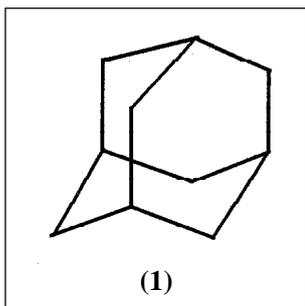# Molecule of the Month

Adamantane – A Plastic Piece of Diamond

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Several facets of adamantane chemistry are highlighted.

Chemists, like others, have long been fascinated by diamond. The challenging goal of making other substances with all the properties of diamond continues to be pursued, with some success. A more limited objective is to make small molecules which resemble diamond only at the structural level. Efforts to make and manipulate such 'diamondoid' systems have yielded interesting results.

The 3-dimensional network structure of diamond, with each carbon having four tetrahedrally arranged neighbours, was figured out as early as in 1913. It is easy to recognise chair cyclohexanes, decalins, etc., (without the hydrogen atoms, of course) in the framework. If we look for something more complex, a cage containing 10 carbon atoms can be spotted. The corresponding hydrocarbon has the formula $C_{10}H_{16}$, and is called adamantane (**1**).

The adamantane molecule has tetrahedral (T_d) symmetry. The four cyclohexane units are all held rigidly in the preferred chair conformation. The molecule must therefore have negligible angle and torsional strain.

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Molecules with the adamantane skeleton are well known (*Figure* 1). The three-dimensional structure of a chemical called urotropine (hexamethylenetetramine) was formulated over 100 years ago. The trioxide and pentoxide of phosphorus are also known to exist as P_4O_6 and P_4O_{10} units with the adamantane structure. Another textbook example with the adamantane skeleton is the arsenic sulfide As_4S_6.

Organic chemists set out to make the hydrocarbon version. Meerwein took the first steps. Others followed, but it was expected to be
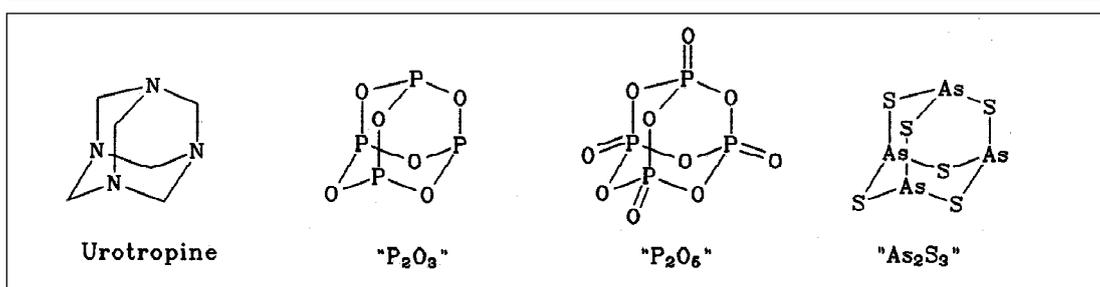
a long struggle. Suddenly, like a genie, adamantane literally popped out of a bottle. In Prague there was a large collection of samples of petroleum from different sources. In one of the samples taken from a village in Moravia (present day Czech Republic; or is it the Republic of Slovakia?) some crystals had formed. Landa, a well-known chemist of his generation, noticed the crystals and carried out a chemical analysis. He found that the substance had a high melting point (270°C)[1] and had the molecular formula $C_{10}H_{16}$. He intuitively proposed that the substance ought to be adamantane. He was vindicated in 1941. After several synthetic steps, Prelog succeeded in making the desired cage compound. It turned out to be identical in all respects to the minor by-product from crude petroleum.

The adamantane story remained fairly dormant for some time. After another 16 years, the molecule made another dramatic appearance. This time it was in the laboratory of Paul von Rague Schleyer at Princeton. He was trying to convert a C_{10} hydrocarbon from its *endo* form to the *exo* isomer, using aluminium chloride as the catalyst (*Figure* 2). After he distilled off the *exo* isomer, some crystals appeared from the nearly empty flask. Yes, it was the same high melting solid with the formula $C_{10}H_{16}$ (mass spectrometry had simplified the task of determining the formula). It was indeed adamantane, formed in one go.
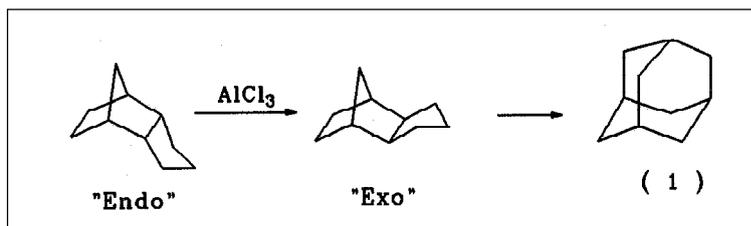
Schleyer and many others took several years to show what had happened. Combining isotopic labelling experiments and calculations, they were able to establish that the spectacular, deep-seated rearrangement occurs through a series of simple hydride and alkyl

[1] It is not easy to determine the melting point of adamantane because it sublimes on heating.

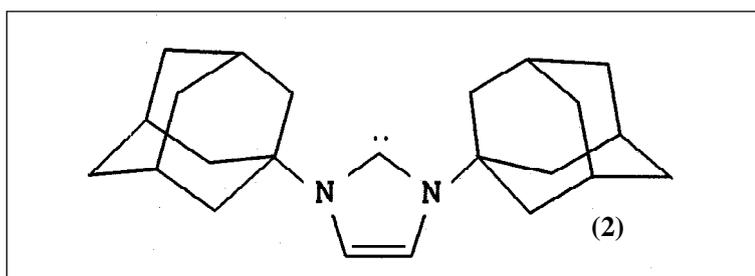shifts involving several carbocation intermediates.[2]

The chemical yield was initially only 15%. But improved methods have since been developed.[3] The rearrangement methodology, with appropriate precursors and catalysts, has been shown to be general enough to make other more complex cage compounds, including dodecahedrane, $C_{20}H_{20}$.

Adamantane is not a hard, lustrous substance like diamond. It is rather soft, white, resembling camphor. Disappointing and perhaps, but not surprising. After all, the molecules are held together only by van der Waals' forces. While the packing of spheroidal molecules would be efficient, there is likely to be a great deal of orientational disorder in the solid state. As a result, adamantane belongs to a class of materials called *plastic crystals*.

Adamantane did not end up as just another computer entry in the voluminous Chemical Abstracts Registry. Instead, the molecule opened up an important chapter in cage hydrocarbon chemistry. The availability of usable quantitites enabled chemists to transform adamantane into a variety of derivatives. These, in turn, have been used as probes to understand many aspects of structure, bonding and reactivity. I shall give a few examples.

Regular *Resonance* readers would be familiar with the simple way of protecting a reactive species by providing bulky substituents at suitable locations. The adamantyl group is an ideal unit for this purpose. A famous example in which the idea was tried out is the carbene, (**2**). While electronic stabilization is provided by the π electrons in the ring, the adamantyl groups shield the reactive site. As a result, the carbene is stable enough to be stored in a bottle. Later,

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it turned out that the electronic effect is more important, since the corresponding carbene with methyl substituents is also stable.

A beautiful example of a species with a 4-centre-2-electron bond was devised around the adamantane skeleton. The dication derived from dehydroadamantane (*Figure* 3) has been shown by Schleyer to adopt the tetrahedral structure, **(3)**. The orbital lobes at the bridgehead positions have 'through-space' overlap. Two electrons are accommodated in the totally symmetric combination. In effect, **(3)** is a 3-dimensionally aromatic species.

Over the years, adamantyl derivatives have been used in mechanistic studies. The study of nucleophilic substitution reactions at saturated centres was often complicated by the occurrence of two processes, S_N1 and S_N2. Although the former is favoured in tertiary systems, contributions from the S_N2 mechanism could not be ruled out. The problem was resolved using 1-adamantyl derivatives. Since backside attack is not geometrically possible at the bridgehead position, the solvolysis reaction follows the S_N1 mode exclusively. The bridgehead cation is also fairly stable, allowing the reaction to occur easily. The 2-adamantyl cation is also an important reference system for secondary carbocations.

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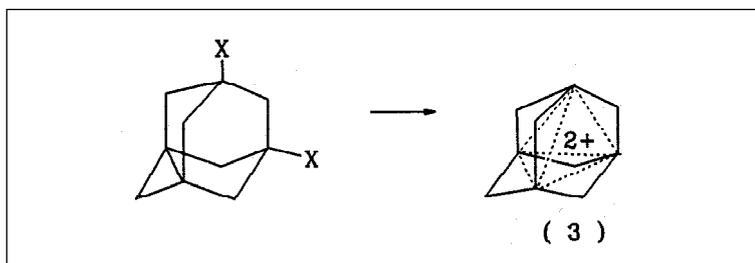
Figure 3. Formation of a 3-dimensionally aromatic species from a dehydro-adamantane derivative (X is a good leaving group).
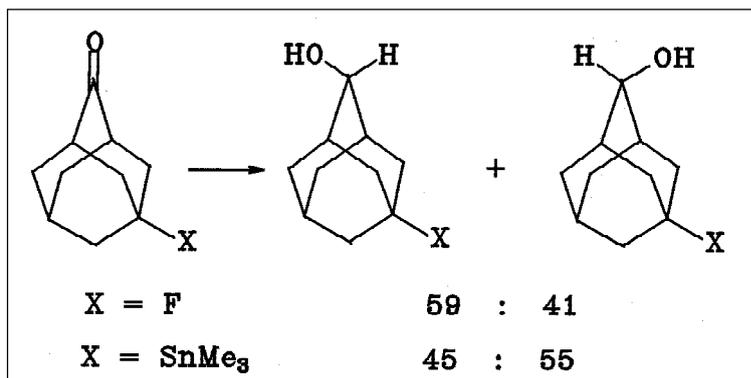
In recent years, the adamantyl skeleton has served as an important probe for studying long-range substituent effects. It has been shown that the preferred direction of approach of a nucleophile towards the carbonyl group of adamantanone can be controlled by substituents at the 5-position (*Figure* 4). Many interpretations have been and are being offered and debated. The problem of π-face selectivity in organic reactions induced by remote substitution is currently an active area of research in physical organic chemistry.

There have been other uses for adamantane. The solid has served as a host for studying small free radicals. On recrystallisation of adamantane, some solvent molecules usually get trapped in the defect sites. Using X-rays or γ-radiation, radicals derived from the solvent can be generated. The *electron spin resonance* spec-trum of the radical is often simple to interpret. This is because the radical tumbles freely in the adamantane matrix, giving rise to simple 'solution' (isotropic) spectrum of the radical.

The adamantyl group is large, inert, and hydrophobic. It can be incorporated suitably to make fat-soluble drugs. Therefore, some medicinal applications have been considered. For example, adamantyl amine shows anti-viral activity. But some applications are quite unusual. High molecular weight fluorocarbons with high symmetry have been proposed as artificial blood substitutes. These chemically inert molecules dissolve oxygen, but little else, and hence may be suited for oxygen transport. Perfluoroadamantane is an important candidate considered in this context.

It is easy to see why chemists are enamoured by adamantane and related cage compounds. Adamantane chemistry is rich. It offers many pleasant surprises. It provides answers to many questions in physical organic chemistry and raises some new questions.

Suggested Reading

◆ *Organic Syntheses.* **Collected Volume 5, ed. H E Baumgarten. John Wiley, pp.16-19, 1973.**
◆ **S Ranganathan.** *Resonance*. **Vol.1, No.1, pp.28-33, 1996.**

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