clean, there is always a fast heterogeneous reaction. However, the active centers of the surface are soon poisoned and the reaction then becomes homogeneous. This is demonstrated by packing the reactor with glass to vary the surface area to volume ratio. After the usual 'poisoning' period, the packed reactor gives the same reaction rate as the unpacked reactor. Hence, the final reaction is not heterogeneous.

For several weeks these two dichlorides decomposed at the same rate by the unimolecular mechanism. But one day, without warning, the ethylene dichloride started to decompose much faster than the 1,1-dichloroethane, such that I could obtain the same conversion at 100 °C lower temperature. After reflection, I realized that the ethylene dichloride used had been recovered from the dry ice trap and then redistilled before use. Normally the 1,1- and 1,2-dichloroethanes were purified by careful fractional distillation. Clearly, my recovered sample contained a catalyst, or lacked an inhibitor. The latter seemed more probable, so I treated the 1,2-dichloroethane with chromic acid or potassium permanganate, shaking overnight. After redistillation, the purified dichloride still gave variable results, some days decomposing very fast and some not. The simply distilled material always had a constant rate of decomposition. The rate for 1,1-dichloroethane was always constant and independent of comparable chemical treatment.

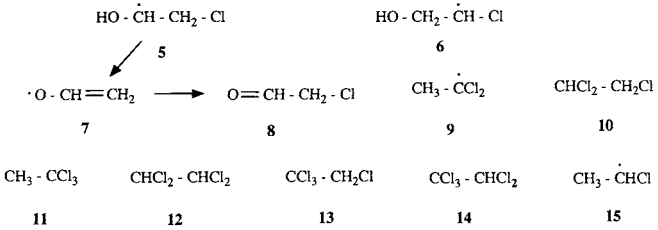
Finally, I identified another factor, a variable air leak. When I eliminated this, both dichloroethanes decomposed slowly by the unimolecular mechanism. When I let in a controlled flow of air (or chlorine), the 1,2-dichloroethane (in contrast to the 1,1-isomer) now decomposed rapidly at a much lower temperature. I had discovered my first new reaction: the radical chain decomposition of the dichloride as in Scheme 2.



Scheme 2

The inhibitor in commercial ethylene dichloride of the 1940 era was ethylene chlorohydrin. The two form an azeotrope and so all my laborious efforts at purification by distillation failed.

Why is ethylene chlorohydrin an inhibitor of the chain (involving radical **4**) depicted in Scheme 2? This must be



because of the formation of either, or both, of the radicals **5** and **6**. The radical **5** is of a type well known[5,6] to eliminate chloride ion and a proton in solution phase to furnish radical **7** which in return would react with Cl· to give **8**. Of course the radical **6** will not eliminate an OH· radical (C–OH bond too strong) so it would also inhibit the chain.

1,1-Dichloroethane **3** always decomposes by the unimolecular mechanism even when oxygen, chlorine, or other radical generators are added. This is because radical attack on **3** gives the derived radical **9** which cannot carry the chain.

All this was later put on a sound basis as a result of more precise measurements of rate constants and of activation energies. However, it did not require precise measurements to predict which chlorinated hydrocarbons would decompose by a radical chain mechanism and which by the unimolecular mechanism. Clearly, if the chlorinated hydrocarbon, or the product from the pyrolysis of the chlorinated hydrocarbon reacted with chlorine atoms to break the chain then the chain mechanism would not exist. Such chlorinated hydrocarbons would decompose by the unimolecular mechanism. Monochlorinated derivatives of propane, butane, cyclohexane, etc. would afford propylene, butenes, cyclohexene, etc. All these olefins are inhibitors of chlorine radical chain reactions because of the attack of chlorine atoms at their allylic positions to give the corresponding stabilized allylic radicals which do not carry the chain.

Chlorinated ethanes could be divided into two types, those that could carry the chlorine atom chain and those that could not. 1,2-Dichloroethane **1**, 1,1,2-trichloroethane **10**, 1,1,1-trichloroethane **11**, 1,1,2,2-tetrachloroethane **12**, 1,1,1,2-tetrachloroethane **13**, and 1,1,1,2,2-pentachloroethane **14** all decomposed with enhanced rates by a chlorine atom chain mechanism. Ethyl chloride and 1,1-dichloroethane **4** did not. The reason for the latter has been explained. Ethyl chloride gave likewise the radical **15** which could not carry the chain. In 1949, in a paper with the late Professor P. F. Onyon,[7] the observations made up to that time were correlated and a number of predictions were made (Table 1). In later work all the predictions were shown to be true.

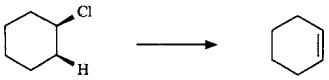
The work on the pyrolysis of chlorinated hydrocarbons, especially the catalyzed synthesis of vinyl chloride, was patented by the Distillers Company and subsequently sold to the Dow Chemical Corp. Perhaps I justified my research career within the first few months! I have never met anyone who could, or would, tell me if ethylene dichloride pyrolysis, which

Table 1.

Chloro compound		Predicted homogeneous first-order mechanism: Unimolecular	Predicted homogeneous first-order mechanism: Radical chain
Ethyl chloride		x (already observed)	
1,1-Dichloroethane	**3**	x (already observed)	
1,2-Dichloroethane	**1**		x (already observed)
1,1,1-Trichloroethane	**11**		x
1,1,2-Trichloroethane	**10**		x
1,1,2,2-Tetrachloroethane	**12**		x (already observed)
1,1,1,2-Tetrachloroethane	**13**		x (already observed)
Pentachloroethane	**14**		x
1-Chloropropane		x	
2-Chloropropane		x (already observed)	
1,2-Dichloropropane		x	
1,2,3-Trichloropropane			x
n-Butyl chloride		x	
tert-Butyl chloride		x (already observed)	
2,2-Dichloroethyl ether			Possibly
β-Chloroethylbenzine			Possibly
α-Chloroethylbenzene		x	

is carried out on an enormous scale, is catalyzed by air or chlorine or not.

The pyrolysis of (say) cyclohexyl chloride by the unimolecular mechanism must involve *syn*-elimination (**16** → **17**) because the product is a *cis*-olefin. When I came across the pyrolysis of steroidal esters[8,9] for the synthesis of olefins it seemed to me that *syn*-elimination (unimolecular mechanism)



16 17

must also be involved. At that time the distinction between *syn*- and *anti*-elimination in the synthesis of cyclic olefins was not established. An analysis of the literature[10] showed the relationship between mechanism (*cis*-elimination) and stereochemistry. Thus a mechanistic study of the pyrolysis of chlorinated hydrocarbons eventually made significant contributions to the stereochemistry of elimination reactions in complex natural products.

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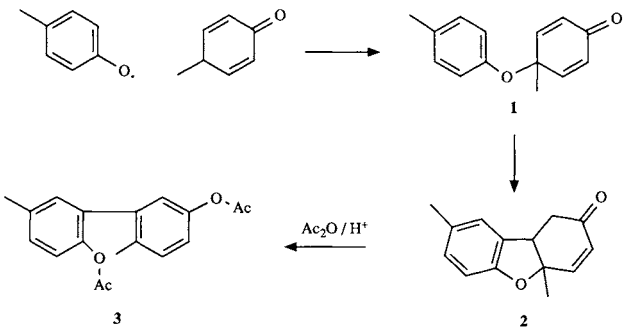
2

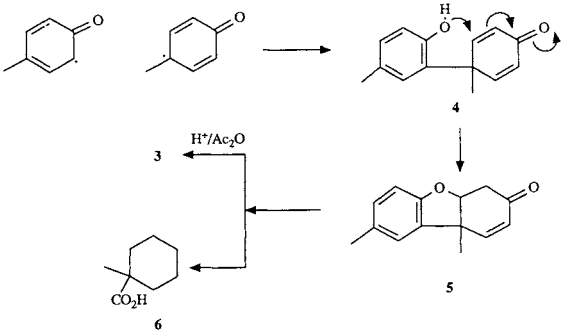
Phenolate radical coupling in synthesis and biosynthesis; Pummerer's ketone

The pioneer in phenolate radical coupling was Pummerer. In 1925 he showed[1] that one electron oxidation of *p*-cresol using potassium ferricyanide afforded a nicely crystalline ketonic dimer of the radical in up to 25% yield. Pummerer's ketone, as it became known, was considered to result from the coupling of two *p*-cresol radicals to give the dienone **1**. This then underwent spontaneous cyclization to furnish **2**. As proof of the structure



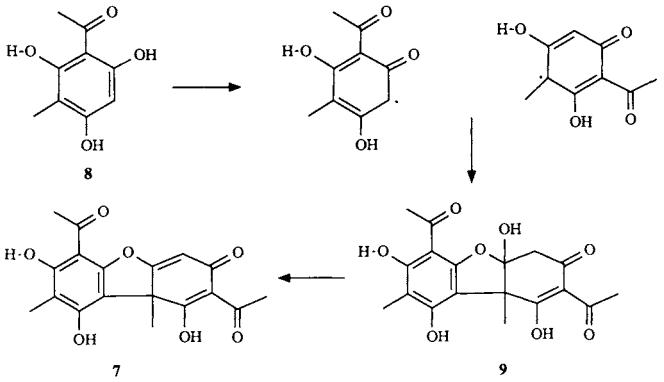
2, Pummerer showed that treatment with acid and acetic anhydride afforded the diphenol diacetate **3** which was identical with the same compound made by total synthesis. Although I could see, perhaps, some driving force in the rearrangement of **1** to **2**, I could not imagine a mechanism which would permit this at room temperature in the presence of only ferro- and ferricyanides as reagents. However, structure **2** was accepted as

true for 30 years and was used by Sir Robert Robinson and Prof. C. Schöpf as a model for the biosynthesis of morphine and sinomenine. It is interesting to reflect why no one before had questioned the structure given by Pummerer. It is possible that Robinson was too busy to look into past literature. Around 1952, it seemed to me that there was a much better way in which to formulate the coupling of two *p*-cresolate radicals to give a different dienone **4** as an intermediate. This only had to add the phenolate anion to the dienone to reach a very acceptable formula **5** for Pummerer's ketone. The formation of **3** would then be the result of an acid catalyzed dienone–phenol rearrangement, a well-known reaction. Still, it was not well known until the deduction by R. D. Haworth of the correct structure for santonin,[2,3] where this rearrangement had complicated the task of structural determination. However, I know that R. D. Haworth, who knew well Pummerer's ketone, did not jump the gap and question the formula **2**.



As soon as I was convinced that I was right, I quickly devised the degradation of **5** to 1-methylcyclohexane-1-carboxylic acid **6**.[4] The formation of this degradation product proved the identity of the original carbon–carbon bond coupling process.

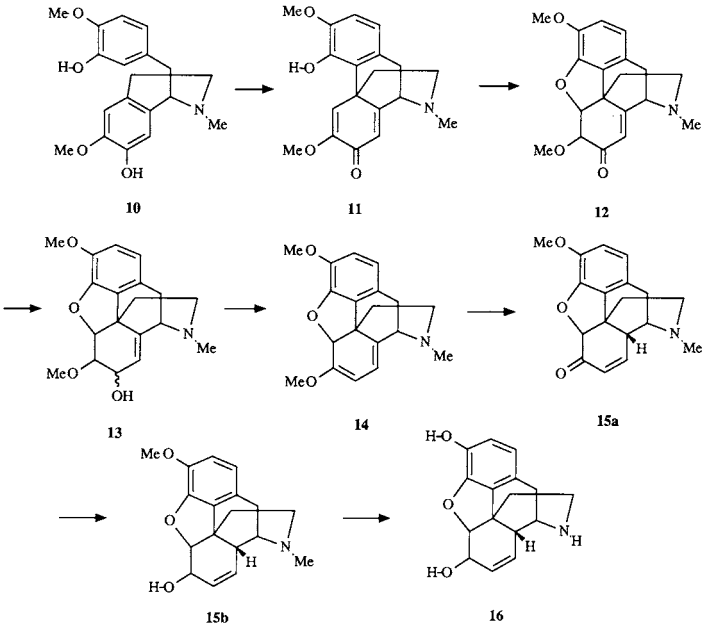
The importance of the revised structure **5** for biosynthesis was impressive. We decided to carry out a synthesis of the important lichen compound usnic acid **7**. Although we,[5] and



others,[6] were by then reconciled to the correctness of **1**, a biogenetic synthesis was welcome. Methylphloracetophenone **8** was oxidized with potassium ferricyanide to give the derived phenolate radical. These radicals coupled together in the desired manner to give usnic acid hydrate **9**, in which all the carbon skeleton had been correctly assembled. Dehydration gave usnic acid, although the overall yield was modest (15% unoptimized). This was an elegant synthesis.[7,8] Later it was proved that usnic acid was indeed biosynthesized by this route.[9,10]

Through accepting the wrong formula for Pummerer's ketone, all the proposals by Sir Robert Robinson on the biosynthesis of morphine and its congeners were in error. It was easy to write a new biosynthetic proposal starting with the benzylisoquinoline alkaloid **10**, then unknown, but later found to be a common natural product, reticuline. I proposed that **10** was oxidized in *Papaver somniferum* to give the dienone **11**, an exact analogue of the primary step of formation of Pummerer's ketone. By ring closure this would give **12**. Reduction of **12** to the allylic alcohol **13** and elimination of water would then furnish thebaine **14**. The steps from thebaine to codeinone **15a** then codeine **15b** on to morphine **16** were logical.

Later, in collaboration with Theodore (Ted) Cohen,[11] I



wrote an article on the biosynthesis of natural products by the coupling of phenolate radicals in pairs to make O–C or C–C bonds. However, we always followed the rules of *ortho*- or *para*-coupling. The theory was applied particularly to phenolic alkaloids. In order to explain what was formally *meta*-coupling, we postulated *para*-coupling followed by a dienone–phenol rearrangement. For certain alkaloids which contained only a benzene ring, we postulated a dienol–benzene rearrangement in biosynthesis before it had even been seen in the chemical laboratory. In fact, all of our proposals, including the existence of a new class of ketonic and phenolic alkaloids, proved, over the years, to be correct as outlined in more detail later.

In the laboratory and associated greenhouse, we gave particular attention to the biosynthesis of the morphine alkaloids.[12–14] At first we purchased *Papaver somniferum* seeds and grew splendid poppies, but they contained no morphine