Carbene Rearrangements, 60.[‡] Supramolecular Structure-Reactivity Relationships: Photolysis of a Series of Aziadamantane@Cyclodextrin Inclusion Complexes in the Solid State

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Received: May 19, 2004; Accepted: August 20, 2004

Dedicated to Professor Johann Mulzer on the occasion of his 60th birthday.

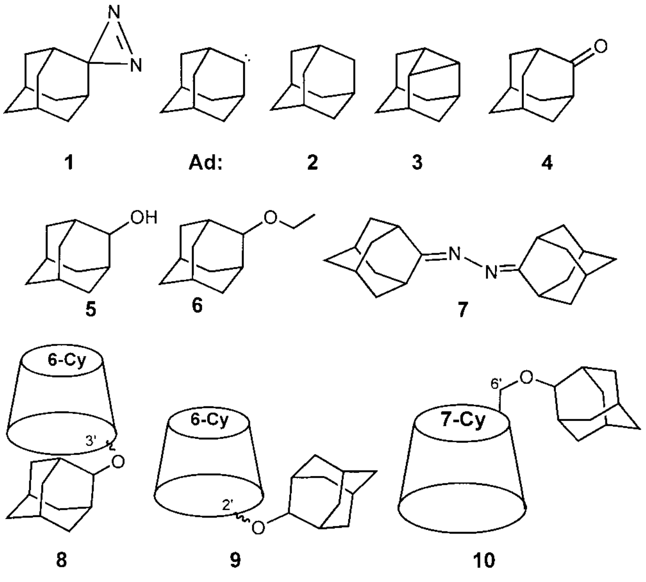
Abstract: Photolyses of the α-, β- and γ-cyclodextrin complexes of 2-aziadamantane (**1**) in the solid state afforded markedly different product distributions, as determined by quantitative GC and HPLC analyses. The results are discussed with respect to the structures of the inclusion complexes.

Keywords: carbenes; cyclodextrins; diazirines; photolysis; supramolecular chemistry

Introduction

The influence of a supramolecular microenvironment on the reaction pathways of reactive intermediates has attracted much interest in recent years.[1] We have been studying in particular reactions of carbenes generated by photolysis of diazirine precursors within cyclodextrin and zeolite hosts in the solid state.[2] 2-Aziadamantane {2-azitricyclo[3.3.1.1^{3,7}]decane; (**1**)} is especially suited for these investigations.[3] A detailed analysis of the complexes of **1** and α-(**6-Cy**), β-(**7-Cy**), and γ-cyclodextrin (**8-Cy**) (Scheme 1) by interpretation of induced circular dichroism (ICD) titrations has already been reported.[4] Moreover, the photolysis of the 1:2 complex of **1** and **6-Cy**, i.e., **1**@2(**6-Cy**), in the solid state has opened up an interesting synthetic route to monofunctionalized 2′- and 3′-substituted α-cyclodextrins.[5]

Here we wish to compare the results obtained earlier with new findings for all three cyclodextrins to reveal interesting structure-reactivity relationships. From these results we expect to gain new insights into the rather complex reaction pathways for the photochemical decomposition of diazirines.



Scheme 1.

Results and Discussion

Photolysis and Analysis of Reaction Products

The photolyses of the solid cyclodextrin complexes of **1** were carried out in the absence of oxygen at defined temperatures using a specially doped medium-pressure mercury lamp to exhibit an emission maximum in the

DOI: 10.1002/adsc.200404142

wavelength region of the diazirine chromophore around $\lambda = 380$ nm.[4,5] Thus, rather short exposure times of 1 to 4 hours could be achieved for complete decomposition of the azi function, which was assessed by UV spectroscopy after each photolysis. Then the solid residue was dissolved in water-dichloromethane and a continuous liquid-liquid extraction was performed. Quantitative GC analysis of the organic extracts provided absolute yields of the adamantane derivatives formed during photolysis within the cyclodextrin host. In contrast, the absolute yields of cyclodextrin and the cyclodextrin derivatives formed were determined after reversed phase (RP) HPLC of the aqueous phase with methanol-water as eluent. For both chromatographic methods response factors were determined using authentic, pure samples. The so-obtained results are summarized in Tables 1–3.

Some of the particular features of the photolysis of the 2 : 1 complex with α-cyclodextrin have already been published.[5] The occurrence of adamantanone-azine **7**,[6] which dominates under almost all photolytic conditions, does not take place at all, owing to the strict separation of the adamantyl moieties by the cyclodextrin hosts. But also the formation of adamantanone (**4**) is negligible, even in the presence of oxygen (compare runs 7 and 9, where the same lot of complex has been photolyzed). This would make the appearance of triplet adamantanylidene (*vide infra*) unlikely. Striking, on the other hand, is the high amount of reduction to adamantane (**2**) which is accompanied by the appearance of oxidized α-cyclodextrins as revealed by UV-Vis detection in the HPLC analysis (coeluting with unsubstituted **6-Cy**). The temperature influence on the course of the reaction is not pronounced, only reduction to **2** and insertion into the hydroxy groups of **6-Cy** become less frequent at 77 K. But, on the other hand, the amount of water present in the crystals is of critical importance eventually giving rise to high yields of the alcohol **5**. Runs 2, 4, 6 and 8 have been performed from the same lot of complex, that had a particularly low content of water. In the presence of water the insertion of adamantanylidene into the hydroxy groups of α-cyclodextrin is markedly reduced. At all temperatures employed about 1–3% of **6** were formed which derives from the insertion reaction of adamantanylidenes **Ad:**[7] into the O–H bond[8] of residual ethanol molecules.[4]

The β-cyclodextrin complexes contain only traces of solvent molecules such as water and ethanol inside the cavity.[4] Therefore, the formation of 2-admantanol (**5**) is very low, while 2-ethoxyadamantane (**6**) is not formed at all. The intramolecular 1,3 C–H carbene insertion to yield 2,4-didehydroadamantane (**3**)[2a, b] is highest at about room temperature and lowest at 203 K, where the reduction to adamantane (**2**) has its maximum. However, the proportions of **2** were always well below the amounts formed from the photolysis of the α-cyclodex-

Table 2. Absolute yields of adamantanyl residues as recovered (in %) after photolysis of **1**@(**7-Cy**) in the solid state under argon and reduced pressure.

Compound	Run	1	2	3	4	5	6
	T [K]	303	283	232	203	77	77
2	AdH$_2$	3.9	3.5	5.0	6.0	3.1	4.0
3	DDHAd	10.8	10.1	7.9	5.0	8.6	7.9
4	Ad=O	2.5	3.0	6.2	5.4	7.1	6.6
5	AdHOH	0.3	0.4	1.0	0.7	2.2	2.0
6	AdHOEt	0.0	0.0	0.0	0.0	0.0	0.0
7	Ad=N-N=Ad	33.4	29.0	33.8	29.9	33.8	32.6
	7-Cy-3′-Ad[a]		0.2		0.6	1.2	1.3
10	7-Cy-6′-Ad	17.4	17.6	14.9	13.4	8.3	8.1
	7-Cy-2′-Ad[a]	7.0	6.5	4.7	7.5	5.4	3.4
	7-Cy-Ad$_2$[a]	5.2	5.9	2.1	4.6	0.5	0.7
	7-Cy-Ad$_2$[a]	3.7	2.8	1.7	2.5	1.3	0.4
	7-Cy-Ad$_2$[a]	1.4	1.3	1.0	1.6	1.0	0.0
Sum (% adamantanyl)		85.5	80.3	78.3	77.2	72.5	67.5
Sum (% cyclodextrin)		82.1	92.6	82.2	91.0	98.7	88.9

[a] The composition of cyclodextrin insertion products was assessed by LC-MS (see Experimental Section). The substitution pattern of monoadamantanyl derivatives is only arbitrary by comparison with isolated compounds and may be different.

Table 1. Absolute yields of adamantanyl residues as recovered (in %) after photolysis of **1**@2(**6-Cy**) in the solid state under argon and reduced pressure.

Compound	Run	1	2	3	4	5	6	7	8	9[a]
	T [K]	303	303	263	263	233	228	77	77	77
2	AdH$_2$	22.4	30.6	29.3	37.3	28.1	37.8	18.3	22.3	18.8
3	DDHAd	7.5	9.3	5.3	8.0	4.9	6.8	3.5	5.4	4.2
4	Ad=O	0.0	0.3	0.0	0.9	0.4	0.7	0.3	0.0	0.3
5	AdHOH	29.6	1.0	8.8	1.0	14.2	1.2	51.1	25.8	48.1
6	AdHOEt	2.7	1.1	2.6	1.0	1.1	0.9	1.0	1.0	1.3
7	Ad=N-N=Ad	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8	6-Cy-3′-Ad	21.2	38.8	32.8	37.4	30.5	37.3	20.4	25.5	13.5
9	6-Cy-2′-Ad	7.8	19.2	10.7	16.7	14.0	16.7	8.4	13.3	6.0
Sum (% adamantyl)		91.2	100.3	89.5	102.3	93.2	101.4	103.0	93.3	92.2
Sum (% 6-Cy)		97.1	97.1	94.6	97.2	98.1	97.3	97.4	94.8	95.5

[a] Run was started under normal atmospheric pressure in the presence of oxygen.

trin complex. The major cyclodextrin insertion product **10** could be isolated by RP-HPLC and characterized. Its structure could be assigned by NMR experiments and was identified as the mono-6′-adamantanyl derivative (*vide infra*). But also the other two possible mono-derivatives could be detected. However, they were formed in significantly smaller amounts and could not be isolated. From LC-MS only their mass is known. As is obvious from Table 2, the formation of cyclodextrin-O–H insertion products in all cases is markedly reduced at lower temperatures. Especially bis-substitution resulting from a two-fold insertion of adamantanylidene (**Ad:**) becomes almost negligible. The recovery of adamantanyl derivatives also is decreased at lower temperatures. Notably, the amount of azine **7** formation (see Scheme 2) is not affected by the temperature.

The photolyses of the γ-cyclodextrin complex reveal not much selectivity which is in accord with the known structural flexibility of **8-Cy**. Conspicuous is the much higher amount of adamantanol (**5**) formed, when compared with the results from the photolysis of **1**@(**7-Cy**). This is due to the presence of more water molecules within the supramolecular arrangement of **1**@(**8-Cy**).[4]

Photolysis of solid *physical mixtures* of α-, β- or γ-cyclodextrin with aziadamantane (**1**) in the appropriate stoichiometry of the corresponding complexes, always gave the same result, i.e., about 20% of reacted adamantanyl moieties were recovered as adamantanone (**4**) and about 60% as azine **7**. The respective cyclodextrin was retrieved nearly quantitatively and found to be unmodified. Identical results were obtained if a concentrated pentane solution of **1** was evaporated in the presence of the appropriate amount of the respective cyclodextrin and the resulting dry powder was photolyzed.

Table 3. Absolute yields of adamantanyl residues as recovered (in %) after photolysis of **1**@(**8-Cy**) in the solid state under argon and reduced pressure.

Compound	Run	1	2	3	4[a]
	T [K]	303	263	77	77
2	AdH$_2$	6.5	4.9	3.1	3.3
3	DDHAd	8.6	5.8	6.3	3.8
4	Ad=O	9.5	11.9	9.2	8.2
5	AdHOH	13.2	12.2	6.6	10.3
6	AdHOEt	2.4	1.5	1.0	1.0
7	Ad=N-N=Ad	29.0	30.1	26.5	28.5
	n.i.[b]	3.4	4.9		
	8-Cy-3′-Ad[c]	9.5	10.7	9.1	6.4
	8-Cy-6′-Ad[c]	4.6	5.3	6.9	4.1
	8-Cy-2′-Ad[c]	3.7	4.2	6.9	3.0
	8-Cy-Ad$_2$[d]			5.0	2.2
Sum (% adamantanyl)		90.3	91.3	80.7	70.8
Sum (% cyclodextrin)		99.2	94.8	102.3	100.6

[a] Run was started under normal atmospheric pressure in the presence of oxygen.

[b] Approximate sum of not identified (n.i.) GC detectable compounds.

[c] The substitution pattern of monoadamantanyl derivatives is only arbitrary by comparison with the isolated compounds (**8**, **9**, and **10**) and may be different.

[d] Several (up to nine) bisadamantanyl derivatives in trace amounts could be detected by RP-HPLC using eluent mixtures more rich in methanol. Here only the sum is listed; their composition was assessed by MS.

Identification of Compound 10 by NMR

The structure of the isolated mono-6′-adamantanyl-substituted β-cyclodextrin (**10**) was determined by various 1D and 2D NMR experiments with DMSO-d_6 as solvent. The linkage position of the adamantane moiety has been identified by HMQC, HMQC-TOCSY, and HMBC and was furthermore verified by ROESY spectra. In the HMBC spectrum the H-2 of the adamantanyl substituent shows a ${}^3J_{CH}$ coupling to the C-6′^{a} of the substituted glucose unit (Glc^a). *Vice versa* both H-6′a^a and H-6′b^a possess a ${}^3J_{CH}$ coupling to C-2 in the adamantanyl moiety. These ${}^3J$ couplings are indicated in Figure 1. The downfield shift of the C-6′^{a} ($\delta_C = 66.6$ ppm) additionally indicates an ether linkage at this position. NOEs between H-5′^{a}, H-6′a^a, and H-6′b^a from Glc^a and H-1 and H-3 from the adamantane moiety indicate the spatial closeness between these nuclei and hence verify the linkage position of the adamantane substituent. Furthermore, H-1, H-2, and H-3 show weak NOEs to H-5′^{b}, H-6′a^b, and H-6′b^b of one other glucose unit in the β-cyclodextrin. This is likely the Glc^b which is 1′-4′ bound to Glc^a and therefore quite close to the adamantanyl moiety. All chemical shifts of **10** are listed in Tables 6 and 7. There the shifts of Glc^a and Glc^b are given in detail. Signals for the five other glucoses (Glc^c to Glc^g) overlap and hence their chemical shifts are only given as shift regions (Table 6). Stereochemical differentiation of the two halves of the adamantane moiety is not very pronounced and hence only two carbons show some shift differences. The other ^{13}C and all proton chemical shifts, however, are not distinguishable (Table 7).

Supramolecular Structure-Reactivity Relationship

As crystallization of 2-aziadamantane-cyclodextrin complexes thus far failed to give crystals suited for X-ray diffraction analysis, structure-reactivity considerations must be deduced indirectly.[4,5] In the case of **1**@2(**6-Cy**) this has been already addressed in part.[5] The comparison of all three types of complexes discussed here reveals some further interesting features. Only in the case of **1**@2(**6-Cy**) are the diazirines totally isolated from each other, since each diazirine is entrapped by two 6-Cy's (see **A** of Figure 2). Therefore, the azine formation is prevented. The chemospecific insertion into the secondary hydroxy groups of **6-Cy** yielding

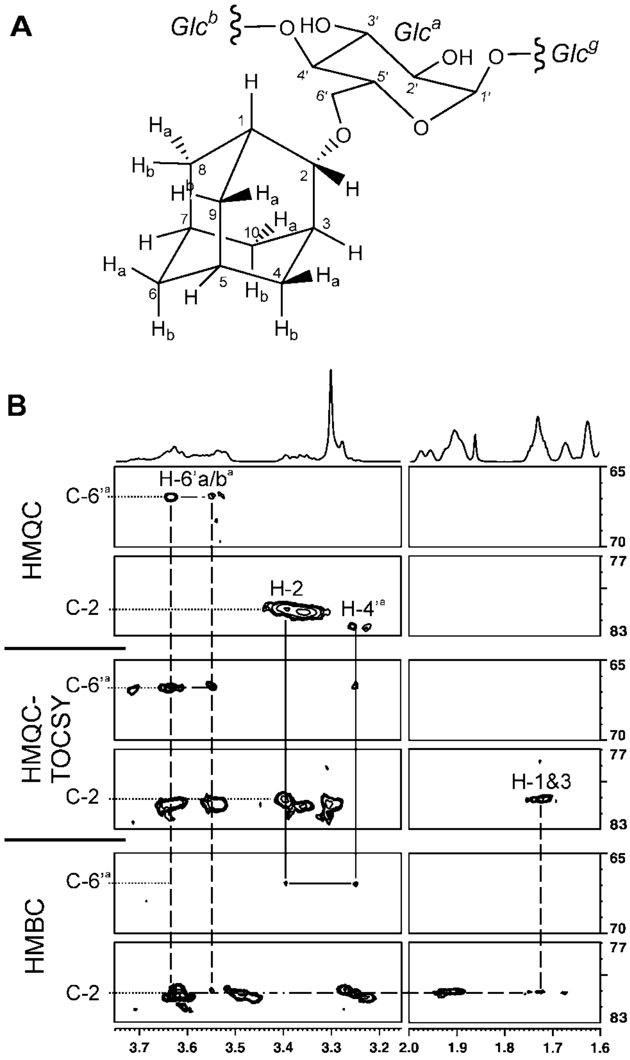


Figure 1. Structure and numbering of the adamantane moiety and the linked glucose unit Glc^{a} (**A**). Sections from HMQC, HMQC-TOCSY, and HMBC indicating the linkage position of the adamantane moiety to the β-cyclodextrin. Dashed lines show the connection from the $^{1}J_{HC}$ (H-6′a/b^{a}/C-6′^{a}) coupling in HMQC and HMQC-TOCSY to the $^{3}J_{HC}$ (H-6′a/b^{a}/C-2) coupling in HMBC. C-2 is further identified by its $^{2}J_{HC}$ coupling to H-1 and H-3 in HMBC and by the coupling in HMQC-TOCSY. This consecutive connection is also visualized by dashed lines. The connection from $^{1}J_{HC}$ (H-2/C-2) in HMQC and HMQC-TOCSY to the $^{3}J_{HC}$ (H-2/C-6′^{a}) is indicated by continuous lines. C-6′^{a} is further identified by its $^{2}J_{HC}$ coupling to H-4′^{a} in HMBC and by the coupling in HMQC-TOCSY. This successive connection is also visualized by continuous lines. Dotted lines indicate the positions of the signals from the C-6′^{a} and C-2 atoms. All further signals belong to other atoms of **10** (**B**).

8 and **9** makes the proposed structure (**A**, Figure 2) highly plausible. Furthermore, the adamantane skeleton must be in close contact with the inner walls of the two α-cyclodextrin molecules – this is corroborated by the very intense ICD.[4] The induced ellipticity of the achiral molecule **1** is strikingly similar to the CD of chiral azicamphane.[9] This close contact with the cyclodextrin obviously also favors the exclusive insertion of **Ad:** into the secondary hydroxy groups of **6-Cy** and the redox reaction yielding adamantane (**2**) and oxidized **6-Cy** derivatives. Apparently, these reactions do occur less within the complexes of hosts providing larger cavities. A reasonable mechanism for the redox reaction yielding a hydrocarbon like **2** from a singlet carbene has – to the best of our knowledge – never been proposed. Naturally, not many suggestions have been put forward because, in general, only small amounts (<5%) of reduced hydrocarbons are formed.[10] This is true for the β- and γ-cyclodextrin complexes of **1** (see Tables 2 and 3). In stark contrast, however, for the photolysis of **1@2(6-Cy)** with adamantane yields of 30–40%, this becomes one of the major reaction paths. Thus, further efforts to explain this fact are justified. The formation of adamantane (**2**) would indicate intersystem crossing (ISC) of adamantanylidene **Ad:** from the singlet to the triplet state followed by H-abstraction. An entrapped carbene might be able to show a different spin multiplicity, when compared with the corresponding mobile carbene. This should especially be true, if the singlet-triplet energy gap is small. Calculations for **Ad:** arrive at an energy gap of 4.8[11a] and 3.1[11b] kcal/mol, respectively, with the singlet being the ground state. There are several mechanisms by which ISC can take place. Compared to **Ad:**, Cy's comprise a large molar mass. Hence, Cy's may provide a collisional mechanism for the ISC of **Ad: 2** from the singlet to the triplet state.[12] On the other hand, the observation that in the presence of air (oxygen) the amount of adamantanone (**4**) obtained is not changed at all when compared with the reaction in the absence of gaseous oxygen, is not indicative of any triplet carbene participation.[13,14] Nonetheless, the selective and very pronounced formation of the 3′- and 2′-cyclodextrin insertion products **8** and **9**, respectively, is indeed chemospecific.[5,15] Also in accord with the proposed structure is the fact that *no* bis-adamantanyl derivatives of **6-Cy** are observed at all.

The dominant formation of azine **7** even at very low temperatures, which is observed in the case of the β-cyclodextrin complex, is in favor of a 2:2 complex where two aziadamantanes (**1**) are facing each other with their respective diazirine moieties. Such a structure has been verified for the crystals of the complex with the more polar guest 5-hydroxy-2-aziadamantane by single-crystal X-ray diffraction.[16] The clear preference for insertion into the 6′-OH group of **7-Cy** is in favor of an arrangement (**B**) as designated in Figure 2. A similar complexation with **7-Cy** was postulated for the 5-hydroxy-2-aziadamantane in solution by NMR spectroscopy.[16] Reliable ROESY spectra of the **1@(7-Cy)** complex could not be obtained, because of the very low solubility of this complex in water. However, the ICD spectra are very similar to those of the corresponding 5-hydroxy de-

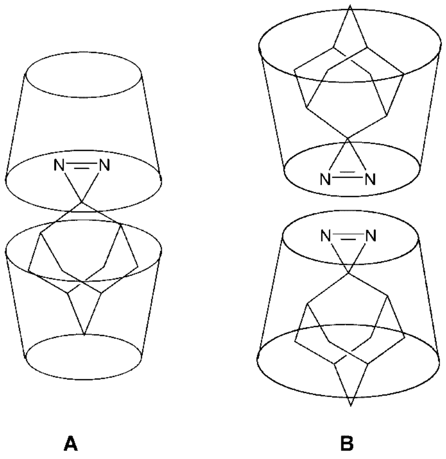
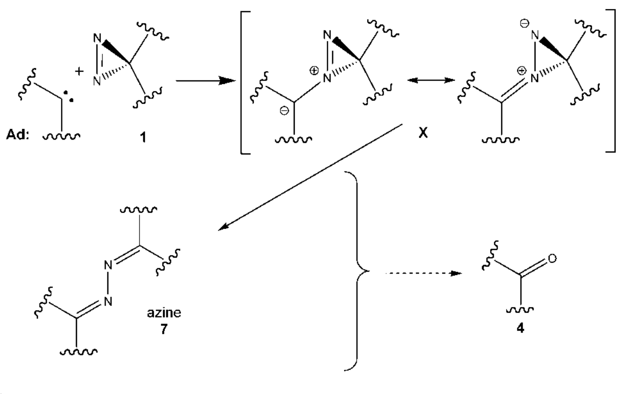


Figure 2. Proposed Structures for **1**@2(**6-Cy**) (**A**) and **1**@(**7-Cy**) (**B**).

rivative.[17] In the solid state the orientation of 5-hydroxy-2-aziadamantane within the β-cyclodextrin host is reversed with respect to the proposed solution structure.[16] Since this can be explained by the special effect of the hydroxy group in the crystal, it should not apply for the unsubstituted adamantane (**2**).

The very low selectivity as shown in the photolysis of the **1**@(**8-Cy**) complex reflects the relatively large space available for adamantane derivatives within the γ-cyclodextrin cavity. This also is corroborated by the rather small complex formation constant K and the faint ICD.[4]

In the photolysis of diazirines three processes can take place: firstly, the direct generation of a carbene, secondly, the rearrangement to the corresponding linear diazo compound, and thirdly, a rearrangement in the excited state (RIES).[18] The formation of all but two of the products obtained in the solid state photolyses of the three cyclodextrin complexes studied has been addressed (*vide supra*). However, for the formation of adamantanone (**4**) and azine **7**, at present no conclusive decisions can be made. As for the azine formation itself, various mechanisms have been proposed.[19,20] More recently an intermediate in the formation of azine **7** by photolysis of **1** could be traced.[20,22] While its structure could not be established, it is formed by direct reaction of **Ad:** with **1**. An intermediate with the structure **X**, as shown in Scheme 2, has been favored based on calculations.[22] It seems likely that adamantanone (**4**) which is only obtained whenever azine **7** is formed (in 50–70% n/n of **7**) either shares a common intermediate with **7** or is a decomposition product under the reaction conditions in the crystal. This is also true for the solid physical mixtures of **1** and cyclodextrins.



Scheme 2.

Conclusion

The photolyses of **1** within cyclodextrin hosts give product distributions that largely depend on the type of cyclodextrin and thus the supramolecular structure. The amount of reduction to hydrocarbon **2**, the proportion of azine **7** and adamantanone (**4**), the formation of cyclodextrin ethers (**8**, **9**, **10**, etc.), and the insertion into solvent molecules yielding **5** and **6** can be widely controlled by the geometry and composition of the complexes. This very interesting influence of the host as "catalyst" or even as co-reactant can be observed especially well for the photolyses of **1**, which primarily yield **Ad:** that cannot easily stabilize intramolecularly. The formation of didehydroadamantane (**3**) has been known to occur only to a small extent, if other inter- and innermolecular reaction channels can be followed. And indeed, its yield (4–11%) is almost invariable for all three complexes studied.

Experimental Section

General Remarks

The following compounds were prepared according to the literature and identified by their respective spectroscopic and analytical data **1**,[3a] **3**,[2b] **6**,[23] **7**,[6] **8**,[5] and **9**[5]. Compounds **2**, **4**, and **5** were purchased from Fluka. Water was highly purified using a Milli-Q system (Millipore®), methanol for HPLC analyses was purchased from Merck (LichroSolv®), ethanol for preparative HPLC was of technical purity (azeotropic mixture with water) and distilled; DMSO-d_6 for NMR was 99.9% D (1 mL ampoules) purchased from Sigma. The supramolecular complexes of **1** with the three cyclodextrins were prepared as already published[4] and are designated as **1**@2(**6-Cy**), **1**@(**7-Cy**), and **1**@(**8-Cy**).

Photolysis

Photolyses were carried out in flasks of Duran® glassware equipped with a septum. The solid material was accurately weighed in as a fine powder (50–400 mg) and evenly distributed on the inner surface of the flask. Then the samples were deaerated and Ar saturated several times on a vacuum line and finally displayed a weak vacuum with some residual Ar. The flasks were rotated in a cooling bath (thermostatted water, ethanol/dry ice or liquid nitrogen) situated below a medium-pressure mercury lamp (Heraeus TQ718-Z4, 700 W, doped with FeI_2). Photolysis was done for 1–4 h depending on the sample amount. Then some mg of sample were dissolved in ethanol-water and a UV spectrum (420–320 nm) was taken to demonstrate complete loss of the diazirine chromophore.

Analysis of Products

Separation of low molecular weight adamantane derivatives from cyclodextrins was performed by dissolving the solid in water (120 mL) and dichloromethane (50 mL) followed by continuous extraction with the appropriate apparatus (100 mL, for extraction liquids of higher density). After 24 h the dichloromethane was replaced by a new portion, thus giving a first fraction, and after 48 h a second dichloromethane extract was collected. In this way one could account for possible evaporation of some quite volatile products. These dichloromethane solutions were diluted with 50% v/v hexane, 0.1% of a standard camphor solution (3.22 mM) was added as internal standard, and then the samples were directly injected into a split-splitless GC injector (5 µL, split *ca.* 1:15). GC analysis was performed on a GC 8160 instrument (Fisons) using a PE-1 column (Perkin Elmer, 30 m, i.d. 0.32 mm, 0.25 µm dimethylpolysiloxane film) using “Chromcard” ® software (Fisons). Detection was accomplished by FID. The flow rate of helium was held constant at 2.1 mL/min; temperature gradient was: 5 min at 100 °C followed by heating up to 150 °C within 10 min and a rapid heating period of 6.7 min to 250 °C. This temperature was held for 5.3 min (total 27 min of analysis) prior to cooling. The retention times and response factors of compounds **2**–**7** were determined by injecting authentic samples (Table 4).

Analytical RP-HPLC analysis was performed using an HP1090 instrument equipped with the RI-detector HP1047 and the interface 35900E (Agilent) using a Nucleosil 300–5C8 5 µm column (4 × 290 mm, FZ Seibersdorf, Austria). The instrument was equipped with an auto-injector and was run with the HP ChemStation (Rev. A.08.03; 2000) software. Isocratic elution with a flow rate of 0.5 mL/min was done with various water-methanol mixtures. Representative data are shown in Table 5. Response factors were determined for each session

Table 4. Representative data for GC analysis.

Compound	Retention time t_R [min]	Response factor[a] [area $(10^5 \cdot \mu V \cdot s) \cdot c^{-1}$ $(mg/mL)^{-1} \cdot v^{-1} (\mu L)^{-1}$]
2	3.95	16.2
3	4.40	14.8
Camphor	4.75	13.0
4	8.75	14.0
5	9.05	13.2
6	9.40	13.1
7	23.5	13.7

[a] Representative values were re-determined for every new session.

Table 5. Representative data for RP-HPLC analysis.

Type of compound	Compound	Methanol content [% v/v]	Retention time t_R [min][a]
underivatized α-cyclodextrin	**6-Cy**	15	12.6
underivatized β-cyclodextrin	**7-Cy**	15	17.4
underivatized γ-cyclodextrin	**8-Cy**	15	12.6
monoadamantanyl α-cyclodextrin	**8**	30	24.5
monoadamantanyl α-cyclodextrin		30	29.0
monoadamantanyl α-cyclodextrin	**9**	30	36.5
monoadamantanyl α-cyclodextrin	**8**	48	10.0
monoadamantanyl α-cyclodextrin	**9**	48	11.8
monoadamantanyl β-cyclodextrin	7-Cy-3′-Ad	30	15.0
monoadamantanyl β-cyclodextrin	**10**	30	19.8
monoadamantanyl β-cyclodextrin	7-Cy-2′-Ad	48	10.9
bisadamantanyl β-cyclodextrin	7-Cy-Ad_2^{I}	48	12.0
bisadamantanyl β-cyclodextrin	7-Cy-Ad_2^{II}	48	21.5
monoadamantanyl β-cyclodextrin	7-Cy-2′-Ad	60	8.7
bisadamantanyl β-cyclodextrin	7-Cy-Ad_2^{I}	60	8.7
bisadamantanyl β-cyclodextrin	7-Cy-Ad_2^{II}	60	10.5
bisadamantanyl β-cyclodextrin	7-Cy-Ad_2^{III}	60	21.4
monoadamantanyl γ-cyclodextrin	8-Cy-3′-Ad	30	11.4
monoadamantanyl γ-cyclodextrin	8-Cy-6′-Ad	30	14.3
monoadamantanyl γ-cyclodextrin	8-Cy-2′-Ad	30	22.3
monoadamantanyl γ-cyclodextrin	8-Cy-2′-Ad	48	10.2
bisadamantanyl γ-cyclodextrins	8-Cy-Ad_2^{I}(2)[b]	48	13–14
bisadamantanyl γ-cyclodextrins	8-Cy-Ad_2^{I}(2)[b]	60	10
bisadamantanyl γ-cyclodextrins	8-Cy-Ad_2^{II}(7)[b]	60	11–20

[a] Representative values that can slightly vary according to small variations in solvent mixture, injection volume, and sample amount.

[b] More than one compound, at least as many as given in brackets.

Table 6. Proton (δ_H [ppm]) and carbon (δ_C [ppm]) chemical shifts of the cyclodextrin moiety.

	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′a/b	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′
Glc^a	4.83	3.29	3.57	3.23	3.68	3.63/3.53	101.7	73.5	72.6	82.2	70.7	66.6
Glc^b	4.83	3.23	3.57	3.40	3.48	3.77/3.51	101.9	72.1	72.5	81.2	71.5	59.5
Glc^c-Glc^g	4.83	3.28	3.61	3.36	3.52	3.64/3.57	101.9	72.2	72.8	81.4	71.8	59.7

Table 7. Proton (δ_H [ppm]) and carbon (δ_C [ppm]) chemical shifts of the adamantane moiety.

H-1, H-3	H-2	H-4a/b, H-9a/b	H-5	H-6	H-7	H-8a/b, H-10a/b	C-1, C-3	C-2	C-4, C-9	C-5	C-6	C-7	C-8, C-10
1.91	3.39	1.73/1.58	1.73	1.63	1.68	1.36/1.94	31.3	81.0	35.9 & 35.7	30.0	37.1	26.8	31.0 & 30.9

with authentic samples of the pure compounds **6-Cy**, **7-Cy**, **8-Cy**, **8**, **9**, and **10**.

LC-MS of the **7-Cy** derivatives was performed using an HP1100 System (Agilent) on a Zorbax Eclipse XDB-C18 column (150 × 4.6 mm, 5 μm) at 25 °C with 0.5 mL/min flow. The MS detector was an MDS Sciex API 365 triple-quadrupole MS (Applied Biosystems) with electrospray ionization (flowing rate 5 μL/min; passive split). As eluents 10 mM ammonium acetate in water and 10 mM ammonium acetate in methanol were used. Analyses were performed by gradient elution but also isocratically (50% methanol) and gave comparable elution profiles as the normal HPLC (above).

Mass spectrometry was accomplished with electrospray ionization using the system Agilent 1100 MSD Trap SL both applying positive and negative ion detection.

All NMR spectra were measured in DMSO-d_6 at 300 K on a Bruker DRX-600 AVANCE spectrometer equipped with a triple resonance *xyz*-gradient inverse probe. Irradiation frequencies were 600.13 MHz for proton (^{1}H) and 150.86 MHz for carbon (^{13}C). Both 1D proton and carbon spectra were recorded with 32,768 data points. After zero filling to 65,536 data points the free induction decay was directly Fourier-transformed to spectra with a spectral range of 6000 Hz and 22,500 Hz for ^{1}H and ^{13}C, respectively. 2D pulse field gradient enhanced COSY, TOCSY, ROESY, HMQC, HMQC-TOCSY, and HMBC spectra were recorded using 1024 data points and 256 experiments for each spectrum. After linear prediction to 512 data points in the t_2 dimension and an appropriate sinusoidal multiplication in both dimensions, the spectra were Fourier-transformed. Mixing times of TOCSY and ROESY were 100 ms and 225 ms, respectively. Analysis of the spectra was performed using the XWINNMR 3.1 software. Chemical shifts were referenced to residual DMSO-d_5 ($\delta_H = 2.49$ ppm) and DMSO-d_6 ($\delta_C = 39.50$ ppm). All chemical shifts (δ) are given in ppm.

6′-*O*-Adamantanyl-β-cyclodextrin (10)

1@(**7-Cy**) (0.405 g, 0.30 mmol) was photolyzed for 4 h at 20 °C. For details about photolysis and work-up see above. Preparative HPLC of the aqueous residue, which was dissolved in ethanol (30%)-water and filtered, afforded under isocratic elution with ethanol (30%)-water a fraction 1, which was almost pure **7-Cy** (yield: 200 mg, 0.17 mmol) and one other homogeneous fraction which was identified as 6′-*O*-adamantanyl-β-cyclodextrin (**10**) (yield: 40 mg, 0.03 mmol, 10%). For HPLC data see Table 5; mp 305–308 °C (dec.); $[\alpha]_D^{20}$: +105.8 ± 0.3°; $[\alpha]_{546}^{20}$: +124.7 ± 0.3° (*c* 1.3, pyridine containing 5% of water); ^{1}H NMR and ^{13}C NMR data for DMSO-d_6 solution see Tables 6 and 7; MS (ESI): (M calcd. 1268.48) found: *m/z* 1291.5 $(M+Na)^+$ and 1267.5$(M-H)^-$, respectively; anal. calcd. for $C_{52}H_{84}O_{35} \cdot 1\ H_2O$: C 48.52, H 6.73; calcd. for 95% content [compare **1**@(**7-Cy**)[4]]: C 46.09, H 6.40; found: C 46.15, H 6.47.

Acknowledgements

We are indebted to the Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (Project P12533-CHE) for financial support. We thank the former American Maize-Products Company and Wacker Chemie for providing the cyclodextrins used in our studies. Dr. A. Leitner of the Institut für Analytische Chemie der Universität Wien (Abteilung Prof. W. Lindner) is thanked for performing the LC-MS and MS experiments.

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[13] Primary products resulting from C–H insertion of **Ad:** into the inner C–H bonds (3′ and 5′ of the glucose moieties) of α-cyclodextrin thus far have never been identified, although the contact with these protons is expected to be quite close. Embedded within the crystal of the **1**@2(**6-Cy**) complex, such a product might be quite strained. Thus the primarily formed tertiary alcohol at C-3′ could be oxidized by a Cannizzaro-like reaction to a ketone with concomitant extrusion of the reduced hydrocarbon **2**. Admittedly, this is a more speculative explanation for the high yield of adamantane (**2**) observed only in this particular case.

[14] Thermal decomposition of the **1**@2(**6-Cy**) complex at 230 °C or 300 °C also yields **2** as the major volatile compound. In these pyrolytic reactions a considerable amount of material decomposed so that quantitative yields are of little significance. An absolute yield of 12% was determined for **2** with a total recovery of adamantanyl residues of only 25% (by analysis of the compounds also found in photolytic experiments).

[15] Minute amounts of a third cyclodextrin derivative can be traced, but only in experiments at low temperature.

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