

# Carbenes in Constrained Systems I: 1,3 C-H Insertion Reaction of Adamantylidene within the $\beta$ -Cyclodextrin Cavity\*\*

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Dedicated to Professor Emanuel Vogel on the occasion of his 65th birthday

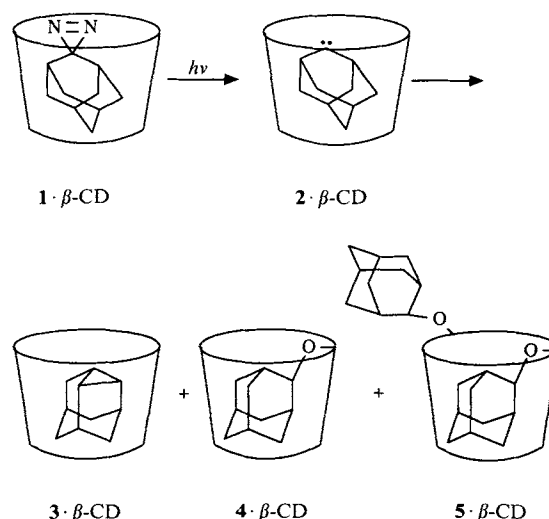
The chemistry of reactive intermediates (guests) within the confined spaces of another species (host) presents interesting opportunities for the discovery of new reactions.<sup>[1]</sup> The reactive behavior of carbenes in constrained systems is expected to be very different from that of free carbenes in solution or in the gas phase. The "tight fit" between the structures of hosts and the guest carbenes should alter both inter- and intramolecular reactions. Furthermore, suitable cavity sizes will restrict the mobility of the entrapped carbenes, which are then anticipated to react more selectively.

Carbene chemistry in different media has been studied extensively over the past decades.<sup>[2]</sup> Nearly nothing, however, is known about carbenes generated in constrained systems. Although  $\alpha$ - and  $\beta$ -cyclodextrin (CD) have been the only molecules employed as hosts,<sup>[3]</sup> the intermediacy of carbenes or the corresponding carbenoids has not been firmly established.<sup>[3]</sup>

The relatively stable<sup>[4]</sup> diazirine **1** derived from adamantane<sup>[5]</sup> was chosen as the guest-carbene precursor and  $\beta$ -CD as the molecular reaction vessel (see Scheme 1). Compound **1** was prepared according to the literature,<sup>[6]</sup> purified by column chromatography (silica gel) under the exclusion of light, and shown to be pure by <sup>1</sup>H NMR spectroscopy. The  $\beta$ -CD complex of **1** (**1** ·  $\beta$ -CD) was synthesized (ratio of host: guest ca. 3:1) and characterized. To avoid the replacement of entrapped guest molecules in the  $\beta$ -CD cavity by solvent molecules, solid-state NMR spectroscopy was used for the characterization. Cross polarization/magic angle spinning (CP/MAS) <sup>13</sup>C NMR spectra provide convincing evidence that an inclusion complex was formed.<sup>[7]</sup> This is further supported by powder X-ray diffraction spectra of **1**,  $\beta$ -CD, **1** ·  $\beta$ -CD, and a physical mixture of **1** and  $\beta$ -CD. Under the conditions of fast atom bombardment (FAB) mass spectrometry, however, the loosely bound complex does not survive, and only the (*M* – H)<sup>–</sup> peak of  $\beta$ -CD is observed.<sup>[8]</sup>

In addition, molecular modeling was used to gain information about the fit and possible position of **1** within the CD cavity.<sup>[9]</sup> According to calculations carried out by using the SYBYL force field with default parameters, **1** is nearly completely submerged into the  $\beta$ -CD cavity with the diazirine function at the wider rim of the truncated cone.

Photolysis (Hanovia 400 W) of the solid inclusion complex of **1** ·  $\beta$ -CD (Scheme 1) yielded the intramolecular carbene insertion product, 2,4-didehydroadamantane, as **3** ·  $\beta$ -CD, and 2-adamantanone azine ·  $\beta$ -CD<sup>[10]</sup> in a ratio of about 35:65.<sup>[11]</sup> Both products were identified by comparison of the NMR spectra with those of  $\beta$ -CD complexes of 2-adamantanone azine and 2,4-didehydroadamantane, synthesized by independent routes. When a physical mixture of  $\beta$ -CD and **1** was photolyzed, only about 1% of 2,4-didehydroadamantane **3** was formed! Furthermore, photolysis of **1** in the solid state leads to no detectable **3**.



Scheme 1. All guest molecules might be positioned differently within and outside the  $\beta$ -CD cavity. Insertion reactions of the carbene might have taken place into the secondary or primary hydroxyl groups at the wider and narrower rims, respectively, of the  $\beta$ -CD molecules.

Our results contrast strongly with the product distribution of the photolysis of **1** in hydrocarbon solvents, in which the carbene insertion product is not<sup>[12]</sup> (or only in traces) formed (0.2% in heptane<sup>[13]</sup>). In the photolysis in solution the formation of azine (76–85%) and adamantanone clearly dominates.<sup>[12]</sup>

Why is **3** ·  $\beta$ -CD, the 1,3 C-H insertion product of **2** ·  $\beta$ -CD, formed in yields as high as approximately 30% in the solid state, whereas yields of 0.2% or less are obtained by the photolysis in solution?  $\beta$ -CD complexation has dramatically altered the reactivity of adamantylidene; the intramolecular 1,3 C-H insertion reaction is now more likely by a factor of 150.

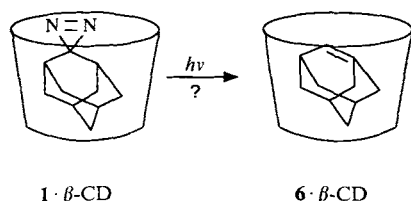
In the clean CP/MAS <sup>13</sup>C NMR spectrum of the product mixture, all signals of 2,4-didehydroadamantane and most of those of the azine can be assigned directly. No clear indication of the formation of products resulting from insertion of adamantylidene into the O–H bonds of  $\beta$ -CD, however, could be found. According to FAB and tandem mass spectrometry, however, adamantylidene inserts into one of the 21 O–H bonds of  $\beta$ -CD<sup>[14]</sup> to make a covalently bound host-guest complex with an (*M* – H)<sup>–</sup> ion of *m/z* 1267. Proof was obtained by treating a sample with D<sub>2</sub>O to exchange the number of active hydrogen atoms left,<sup>[14]</sup> and by collisionally activating the *m/z* 1267 ion; no loss of 2,4-didehydroadamantane could be detected. A low abundance ion of *m/z* 1401.5 was also observed in the FAB mass spectra; it is probably due to a  $\beta$ -CD with two C<sub>10</sub>H<sub>14</sub> moieties attached. This is confirmed by the fact that only 19 hydrogen atoms

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[\*\*] Carbene Rearrangements, Part 41. We thank the American Maize-Products Company, Hammond, Indiana, for providing the cyclodextrins used in this study. Part 40: L. Xu, G. Lin, F. Tao, U. H. Brinker, *Acta Chem. Scand.*, **1992**, *46*, 650.

can be exchanged with D<sub>2</sub>O. Thus, two insertions of two adamantylidenes into two different O–H bonds of  $\beta$ -CD have taken place. The absolute amount of OH insertion products **4** ·  $\beta$ -CD and **5** ·  $\beta$ -CD detected by FAB mass spectrometry (Scheme 1) is not yet known. Since these compounds could not be found by CP/MAS <sup>13</sup>C NMR spectroscopy, they must have been formed each in less than 5% yield.

Adamantylidene is believed to be a ground-state singlet carbene, and the generation of the triplet state fails even in the presence of photosensitizers.<sup>[15]</sup> The question of whether adamantylidene entrapped in  $\beta$ -CD is also a singlet cannot be answered at this time. Laser flash photolysis studies may solve this problem, as well as answer questions concerned with the detailed differences in the reactive behavior of a "free" adamantylidene and a (partially) entrapped one.



If the carbene **2** ·  $\beta$ -CD cannot easily encounter another reaction partner, it could rearrange to the highly strained adamantene **6**, which is known to dimerize<sup>[16]</sup> immediately, although it has been shown to exist in a matrix at low temperature.<sup>[17]</sup> This reaction, however, does not appear to take place if adamantylidene **2** is entrapped in  $\beta$ -CD.<sup>[18]</sup>

In conclusion, our results strongly suggest that we have established the first intra- and intermolecular carbene insertions within any constrained molecular reaction vessel.

### Experimental Procedure

**1** ·  $\beta$ -CD: A solution of **1** (0.49 g, 3 mmol) in diethyl ether (12 mL) was added to a solution of  $\beta$ -CD hydrate (3.4 g, 3 mmol) in water (150 mL). After the mixture had been stirred for one day, the precipitate was filtered off, washed several times with water and ether, and then dried in the desiccator. Yield: 2.9 g (2.4 mmol, 81%).

Received: March 17, 1993

Revised: April 30, 1993 [Z 5933 IE]

German version: *Angew. Chem.* **1993**, *105*, 1427

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- [7] In **1** ·  $\beta$ -CD the signals at  $\delta = 27$ –28 and 37 appear as doublets; when resolution enhancements were applied they became two distinct signals. For a physical mixture, these signals remained singlets. Cross polarization dynamics, as measured by the contact time and the proton rotating-frame relaxation time  $T_{\rho}(H)$ , differed between **1** ·  $\beta$ -CD and the physical mixture, indicating a single proton-spin reservoir for the complex and two distinct proton-spin reservoirs which are separated in space for the physical mixture (see J. R. Garbow, B. J. Gaede, *J. Agric. Food Chem.* **1992**, *40*, 156).

- [8] FAB mass spectra were obtained by bombarding the samples in a glycerol or triethanolamine matrix with approximately 33 keV beam of Cs<sup>+</sup> ions, and the desorbed ions were analyzed with the first stage of a VG analytical ZAB-T four-sector mass spectrometer. Exact mass measurements were within <3.8 ppm of theoretical values. Collisional activation of the  $m/z$  1267.4 ion and mass analysis of products with the second stage produces evidence for rupture of the CD ring but not for loss of C<sub>10</sub>H<sub>14</sub>. The mass spectrometer was briefly described by M. L. Gross *Methods Enzymol.* **1990**, *193*, 131.
- [9] The calculations were performed with the SYBYL 6.0 version from Tripos Associates, Inc., on an 4D/35 IRIS workstation from Silicon Graphics, Inc. The "dock molecules" program was used to obtain the total energy of the complex with consideration of different possible conformations of **1** within  $\beta$ -CD.
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- [14] This sample which contained "empty" and "filled"  $\beta$ -CD molecules (ratio: ca. 2:1, determined by NMR spectroscopy) was treated with D<sub>2</sub>O in order to exchange the number of active hydrogen atoms. The ( $M - H$ )<sup>+</sup> ion of  $\beta$ -CD shifts from  $m/z$  1133.4 to 1153.4, indicating that all 21 active hydrogen atoms of  $\beta$ -CD had been replaced with deuterium atoms, and that an ( $M - D$ )<sup>+</sup> ion had been desorbed. The exchange was not complete; there were still some isomers with 20, 19, 18, and 17 deuterium atoms, but it was the most exchange that could be accomplished. For **4** ·  $\beta$ -CD, 20 active hydrogen atoms could be exchanged as indicated by a shift from  $m/z$  1267.4 for ( $M - H$ )<sup>+</sup> to  $m/z$  1286.5 for ( $M - D$ )<sup>+</sup>. One active hydrogen atom was lost owing to carbene insertion into an O–H bond.
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- [18] This could also mean that adamantene **6** is not formed from the carbene **2** but from the diazirine **1** or the rearranged linear diazo precursor (see J. E. Jackson, M. S. Platz in *Advances in Carbene Chemistry*, vol. 1 (Ed.: U. H. Brinker), JAI, Greenwich, CT, in press).

## Conjugated, Liquid Crystalline Polymers\*\*

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Liquid crystalline (LC) polymers are of great interest in fundamental science and the development of advanced materials.<sup>[1]</sup> Three main types of LC polymers have been extensively studied: 1) side-chain LC polymers, 2) main-chain LC polymers with flexible spacers, and 3) rigid main-chain LC polymers. The study of type 3 LC polymers stemmed from the discovery that poly(*p*-phenyleneterephthalamide) forms an LC solution from which high-modulus fibers may be spun.<sup>[2,3]</sup> These polymers are particularly important because of their exceptional strength and high-temperature properties induced by the LC ordering. However, since these materials are not very soluble, fabrication is extremely difficult. To overcome these problems, in recent years there has been considerable efforts to prepare LC polymers with a rigid

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[\*\*] This work was supported by the Office of Naval Research (grants N00014-93-1-0092), the Camille & Henry Dreyfus Foundation (New Faculty Award), and The Petroleum Research Fund, administered by the American Chemical Society.