List of Contents of this Book:

- Molecular Structure and Chemistry of Diamondoids
- Diamondoids in Petroleum and Other Fossil Fuels
- Physical Properties of Diamondoids
- Diamondoids as Nanoscale Building Blocks
- Properties of Diamondoids Through Quantum Calculations
- Biomedical Applications of Diamondoids
- Diamondoids in Materials Science


See 7 major reviews of this book at: trl.lab.uic.edu/Diamondoids/Dia.html

To order copies please visit:
www.worldscientific.com/worldscibooks/10.1142/7559#t=aboutBook

Or visit:
Chapter 1
Molecular Structure and Chemistry of Diamondoids

1.1. Introduction
Diamondoid molecules are cage-like, ultra stable and saturated hydrocarbons. The basic repetitive unit of the diamondoids is a ten-carbon tetracyclic cage system called “adamantane” (Fig. 1.1). They are called “diamondoid” because they have at least one adamantane unit and their carbon–carbon framework is completely or largely superimposable on the diamond lattice (Balaban and Schleyer, 1978; Mansoori, 2007). The diamond lattice structure was first determined in 1913 by Bragg and Bragg using X-ray diffraction analysis (Bragg and Bragg, 1913).

Diamondoids show unique properties due to their exceptional atomic arrangements. Adamantane consists of cyclohexane rings in “chair” conformation. The name adamantane is derived from the Greek language word for diamond since its chemical structure is like the three-dimensional diamond subunit as it is shown in Fig. 1.2.

1.2. Classification and Crystalline Structure of Diamondoids
The first and simplest member of the diamondoids group, adamantane, is a tricyclic saturated hydrocarbon (tricyclo[3.3.1.1(3.7)]decane, according to the von Bayer systematic nomenclature). Adamantane is followed by its
Fig. 1.1. Three-dimensional molecular structures of (from left to right) adamantane, diamantane and triamantane, the smallest diamondoids, with chemical formulas C_{10}H_{16}, C_{14}H_{20}, and C_{18}H_{24}, respectively. Note that the bridgehead position 1 in adamantane is equivalent to positions 3, 5, and 7, while all four secondary or bridge positions are equivalent to each other. Note that diamantane and triamantane have two types of bridgehead carbons: atoms at positions 4 and 9 of diamantane and 9 and 15 in triamantane are in equivalent *apical* positions. Carbon atoms 1, 2, 6, 7, 11, and 12 in diamantane are medial or belt; as are atoms 2 (equivalent to 12), 6 (equivalent to 4), 7 (equivalent to 11), 3 (equivalent to 13) in triamantane (Fort, 1976; Olah, 1990a; Ramezani *et al.*, 2007).

Fig. 1.2. The relation between lattice diamond structure and (i) adamantane, (ii) diamantane, and (iii) triamantane structures (Mansoori, 2007).
polymantane homologs (adamantologs): diamantane, tria-, tetra-, penta-, and hexamantane. These molecules are particularly denominated polymantanes because they are completely superimposable on the diamond lattice (see Fig. 1.2) and all carbon atoms belong in a whole adamantane unit, in addition, each pair of units is face-fused (Balaban and Schleyer, 1978). In other words, each adamantane shares six carbon atoms with an adjacent unit. Figure 1.1 illustrates the smaller diamondoid molecules, with the general chemical formula $C_{4n+6}H_{4n+12}$: adamantane ($C_{10}H_{16}$), diamantane ($C_{14}H_{20}$), and triamantane ($C_{18}H_{24}$). Each of these three lower adamantologs has only one isomer.

In 1978, Balaban and Schleyer created a systematic enumeration of polymantanes (Balaban and Schleyer, 1978). At that time, the larger known adamantolog was tetramantane, nevertheless the authors proposed a new code, based on graph-theory approach using dual-graphs. This was in anticipation of eventual preparation of higher diamondoids and to avoid use of trivial names which would probably be invented to distinguish isomeric polymantanes. Dual-graphs or dualist graphs of polymantanes are built by joining the centers of fused adamantane units. These graphs are coded using digits 1–4 as symbols of the four possible orientations in space of adamantane units in a polymantane structure (Fig. 1.3a).

Using these concepts, one could represent adamantane as a point and diamantane as an edge. Figure 1.3b shows a representation of the dualist graph for one of the isomers of tetramantane called anti-tetramantane (the same as [121]tetramantanes shown on Fig. 1.4). Note that this graph is acyclic linear, while Fig. 1.3c exhibits an acyclic branched graph for iso-tetramantane (the same as [1(2)3]tetramantane shown on Fig. 1.4).

Both isomers are classified as cata-condensed isomers or catamantanes as their dual graphs are open. Molecules like [12312]hexamantane (Fig. 1.4), in their turn, are peri-condensed polymantanes or periamantanes, as their dual-graphs are cyclic. To code polymantanes according to Balaban and Schleyer, it is necessary to number each different direction taken by the dual graph, starting from one endpoint of the longest chain. The final set of digits has to form the smallest number possible. For example, diamantane has code 1, because its dual graph is a straight line (one possible direction, smallest possible number), and triamantane has code 12 (two lines forming a $109^\circ 28'$ angle, first direction is 1, second is 2). Anti-tetramantane is [121]tetramantane, and iso-tetramantane, with its tree-like dualist graph, is coded [1(2)3] (parentheses indicate a branch).
Balaban and Schleyer nomenclature is widely used for diamondoids and will be preferably used in this book.

Depending on the spatial arrangement of the adamantane units, higher polymantanes \( (n \geq 4) \) can have several isomers and nonisomeric equivalents. There are three possible tetramantanes, all of which are isomeric. They are depicted in Fig. 1.4 as \([1(2)3]\) (or \(iso\)-), \([121]\) (or \(anti\)-), and \([123]\) (or \(skew\)) tetramantane (only one enantiomer is shown). \([121]\) and \([123]\) tetramantanes each possess two quaternary carbon atoms, whereas \([1(2)3]\) tetramantane has three. The number of diamondoid isomers increases appreciably after tetramantane.

With regard to the remaining members of the diamondoid group, there are ten possible pentamantanes, nine of which are isomeric \((C_{26}H_{32})\) and follow the molecular formula \((C_{4n+6}H_{4n+12})\) of the homologous series and one is nonisomeric \((C_{25}H_{30})\). For hexamantane, there are 39 possible structures: 28 are regular \(cata\)-condensed isomers with the chemical formula \(C_{30}H_{36}\), 10 are

---

**Fig. 1.3.** Dualist graphs of polymantanes. (a) Four possible relative directions for face-fused adamantane units, (b) \(Anti\)-tetramantane and (c) \(Iso\)-tetramantane with their dual-graph showing the numbering of each direction (Balaban and Schleyer, 1978).
Fig. 1.4. Some of the higher diamondoids up to heptamantane. All tetramantanes are regular cata-condensed polymantanes. Shown pentamantanes are also regular catamantanes. Peri-condensed [12312] hexamantane (C_{26}H_{30}) and [121321] heptamantane (C_{30}H_{34}) and other higher diamondoids may become fundamental components in nanometric devices (see also Fig. 4.13). Adapted from CDV Diamond Group {www.chm.bris.ac.uk/pt/diamond/diamondoids.htm} 2010.
irregular *cata*-condensed isomers with the chemical formula \( \text{C}_{29} \text{H}_{34} \) and one is *peri*-condensed with the chemical formula \( \text{C}_{26} \text{H}_{30} \) (Carlson *et al*., 2007). Irregular catamantanes do not follow the general formula \( \text{C}_{4n+6} \text{H}_{4n+12} \). Their codes have at least two identical digits separated by any two other digits (excluding parentheses with their contents). Figure 1.4 shows structures of some higher diamondoids. Among the diamondoids of this figure, only [12312] hexamantane and [121321] heptamantane are irregular. Table 1.1 lists some physical properties of diamondoids including their molecular weights, melting points, apparent boiling points, and normal densities.

Diamondoids melt at much higher temperatures than other hydrocarbon molecules with the same number of carbon atoms in their structures. The melting point of adamantane (269°C) is probably the highest among all organic molecules with the same molecular weights. Since diamondoids also possess low strain energy, they are more stable and stiff, resembling diamond in a broad sense. They possess superior strength-to-weight ratio.

It has been found that adamantane crystallizes in a face-centered cubic lattice, which is extremely unusual for an organic compound. The molecule therefore should be completely free from both angle strain (since all carbon atoms are perfectly tetrahedral) and torsional strain (since all C–C bonds are perfectly staggered), making it a very stable compound and an excellent candidate for various applications, as will be discussed later in this book.

At the initial growth stage, crystals of adamantane show only cubic and octahedral faces. The effects of this unusual structure on physical properties are interesting (Kabo *et al*., 2000).

Many of the diamondoids can be brought to macroscopic crystalline forms with some special properties. For example, in its crystalline lattice, the pyramidal-shaped [1(2,3)4]pentamantane has a large void in comparison to similar crystals (Table 1.1). Although it has a diamond-like macroscopic structure, it possesses weak, noncovalent, intermolecular van der Waals attractive energies that are involved in forming a crystalline lattice (Dahl *et al*., 2003; Mansoori *et al*., 2003). Another example is the crystalline structure of 1,3,5,7-tetracarboxyadamantane, which is formed via carboxyl hydrogen bonds of each molecule with four tetrahedral nearest neighbors. The similar structure in 1,3,5,7-tetraiodoadamantane crystal would be formed by I–I interactions. In 1,3,5,7-tetrahydroxyadamantane, the hydrogen bonds of hydroxyl groups produce a crystalline structure
### Table 1.1. Some physical properties of diamondoids (Mansoori, 2007).

<table>
<thead>
<tr>
<th>Diamondoid Chemical Formula</th>
<th>Molecular Structure</th>
<th>Mw</th>
<th>MP [°C]</th>
<th>aBP [°C]</th>
<th>ρ[g/cc]</th>
<th>Crystal Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adamantane C_{10}H_{16}</td>
<td></td>
<td>136.240</td>
<td>269</td>
<td>135.5 @ 10 nm Hg</td>
<td>1.07</td>
<td>Cubic, fee</td>
</tr>
<tr>
<td>Diamantane C_{14}H_{24}</td>
<td></td>
<td>188.314</td>
<td>236.5</td>
<td>272</td>
<td>1.21</td>
<td>Cubic, Pa₃</td>
</tr>
<tr>
<td>Triamantane C_{18}H_{24}</td>
<td></td>
<td>240.390</td>
<td>221.5</td>
<td>330</td>
<td>1.24</td>
<td>Orthorhombic, Fddd</td>
</tr>
<tr>
<td>Tetramantanes C_{22}H_{28}</td>
<td></td>
<td>292.466</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Diamondoid Chemical Formula</th>
<th>Molecular Structure</th>
<th>Mw</th>
<th>MP [°C]</th>
<th>aBP [°C]</th>
<th>ρ [g/cc]</th>
<th>Crystal Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentamantanes</td>
<td>[1212]</td>
<td>344.543</td>
<td>NA</td>
<td>NA</td>
<td>1.26</td>
<td>Orthorhombic, P2_{1}2_{1}2_{1}</td>
</tr>
<tr>
<td>C_{26}H_{32}</td>
<td>[12(3)4]</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Monoclinic, P2_{1}/n</td>
</tr>
<tr>
<td></td>
<td>[1234]</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1.30</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>[1(2,3)4]</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1.33</td>
<td>Orthorhombic, Pnma</td>
</tr>
<tr>
<td></td>
<td>[12131]</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1.36</td>
<td>Triclinic, P-I</td>
</tr>
<tr>
<td></td>
<td>[12(1)3]</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Diamondoid Chemical Formula</th>
<th>Molecular Structure</th>
<th>Mw</th>
<th>MP [°C]</th>
<th>aBP [°C]</th>
<th>ρ [g/cc]</th>
<th>Crystal Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexamantane (peri-condensed)</td>
<td><img src="image" alt="Molecular Structure" /></td>
<td>342.528</td>
<td>&gt;314</td>
<td>NA</td>
<td>1.38</td>
<td>Orthorhombic, Pnma</td>
</tr>
<tr>
<td>Heptamantanes C$<em>{30}$H$</em>{34}$</td>
<td><img src="image" alt="Molecular Structure" /></td>
<td>394.602</td>
<td>NA</td>
<td>NA</td>
<td>1.35</td>
<td>Monoclinic, C$_{2}$/m (#12)</td>
</tr>
<tr>
<td></td>
<td><img src="image" alt="Molecular Structure" /></td>
<td>394.602</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

aBP = apparent boiling point; MP = melting point; Mw = molecular weight; ρ = normal density. Adapted from ChevronTexaco (www.moleculardiamond.com).
similar to inorganic compounds, like cesium chloride (CsCl) lattice (Desiraju, 1996) (Fig. 1.5).

The presence of chirality is another important feature in many diamondoids. It should be pointed out that [123]tetramantane is the smallest of the higher diamondoids to possess chirality (Balaban and Schleyer, 1978).

The vast number of structural isomers and stereoisomers is another property of diamondoids. For instance, octamantane possesses hundreds of isomers in five molecular weight classes. The octamantane class with formula $\text{C}_{34}\text{H}_{38}$ and molecular weight 446 has 18 chiral and achiral isomeric structures. Furthermore, there is unique and great geometric diversity within these isomers. For example, rod-shaped diamondoids (with the shortest one being 1.0 nm long) and disc-shaped and screw-shaped diamondoids (with different helical pitches and diameters) have been recognized (Dahl et al., 2003), as shown in Table 1.1. Very interesting nanotechnology applications are proposed for these molecules, such as structural components of nanosystems (see Sec. 4.4.2 for details).

Fig. 1.5. The quasi-cubic units of crystalline network for 1,3,5,7-tetrahydroxyadamantan. Molecules are shown as spheres and hydrogen bonds as solid linking lines. This crystalline structure is similar to that of CsCl (Desiraju, 1996).
1.3. Distinction between Diamondoids and Nanodiamonds

At this point, it is important to make a distinction between diamondoid molecules and nanodiamonds (NDs). Adamantane and other diamondoids are cage-shaped hydrocarbons, constituents of petroleum, gas condensate (also called NGL or natural-gas-liquid) and natural gas reservoirs (King, 1988; Alexander and Knight, 1990; Alexander et al., 1990a, 1990b; 1991; Mansoori, 2007). Diamondoid molecules can also be synthesized from a variety of organic precursor (see Sec. 1.4). ND is generally referred to diamond films with nanoscale thickness, diamond nanoparticles which may be produced as a result of crushing diamond crystals, and various other diamond-based materials at the nanoscale (see Fig. 1.6).

In comparison, there are no natural sources of NDs, except for samples found in meteorites (Grady et al., 1995; Daulton et al., 1996; Huss, 2005). Nevertheless, synthetic ND material is readily available from large-scale production methods of detonation synthesis (Vityaz, 2004; Dolmatov et al., 2004). Nanosized diamonds can also be prepared as thin pure or doped films by microwave plasma enhanced chemical vapor deposition (MPECVD). Several substrates like glass, silicon, or metals are suitable for supporting ND crystal growth (Williams and Nesladek, 2006). Many

![An optimized (PM3) molecular model of nanodiamond (Redrawn for this book from the presentation made by Mochalin et al. (2007)) surrounded by oxygen and hydrogen atoms and purified by oxidation in air.](image-url)
precursor gas mixtures, e.g., C\textsubscript{60}/argon (Gruen et al., 1994; Qin et al., 1998), methane/hydrogen (Sung et al., 1998; Zhang et al., 2004) and methane/argon (Sung et al., 1998) are used for carbon deposition to form ND. Diamond nanograins obtained by chemical vapor deposition (CVD) are frequently called nanocrystalline diamonds (NCD) and ultrananocrystalline diamonds (UNCD) (Williams and Nesladek, 2006).

The first publication related to diamond synthesis was by DeCarli and Jamieson (1961). They submitted samples of graphite to explosive shocks of high intensity (about 300,000 atm) and were able to separate and identify small particles of diamond having 10 \(\mu\)m, or less, diameter from the shocked graphite. Nanometer-sized diamonds or NDs were first produced by Danilenko and collaborators in the 60’s, through detonation as it is reported in the history of the discovery of ND synthesis by Danilenko (2004). This method is nowadays used for industrial production of NDs and consists of submitting mixtures of organic explosives, such as TNT, hexogen, and octogen to an incomplete combustion reaction, inside of a detonation chamber, in vacuum or inert gas atmosphere. Hydrogen, argon, nitrogen, or carbon dioxide can be used to fill the detonation chamber when performing this dry synthesis technique. Alternatively, a wet synthesis can be carried out when ice-water or another coolant is placed into the chamber with the detonation charge (Dolmatov et al., 2004) which could cool the detonation products. Carbon atoms are supplied by the mixture of explosives, thus, graphite is not added. After the detonation, the products of the condensed carbon are grinded, averaged, and purified by mechanical and magnetic methods. Then, they are treated by thermooxidation into pressurized equipments and washed to remove acids and water-soluble impurities, suspended in distilled water or dried to give homogeneous powder. The resulting product is called ultrafine-dispersed diamond (Dolmatov, 2001; Dolmatov et al., 2004), ultradispersed diamond (Aleksenskii et al., 1999; Danilenko, 2004a) (UDD) or nanocrystalline diamond powder (Holt, 2007).

A model for the structure of ND powder obtained through detonation synthesis is shown in Fig. 1.7.

The primary particle is made up of a ND core which is coated with an onion-like carbon shell. An external nondiamond carbon phase containing graphite inclusions and metal-oxide impurities is distributed on top of the
onion-like shell. Cleaning procedures consecutively etch off the bulky graphite phase, impurities, nanosized carbon platelets and may remove the onion-like shell, exposing the diamond core (Aleksenskii et al., 1999).

Despite the possibility of the extraction of primary diamond nanoparticles presented in this model, transmission electron microscopy (TEM) images of detonation ND powders both before and after thermooxidation treatment show large aggregates (Fig. 1.8a–c).

These aggregates have firmly tight cores, designed as “agglutinates” and are not greatly affected by thermooxidation treatment. Nevertheless, they can be disintegrated through milling with micron-sized ceramic beads followed by sonication treatment to yield a clear colloidal solution of de-aggregated ND, as illustrated in Fig. 1.9 (Kruger et al., 2005; Osawa, 2007).

While diamondoids are structurally well-characterized chemical compounds, NDs are frequently a mixture of several carbonaceous compounds. Their characteristics are governed by many factors, such as starting materials, methods of fabrication and processing (Aleksenskii et al., 1999; Shenderova et al., 2002; Chiganov, 2004; Dolmatov et al., 2004; Larionova et al., 2006; Krueger, 2008a; Nekhaev et al., 2011).
addition, oxygenated groups, such as –COOH, –C=O and –OH (Kusnetsov et al., 1991) and NO$_3^-$ (Aleksenskii et al., 2001) are frequently present at the surface of the ND particle aggregates, either formed during synthesis reactions or processing. The presence of reactive functional groups is important for easing surface modification in ND, but brings uncertainties concerning chemical composition of these materials. Table 1.2 shows a comparison between diamondoids and NDs.

Scientific interest in NDs has increased over the last decade primarily due to the discovery of their promising physicochemical (Aleksenskii
et al., 2001; Shenderova et al., 2007) and biological properties (Krueger et al., 2006; Kruger, 2008b). For example, sub-micron diamond particles (800–1000 nm in diameter) fabricated by dual radiofrequency/microwave plasma activated chemical vapor deposition (RF/MW PACVD) are able to suppress the expression of cancer-related human genes while graphite powder has no such capability (Barkowicz-Mitura et al., 2007). Detonation NDs are able to absorb UV light due to the presence of sp\(^2\) carbons and impurities at the aggregates surface while are practically transparent to the visible light. Therefore, they can be included in sunscreen formulations for a number of applications (Shenderova et al., 2007). Functional groups at the NDs surface allow adsorption of complex biomolecules such as
proteins, on diamond nanoparticles for use in separation methods and analysis (Bondar et al., 2004; Kong et al., 2005).

In this book, our aim is to present the state-of-the-art in diamondoid research. Although NDs are a fascinating R&D field, they will not be studied in further details.

1.4. Synthesis and Functionalization of Diamondoid Cages

In 1990, Professor George A. Olah (Nobel Prize Laureate in Chemistry in 1994) edited a book entitled: Cage Hydrocarbons dedicated to “Paul Schleyer for Thirty Years of Adamantane Chemistry and His Sixtieth
“Birthday” (Olah, 1990a). In that book, Professor Olah and coauthors highlighted many aspects of diamondoids as well as nondiamondoid cage compounds, with an emphasis on synthesis, and offered a comprehensive review of the, then, past, present, and future of the chemistry of these substances. Thus, the reader interested in details on diamondoids synthetic routes will find a great deal of information in Olah’s book, as well as in a number of original articles on adamantane (Prelog and Seiwerth, 1941; Stetter et al., 1956; Schleyer, 1957; Schleyer and Donaldson, 1960; Schleyer et al., 1962; Olah et al., 1984), on diamantane (Cupas et al., 1965; Gund et al., 1970; Gund et al., 1973) and triamantane (Williams et al., 1966; Hollowood et al., 1980) and on [121]tetramantane (Burns et al., 1976, 1978). There are also review papers published on the chemistry of adamantane (Sevostyanova et al., 1970; Moiseev et al., 1999; Schwertfeger et al., 2008) including the first review on adamantane, published in 1964, by Fort and Schleyer (1964a). In the next sections, we will mainly focus our discussion on new methods for the introduction of functional groups to the diamondoid cages. In addition, a general overview of established methods for cage moiety synthesis will be presented.

1.4.1. Adamantane syntheses: from nearly trace amounts to semi-quantitative yields

Originally diamondoids were considered as hypothetical molecules since they could neither be isolated from a natural repository nor made through rational organic synthesis until 1933 when adamantane was discovered and isolated from petroleum (Landa et al., 1933). The natural source of diamondoids was the only effective source until 1941 when adamantane was synthesized for the first time, though the yield was very low (McKervey, 1980; Prelog and Seiwerth, 1941; Navratilova and Sporka, 2000).

In 1941, Prelog and Seiwerth published the first route to adamantane cage synthesis (Prelog and Seiwerth, 1941) but they achieved practically trace amounts of the target compound. Nevertheless, adamantane crystalline and its high-melting point served to confirm its structure to be the same as the natural adamantane found by Landa and Machacek in petroleum samples from Hodonin Oil field, in Moravia, Czechoslovakia, in 1933 (Landa et al., 1933). Later, the 1956 Stetter’s synthesis (Stetter
et al., 1956) represented an important increase in the overall yield of adamantane to 6%, although their proposed relatively complex four-step process still left room for improvement.

In 1957, Schleyer introduced a Lewis acid-catalyzed rearrangement to produce adamantane (Schleyer, 1957). A Lewis acid is any acid that can accept a pair of electrons and form a coordinate covalent bond [45]. According to Schleyer endo-trimethylenenorbornane, which could be produced readily, rearranged to adamantane when refluxed overnight with aluminum chloride (AlCl₃) as shown in Fig. 1.10.

This reaction allowed a simple preparation of adamantane with 10% overall yield, which was unprecedented at that time, and opened up the field of diamondoids synthesis and application for further studies worldwide. For example, the number of patents related to adamantane increased rapidly after the publication of Schleyer’s synthesis of adamantane (see Fig. 1.20).

Fig. 1.10. Various stages in synthesis of adamantane (Mansoori, 2007) based on the work reported by Schleyer (1957) and Schleyer and Donaldson (1960).
Schleyer’s AlCl₃ catalyzed isomerization and subsequent improved synthetic routes involving replacement of AlCl₃ by AlBr₃/HBr sludge (Schleyer and Donaldson, 1960; Schleyer et al., 1962) were responsible for “the breaking of the cage molecule bottleneck”, as referred to by Schleyer (Schleyer, 1990).

Further studies on superacids applied to isomerization of hydrocarbons, performed by Olah and co-workers, allowed up to 98% yields. These semi-quantitative yields can be explained by the higher stability of the 1-adamantanyl cation formed during the isomerization process; thus, all intermediate ions generated in the cationic reaction of C₁₀ hydrocarbon are converted into this species. Table 1.3 shows superacid systems used for the isomerization of endo- and exo-trimethylenenorbonane to adamantane. In Fig. 1.11, we report a comparison of adamantane synthesis by various investigators as discussed above.

### 1.4.2. Diamantane and triamantane syntheses

In 1963, a then unknown C₁₄ cage compound was used as the official emblem of the London IUPAC conference. “Congressane” was the
A suggested name for this compound and a challenge for its synthesis was posed to the chemical community of that time (Schleyer, 1990). Two years later Cupas and co-workers published the first synthesis of congressane (later renamed as diamantane as shown by Fig. 1.1b) using the same Lewis acid-catalyzed rearrangement synthesis approach as was used for adamantane synthesis (Cupas et al., 1965). Figure 1.12 shows this route for diamantane preparation, with a yield of only 1%, and two additional AlBr₃-catalyzed syntheses, also published by Gund and co-workers in 1970 (Gund et al., 1970) and 1973 (Gund et al., 1973), in which yields were improved to 30% and 60%, respectively.

The synthesis of the next member of the lower diamondoid, trimantane, was accomplished shortly after the first diamantane synthesis. Williams and
Molecular Structure and Chemistry of Diamondoids

colleagues found an appropriate C18 candidate to undergo bromide halide-catalyzed isomerization reaction (compound III, Fig. 1.13) (Williams et al., 1966). The starting material for their synthesis of triamantane is cyclooctatetraene. This compound undergoes dimerization and thermal rearrangements to give the C16 diene I. The two extra carbon atoms needed to build the target diamondoid were added through cyclopropanation of the double bonds, resulting in compound II. The next step was the hydrogenolysis of the highly strained cyclopropane rings to give C18 precursor III. The yield of the isomerization step from III toward triamantane was 2–5%.

Hollowood et al. (1980) improved triamantane synthesis by starting it from norbonadiene, in five stages (Fig. 1.13). Binor-S, the norbonadiene [4 + 4] dimer gives a mixture of precursors IV and V in three steps, which is isomerized into triamantane with 60% yield.

Near quantitative yield of triamantane was achieved through superacid-catalyzed isomerization, similar to what was obtained for adamantane and diamantane. Farooq et al. (1988) prepared triamantane from C18 precursors and a variety of superacidic catalysts, including mixtures of triflic acid and SbF5 (CF3SO3H:SbF5) and boron tris-triflate (B(OSO2CF3)3) to obtain triamantane with 70–74% yield. When bromoadamantane is added in small quantities, it acts as a carbocation initiator, and increases the yield of the isomerization reaction to 95% (Fig. 1.13).

It should be pointed out that the Schleyer’s Lewis acid-catalyzed rearrangement method, which is based on diamondoids thermodynamic stability during carbocation rearrangements, has had little or no success to synthesize higher diamondoids beyond triamantane. While attempts to

Fig. 1.12. Syntheses of diamantane from various C14-precursors. aCupas et al., 1965; bGund et al., 1970; cGund et al., 1973, conditions: CoBr2, 2Ph3P; BF3; dH2, PtO2, HCl.
synthesize lower diamondoids (adamantane, diamantane, triamantane) have been successful through Lewis acid-catalyzed rearrangement, it is no longer a method of choice for synthesis of higher polymantanes (McKervey, 1980). Producing these heavier diamondoids via the above-mentioned

rearrangement synthesis method has not been convenient because of their complex structural properties and their lower thermal stability.

The synthesis of higher diamondoids is a challenging and difficult process. For example, after numerous efforts, the anti isomer of tetramantane was synthesized with only 10% yield (McKervey, 1980). The usage of zeolites as the catalyst in synthesis of adamantane has been investigated and different types of zeolites have been tested for achieving better catalyst activity and selectivity in adamantane formation reactions (Navratilova et al., 2000). In the early 2000’s, Shibuya et al. (2002) represented two convenient methods for synthesis of enantiomeric adamantane derivatives. Recently a short report on the synthesis of hexamantane is reported using low-temperature plasmas generated in supercritical xenon with limited success (Stauss et al., 2010). Otherwise, high molecular weight diamondoids have not been synthesized as of this date. Present day efforts are towards more economical separation of high molecular weight diamondoids from petroleum fluids and synthesis of lower molecular weight diamondoids (Dahl et al., 2003; Vakili-Nezhaad et al., 2005; Mansoori, 2007).

We envision that with advances in our knowledge about inter- and intra-molecular interactions through ab initio methods, dynamic combinatorial chemistry, molecular design and nano-catalysts new routes for synthesis of higher diamondoids would be discovered (Mansoori, 2005).

1.4.3. **Functionalization of diamondoids**

Diamondoid derivatives are becoming of increased importance as nanoscale building blocks (Chapter 4), as carriers for biologically active substances (Chapter 6), as well as new material for polymer applications, among others (Chapter 7). Most of the diamondoid applications are based on adamantane chemistry; hence, methods for the substitution of adamantane H+ ions for a variety of functional groups have been intensively studied over the last five decades (Fort and Schleyer, 1964a, 1964b; Sevostyanova et al., 1970; Moiseev et al., 1999; Mansoori, 2007; Xue and Mansoori, 2008; Bagrii et al., 2010). Some of the first reported direct substitution reactions were adamantanes halogenation (Stetter et al., 1968; Peterson and Wahl, 1968), carboxylation (Koch and Haaf, 1960), cyanation followed by hydrolysis to produce amides (Haaf, 1961), and
Diamondoid Molecules

nitrates (Smith and Williamson, 1961). From simple 1-substituted adamantanes, such as bromoadamantanes, adamantyl carboxylic acid and amides, a great variety of derivatives were synthesized using well-established methods (Fort and Schleyer, 1964a).

Bromination, nitration, and carboxylation of adamantane are nucleophilic substitution reactions of hydrogen leading to bridgehead-substituted derivatives. Such mechanisms probably involve the formation of 1-adamantanyl cation, for example, as shown in Fig. 1.14 for adamantane bromination reaction substitution (Stetter et al., 1959; Stetter and Wulff, 1960).

In contrast, bridge 2-substituted derivatives are more difficult to obtain, since the position 2 (bridge) in adamantane (see Fig. 1.1) is less reactive than the bridgehead position (Fort and Schleyer, 1964b; Schleyer et al., 1964).

Substitution at the bridge positions frequently involves 1,2-hydride transfer. As an example, the direct oxidation of adamantane to adamantane in concentrated sulfuric acid (Fig. 1.15) occurs in multiple stages (Geluk and Schlatmann, 1967, 1968).

First, adamantane is oxidized to 1-adamantanol, then hydroxyl elimination and 1,2-hydride transfer leads to the equilibrium between 1- and 2-adamantanyl cations. Then 2-adamantanol is formed from 2-adamantanyl cation reaction with water. Intermolecular hydride transfer occurs between adamantanyl cation and 2-adamantanol, in which the cation acts as a hydride ion acceptor. This disproportionation reaction yields adamantane and adamantane (Geluk and Schlatmann, 1967, 1968).

Functionalization of diamantane, triamantane, and tetramantane are also gaining importance in diamondoids chemistry. These functionalized molecules are explored through combinatorial chemistries for their expected biological activity and their possible nanotechnology applications. Moreover, natural occurrence of diamantane, triamantane, and higher diamondoids in petroleum and other fossil fuels of different origins is allowing

![Fig. 1.14. Bromination of adamantane with Br₂.](image)
Thus, methods to chemically modify diamondoids other than adamantane have been published over the past years (Liu et al., 2002; Davis and Liu, 2006; Tkatchenko et al., 2006; Schreiner et al., 2006; Fokin et al., 2007; Fokina et al., 2007; Davis et al., 2008; Schwertfeger et al., 2008, 2009). Since 2002, many patents on functionalized higher diamondoids have been filed. These patents show broad spectra of the utility of these molecules for biomedical, chemical, nanotechnology, pharmaceutical, and other applications (Dahl et al., 2002a, 2002b, 2004; Liu et al., 2002, 2003, 2009; Dammel, 2006; Sciamanna et al., 2007; Mansoori, 2007; Yang et al., 2008) including higher heterodiamondoids, as well (Liu et al., 2010).

Figure 1.16 shows an example of selective bromination of diamantane to give bis-apical derivative 4,9-dibromodiamantane. For numbering and
positions of “4 and 9” see diamantane in the top row in Fig. 1.1. Reaction conditions include Freon-113 as solvent and iron as catalyst to give 62% yield (Davis and Liu, 2006).

This method differs from classical *apical* bromination of diamantane, in which aluminum bromide is used as catalyst to give a mixture of *apical* 4-bromodiamantane, *bis-apical* 4,9- and *medial-apical* 1,4-dibromodiamantane obtained along with traces of both medial 1-, and *bis-medial* 1,6-bromodiamantane; then products are separated by column chromatography over alumina (Gund *et al.*, 1971). Diamantane medial positions are more reactive than *apical* positions (Gund *et al.*, 1970; Olah *et al.*, 1985), hence, bromination at room temperature in the absence of Lewis acid catalysts leads to 1-bromodiamantane with 80% yields, which can be further brominated to 1,4- and 1,6-derivatives with bromine under reflux (Gund *et al.*, 1974).
et al., 1971). Dibromine derivative can be conveniently converted into dihydroxy or dicarboxy diamantane, as shown in Fig. 1.16.

Bifunctional diamondoid derivatives, especially highly symmetrical bis-apical 4,9-dibromodiamantane are useful as starting materials for the synthesis of polymers containing cage moieties in the backbone. Such polymers are reported to be thermoset resins of high thermal and thermo-oxidative stability (Malik et al., 1991). Apically-substituted diamondoids are promising molecular building blocks for nanotechnology applications; for example, as improved AFM tips (see Figs. 4.6e and 4.6f) (Carlson et al., 2007), or components of self-assembled monolayers (Dameron et al., 2005).

Triamantane substitution reactions are even more challenging when it comes to selectivity, due to their increased number of tertiary C–H bonds. Again, a mixture of several monobromo-derivatives is obtained by reaction with neat bromine, which gives medial 2-bromotriamantane as main product (37% in preparative yield) after recrystallization from n-hexane (Schreiner et al., 2006). Reaction of triamantane with 100% nitric acid followed by hydrolysis also resulted in a mixture of medial 2-hydroxytriamantane (20%), and 3-hydroxy (38%), and apical 9-hydroxytriamantane (21%) derivatives (Schreiner et al., 2006).

Extended reaction times of triamantane with excess of nitric acid yielded a mixture of triamantanediols after hydrolysis (Fig. 1.17) (Fokina et al., 2007), in which 3,9-dihydroxytriamantane (Fig. 1.16b) was the main product, while the bis-apical 9,15-derivative (Fig. 1.17f) had only 4% in yield. Thus, in such conditions, where disubstitution reaction is

![Fig. 1.17. Bis-apical nitroxylation of triamantane (data from Fokina et al., 2007).](image-url)
kinetically controlled, there is poor selectivity and low percentage of apically-substituted compounds.

Conversely, selective formation of 9,15-dyhydroxytriamantane was obtained after thermodynamically controlled isomerization of the mixture of triamantanediols (a)–(f) (Fig. 1.17) with 98% H₂SO₄. This result is explained by the higher calculated relative stability of *bis-apical* derivative (f) in comparison with diols (a)–(e). For example, *bis-medial* compound (d) is the least stable of the mixture and its formation ΔG°₂⁹⁸ is 6.0 kg/mol higher than ΔG°₂⁹⁸ of compound f (Fokina et al., 2007). It is worthwhile to mention that *bis-apical* nitroxylation may also be performed as a one-pot reaction, starting from triamantane and nitric acid. After reaction first step, acid excess is removed by evaporation, then, isomerization with H₂SO₄, followed by hydrolysis, gives compound (f) with 80% yield.

*Apical* derivatives of tetramantane are more difficult to produce. Their reactions with electrophiles present high selectivity towards *medial* 2-derivatives of [121]tetramantane, possibly due to the high stability of correspondent 2-tetramantanyl cations relative to other cations to be formed from the same structure. The 6-tetramantanyl cation, for example, is the least stable of the family and its calculated formation ΔG°₂⁹⁸ is c.a. 5 kcal/mol higher than formation ΔG°₂⁹⁸ of 2-tetramantanyl cation. Thus, a simple functionalization reaction, such as mono-bromination with bromine in chloroform gives *medial* 2-bromo[121]tetramantane in high yields (Schreiner et al., 2006). Figure 1.18 summarizes the results of bis-functionalization reactions in [121]tetramantane. The data reported in this figure verify how 2-derivatives predominate in dibromination: (b) 2.17%, (c) 2.18%, (d) 2.6%, and (e) 2.13% diols represent 75% of the product of bromination/hydrolysis reaction.

In addition, *bis-medial* 2,17-dibromo[121]tetramantane (compound f) could still be recovered with 17% yield even after hydrolysis procedure, while only traces of *bis-apical* 6,13-dihydroxy[121]tetramantane (compound a) is produced. Nitroxylation reaction exhibited lower selectivity and predominance of *apical*-derivatives (d) and (a). Nevertheless, the same isomeric tertiary diols were also present. Similarly to what was obtained with triamantane, these mixtures of tetramantanediols yielded *bis-apical* derivative (a) when subjected to thermodynamically-controlled isomerization reaction allowing yields of up to 85% for *bis-apical* derivative (a). Another evidence
of compound (a) higher stability, when compared to medial derivatives, relies on difference in formation free energies, $\Delta G_{298}$, between (a) and (b) which is c.a. 3 kcal/mol in favor of the bis-apical isomer (a) (Fokina et al., 2007).

Thermodynamically-controlled functionalization reactions show a favorable outlook for large-scale production of functionalized diamondoids, especially for preparation of rather attractive and amenable bis-apical diamondoid diols, as these reactions present high selectivity, good yields and give bifunctional products easily convertible into a number of different compounds.

Other approaches for apical diamondoids involve oxidation under UV irradiation and are described in the following paragraphs. Such procedures demand strong oxidant agents and are more efficient in producing monofunctional diamondoids.

Good yields for preparation of mono-apical 9-derivatives of triamantane were achieved with photooxidation with diacetyl to produce 9-acetyl-triamantane (43% yield). As this reagent (diacetyl) preferentially chooses
less sterically hindered positions, the second substitution occurs at the apical position 15, to give the bis-apical diacetyl derivative as a minor product (Fig. 1.19) (Schreiner et al., 2006).

Single-electron-transference (SET) oxidation conditions also have rendered selective apical substitution in triamantane. In SET oxidation, triamantanyl radical cation is formed under UV photoirradiation in the presence of 1,2,4,5-tetracyanobenzene (TCB) and excess of triamantane, to yield 9-(2,4,5-tricyanophenyl)triamantane exclusively, in 43% preparative yield (Fig. 1.19) (Schreiner et al., 2006).

Both photooxidation with biacetyl and SET oxidation with TCB were used to selectively produce apical derivatives of [121]tetramantane. Apical 6-acetyl[121]tetramantane was the main product of photoacetylation (57%) along with the bis apical product (11%), while oxidation with TCB resulted in the apical aromatic compound with 100% selectivity, in 40% yield (Schreiner et al., 2006).

1.5. Concluding Remarks

In this chapter, we have presented the diamondoid molecules which are cage-like organic (saturated hydrocarbons) with unique structures and properties. These molecules are ringed compounds, which have a
diamond-like structure consisting of a number of six-member carbon rings fused together. More explicitly, they consist of repeating units of ten carbon atoms forming a tetra-cyclic cage system. They are called “diamondoid” because their carbon–carbon framework constitutes the fundamental repeating unit in the diamond lattice structure.

Also we have introduced, the general aspects of how to define and classify diamondoids. Difference between diamondoids and NDs are pointed out. The Lewis acid-catalyzed rearrangement of hydrocarbons to synthesize lower diamondoids is presented and its limitations for the synthesis of higher diamondoids are discussed. Classical methods of diamondoid cage chemical syntheses and functionalization, along with recent methods for higher diamondoid chemical modification set the tone for organic chemistry of diamondoids.

The discovery of adamantane cage in 1933 and its direct synthesis in 1957 has turned this diamondoid and its derivatives into readily available compounds. Since 1960, the interest in practical applications of diamondoid molecules has steadily increased. A consequence of these findings can be seen through the number of adamantane-related issued US Patents in the past 55+ years (Fig. 1.20).

The first issued patent, in May 1960, was filed by Richard E. Ludwig (1960) (du Pont & Co., Wilmington, DE) a few years after the publication

![Fig. 1.20. US issued patents related to adamantane (black columns, left Y-axes) and percentage of patents on pharmaceutical/medical application of adamantane and its derivatives (empty circles/black line, right Y-axes), from January 1950 to December 2009.](image-url)
Diamondoid Molecules

of Schleyer’s 1957 work, and presented an improved synthesis of adamantane. Since the 1990’s, the rate of claims of products and processes related to diamondoids has rapidly increased. By the second half of the 2010 decade, total patents issued on adamantane alone reached more than 3,200 (Fig. 1.20, black columns).

Diamondoids family of compounds and their derivatives (with over 20,000 variants) is one of the best candidates for templates and molecular building blocks for synthesis of high temperature polymers, nanotechnology, drug design, drug delivery, drug targeting, DNA-directed assembly, DNA-protein nanostructure formation, and in host-guest chemistry. In the rest of this book, we present various aspects of diamondoids and their applications.

Bibliography


Molecular Structure and Chemistry of Diamondoids


Diamondoid Molecules


Molecular Structure and Chemistry of Diamondoids

Diamondoid Molecules


DOI: 10.1002/cber.19560890821.