Photoelimination of nitrogen from adamantine and pentacycloundecane (PCU) diazirines: a spectroscopic study and supramolecular control

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Photochemical reactivity of pentacycloundecane (PCU) and adamantane diazirines was investigated by preparative irradiations in different solvents, laser flash photolysis (LFP) and quantum chemical computations. In addition, formation of inclusion complexes for diazirines with cucurbit[7]uril, β- and γ-cyclodextrin (β- and γ-CD) were investigated by ^{1}H NMR spectroscopy, isothermal microcalorimetry and circular dichroism spectroscopy, followed by investigation of photochemical reactivity of the formed complexes. Diazirines undergo efficient photochemical elimination of nitrogen (Φ_R > 0.5) and deliver the corresponding singlet carbenes. Singlet carbenes react in intra- and intermolecular reactions and we found a rare singlet carbene pathway in CH_3OH involving protonation and formation of a carbocation, detected due to the specific rearrangement of the pentacycloundecane skeleton. Singlet diazirines undergo intersystem crossing and deliver triplet carbenes that react with oxygen to form ketones which were isolated after irradiation. Our main finding is that the formation of diazirine inclusion complexes with β-CD and γ-CD changes the relative ratio of singlet *vs.* triplet pathways, with singlet carbene products being dominant from the chemistry of the irradiated complexes. Our combined theoretical and experimental studies provide new insights into the supramolecular control of carbene reactivity which has possible applications for the control of product distribution by solvent effects and choice of constrained media.

Introduction

Carbenes are reactive intermediates that have drawn scientific attention for more than 60 years. Seminal papers of Hine[1] and Doering[2] initiated a rapid development of carbene chemistry[3] and the advancements have been documented in several reviews.[4,5] Of particular importance are stable carbenes[6] applicable as useful ligands[7] in modern catalysis.[8] Despite significant progress in understanding carbene reaction mechanisms and reactivity, physical-organic aspects of carbene chemistry are still under intensive investigation.[9] We became interested in carbenes as intermediates during the preparation of strained polycyclic molecules,[10] particularly propellanes.[11,12]

Convenient precursors for photochemical or thermal formation of carbenes are diazirine derivatives.[13] Elimination of nitrogen occurs upon photochemical excitation or at elevated temperatures, thus delivering carbenes.[14] Adamantane diazirine is an especially convenient precursor for carbene investigation since it is stable and easy to handle.[15] Moreover, the formed adamantylidene can only undergo one type of intramolecular reaction: insertion into the γ-CH bond.[16-19] A rigid adamantane backbone and its inability to form anti-Bredt olefins results in a somewhat longer lifetime of the generated carbene, rendering it appropriate for the study of reactivity in intermolecular reactions.[20,21] Photochemical reactivity of adamantane diazirine has been investigated by irradiation experiments,[22] spectroscopically by fluorescence[23,24] and laser flash photolysis,[25-27] and theoretically.[28-30] The carbene formed in photolysis was also isolated in a matrix and spectroscopically characterized.[31] Additionally, complexation of adamantane diazirine with macrocyclic hosts[32] and zeolites[33] was conducted and the effects of supramolecular containers on photochemical reactivity were investigated. [34]

Herein we report the investigation of the photochemical reactivity for pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-diazirine (**1**) (PCU diazirine **1**) and adamantane diazirine **2**. PCU diazirine **1** was chosen as a probe for the formation of carbocations by carbene protonation. The rearrangement of this carbocation is anticipated due to the known nonclassical

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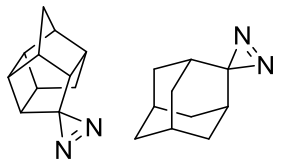
Electronic Supplementary Information (ESI) available: selected experimental procedures, UV-vis and fluorescence spectra of **1** and **2**, ITC, CD and ^{1}H NMR titrations, LFP and computational data, and ^{1}H and ^{13}C NMR spectra of prepared compounds. This material is available free of charge *via* the internet, see DOI: 10.1039/x0xx00000x

nature of the carbocation on the PCU skeleton.[35-37] Polycyclic carbenes have a nucleophilic character leading to the facile protonation with strong acids.[20,21,25,28] Protonation of carbenes is well known.[4] However, protonation of dialkyl carbenes by weak acids, such as alcohols, is usually not considered a plausible reaction pathway since reports of such reactivity are scarce.[19,38] In these systems, the reactivity of carbenes has usually been articulated as an concerted OH insertion reaction. In addition, the photochemical reactivity of **2** was investigated as a benchmark control in order to compare our experimental and computational results with previous reports.[22-34] Photoelimination of nitrogen was studied by preparative irradiations in different solvents and we also investigated the effects of host complexation on this reactivity. We found differences in product distribution upon irradiation of **2**, which provide new insights into the supramolecular control of carbene reactivity. The supramolecular reactivity is not only based on the cage effect of the host molecules which prevent bimolecular reactions,[32,34] but also on differences in population of singlet *vs.* triplet carbenes in the inclusion complexes. Furthermore, photoproducts derived from the PCU derivative **1** indicated reactivity of the carbene with an alcohol involving protonation to carbocations, a reaction that is not ubiquitous in dialkylcarbene chemistry. Laser flash photolysis (LFP) experiments in cooled solutions allowed for the detection of singlet carbenes in these systems. Our mechanistic investigation provides a detailed overview of plausible carbene reaction pathways, filling gaps that were not apparent in previous work. We also conducted theoretical studies of these polycyclic compounds to further confirm the interpretation of the obtained experimental results and to better understand the reaction mechanisms.



1 **2**

Results

Synthesis

Diazirines **1** and **2** were prepared in good yields from pentacyclo[5.4.0.0$^{2.6}$.0$^{3.10}$.0$^{5.9}$]undecan-8-one (**3**) and adamantan-2-one (**4**), respectively, according to the previously published procedure (Schemes S1 and S2 in the ESI).[39,40] A simple Jones oxidation of the intermediate diaziridine **6** gave **2** in 75% yield over two steps.[39] On the contrary, oxidation of diaziridine **5** could not be conducted in acidic conditions due to the known rearrangement of the PCU skeleton.[35-37] We therefore used a modified protocol with a silver salt, giving **1** in 71% yield in two steps (Scheme S1 in the ESI).[40]

Photophysical properties

The only chromophore in diazirines **1** and **2** is a N=N double bond that is characterized by a n→π* transition corresponding to the absorption maximum at ≈ 350 nm that populates the S_1 state. We measured absorption spectra in benzene, cyclohexane, and CH_3OH (see Figs. S1 and S2 in the ESI). The molar absorption coefficients are small (ε_{350} ≈ 100 $M^{-1}cm^{-1}$), in agreement with a symmetry forbidden transition. Accordingly, **1** and **2** are weakly emissive with maxima in their emission spectra at ≈ 400 nm. Quantum yields of fluorescence (Φ_f) for **1** and **2** were measured using quinine sulfate in 0.05 M H_2SO_4 as a reference[41] and amount to (2.5 ± 0.5) × 10^{-4} and (4.5 ± 0.3) × 10^{-4}, respectively (see experimental and the ESI). We attempted to measure singlet excited state lifetimes by single photon counting (SPC) but due to a very fast decay at the limits of the time resolution of the setup used and a fast decomposition of the samples (*i.e.*, their high photochemical reactivity), we can only state that both diazirines have S_1 lifetimes shorter than 100 ps, in accord with literature precedent for **2**.[24]

Formation of host@guest complexes

Ramamurthy *et al.* have shown that **2** forms an inclusion complex with cucurbit[7]uril (CB[7]) with a 1:1 stoichiometry and the association constant for **2**@CB[7] was measured by isothermal microcalorimetry (ITC) (DMSO-H_2O 3:2, $K_{1:1}$ = 6.5 × 10^5 M^{-1}).[34] Moreover, Brinker *et al.* have demonstrated formation of inclusion complexes of **2** with β- and γ-cyclodextrin (β-CD and γ-CD), where complexation led to induced circular dichroism signals. The association constants were determined from these signals (in EtOH-H_2O 3:7, **2**@β-CD $K_{1:1}$ = 6200 M^{-1}, **2**@γ-CD $K_{1:1}$ = 2700 M^{-1}).[32] The binding of **2** to β-CD and γ-CD was further investigated by molecular dynamics simulations.[42,43] Since complexation of **2** with macrocyclic hosts affects its photochemistry, irradiation of an aqueous solution of **2**@CB[7] gave predominately the intramolecular photoproduct dehydroadamantane (>90%),[34] whereas irradiations of solid state inclusion complexes **2**@β-CD and **2**@γ-CD gave dehydroadamantane together with the products where adamantane was covalently bound to β-CD or γ-CD, respectively.[44,45] Our approach was to conduct a systematic investigation of the complexation of **1** with CB[7], β-CD, and γ-CD by ^{1}H NMR spectroscopy, ITC and circular dichroism experiments. Moreover, we investigated the effects of complexation on the photochemical reactivity of these compounds. Titrations and irradiations in the presence of host molecules were all performed in DMSO-H_2O (1:1 or 1:9). Thus, constants measured in the supramolecular studies can be used for the calculation of the concentrations of the various species in the irradiated solutions, but these constants cannot be compared to literature precedent where measurements were performed in different solvents or in the solid state.

^{1}H NMR titrations of **1** and **2** with CB[7], β-CD, and γ-CD were conducted in DMSO-d_6-D_2O (1:9). In addition, due to problems with solubility, the titrations with β-CD and γ-CD were also

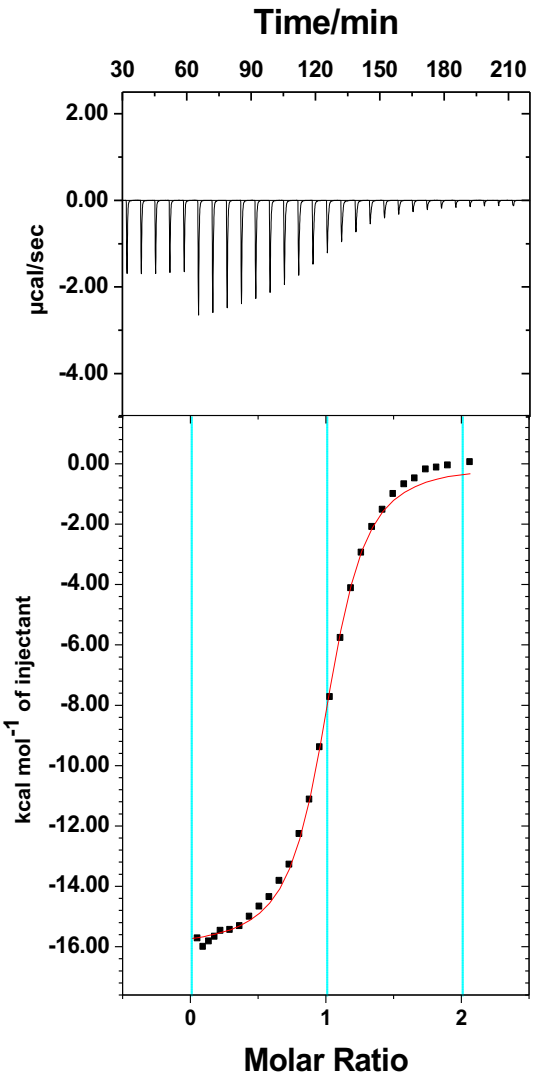


Fig. 1. Calorimetric titration of CB[7] (c = 0.05 mM) with **1** (c = 1 mM) at 25 °C in DMSO-H_2O (1:1). Top: raw ITC data; Bottom: dependence of the successive enthalpy change per mol of titrant on **1**:CB[7] ratio. The red line corresponds to the fit of the data to 1:1 complex stoichiometry.

performed in DMSO-d_6-D_2O (1:1) (for the corresponding spectra see Figs. S3-S12 in the ESI). The signals corresponding to **1** or **2** were shielded upon addition of the hosts, as expected for the formation of inclusion complexes. A more pronounced shielding effect was observed with CB[7] and γ-CD than with β-CD. In the titrations with β-CD and γ-CD, the exchange rate between free and complexed guest was fast on the ^{1}H NMR timescale because no distinct resonances for the protons of the free and bound guests were observed. On the other hand, in titrations with CB[7] when the concentrations of guests were higher than those of CB[7], the signals of the unbound guest were observed along with the complex, indicating a slow exchange between the complexed and the free form, probably due to the formation of a very stable complex with a 1:1 stoichiometry. In the NOESY spectrum for **1** and CB[7], no NOE interaction was observed between the host and the guest H-atoms, although the inclusion complex was formed (*vide infra*). The absence of NOE interactions is due to low quality of the NOESY spectrum imposed by low solubility of the host and the guest in DMSO-H_2O. On the other hand, data from NOESY spectra for **1** and β-CD or γ-CD, as well as NOESY for **2** and all hosts support the formation and the structures of inclusion complexes (for all NOESY spectra and data see Figs. S13-S20 and Table S1 in the ESI). NOESY spectra for **2** and CB[7] (Fig. S15 in the ESI) are in agreement with the computed structures by Ramamurthy *et al.*[34] and Brinker *et al.*,[45] where the lipophilic part of molecules enters into the CB[7] or β-CD cavities while the diazirine chromophore remains outside the host and is exposed to water molecules.[34] Furthermore, the much larger γ-CD cavity can probably accommodate the whole molecule of **1** or **2** (Fig. S19 in the ESI).

ITC titrations were conducted in DMSO-H_2O (1:1) (Figs. 1, S21, S22 and Table S2). Binding of **1** and **2** with CB[7] is enthalpically favored but entropically disfavored. The equilibrum constants for 1:1 complexes are large (Table 2) and similar to those

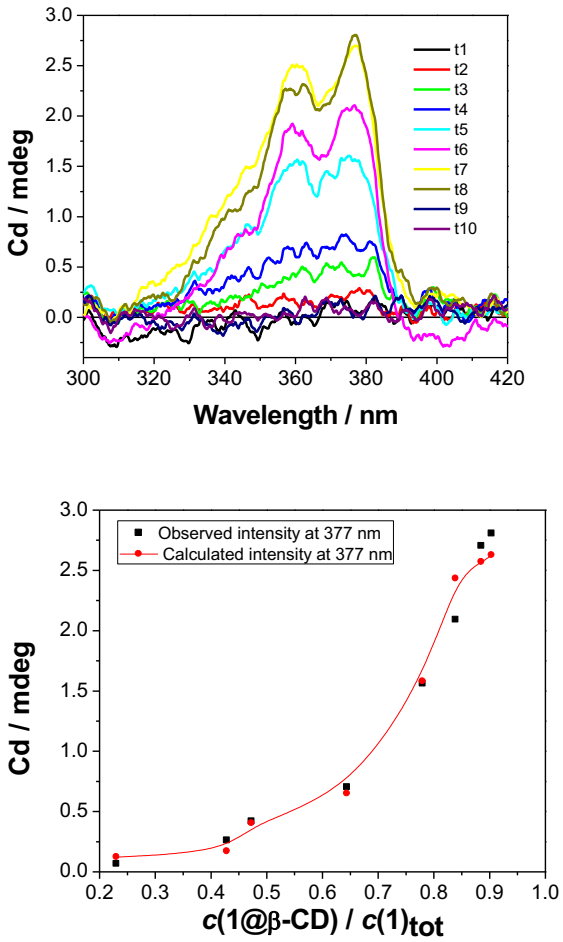


Fig. 2. Top: Circular dichroism spectra of solutions containing **1** (0.14-1.00 mM) and β-CD (0.4-12 mM, according to Table S3) in DMSO-H_2O (1:1). Bottom: Dependence of the intensity for the circular dichroism signal (mdeg) on the increase in complex **1**@β-CD concentration expressed as c(**1**@β-CD)/c(**1**)$_{tot}$. The red line only connects the calculated points and does not correspond to a fit of the experimental data.

reported by Ramamurthy *et al.* in a solvent containing more DMSO.[34] On the other hand, the heat evolution for the binding of **1** and **2** with β-CD and γ-CD was too low to reliably determine the association constants using ITC. Only for **2**@β-CD we obtained ITC results which could be processed, however, the determined thermodynamic parameters contained large errors (Table S2). We therefore determined the binding constants with β-CD and γ-CD by circular dichroism spectroscopy (for all circular dichroism data see Figs. S23-S28 and Tables S3-S5 in the ESI).

Diazirine **2** is an achiral molecule, whereas **1** is chiral but present as a racemic mixture in our studies. Upon binding of **1** or **2** to chiral β-CD and γ-CD, induced circular dichroism signals were observed at the wavelengths where **1** and **2** absorb light (for **1** see Fig. 2), clearly indicating the formation of complexes. Since the induced circular dichroism signal is directly proportional to the concentration of the inclusion complex, the spectra were processed by nonlinear regression analysis and the association constants for the complexes were determined (Table 1). In contrast to the association constants measured by Brinker *et al.* in EtOH-H_2O,[32] our measurements for both **1** and **2** in DMSO-H_2O (1:1) indicate the formation of a more stable complexes with γ-CD than with β-CD. It should be noted that the racemic diazirine **1** probably forms two different complexes, with different values of the association constant for each enantiomer. The obtained results therefore represent an averaged value for the binding of both isomers. Stereodifferentiation of enantiomers of **1** with β-CD and γ-CD is beyond the scope of this work and does not affect the interpretation of photochemical studies reported herein.

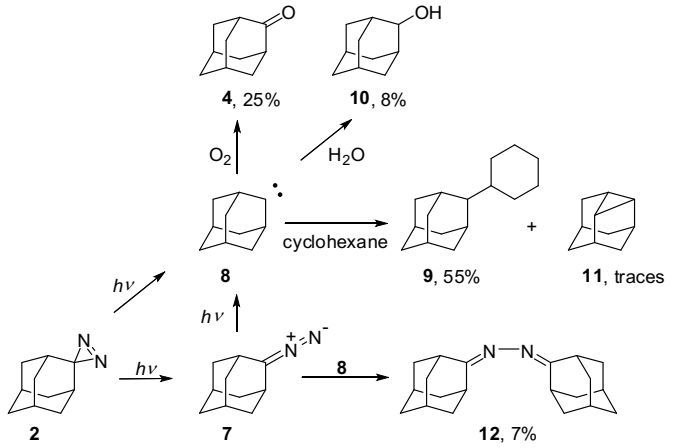
Table 1. Stability constants, log ($K_{1:1}$ / M^{-1}), for the inclusion complexes of **1** and **2** with CB[7], β-CD and γ-CD.[a]

	1	2
CB[7]	5.9 ± 0.1 [b]	6.4 ± 0.1 [b]
β-CD	2.98 ± 0.01 [c,d]	3.4 ± 0.3 [b]
		2.93 ± 0.03 [c]
γ-CD	3.50 ± 0.02 [c,d]	4.0 ± 0.1 [c]

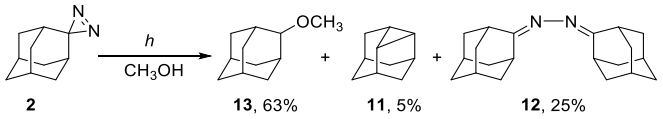
[a] Measurements were conducted in DMSO-H_2O (1:1) at 25 °C. The quoted errors are obtained from nonlinear regression analysis and not from independent measurements. [b] Determined by ITC. [c] Determined by circular dichroism. [d] Average constant determined for a racemic mixture.

Photochemistry

The photochemistry under different conditions was studied and the products were fully characterized in order to understand the photochemical reactivity of diazirines **1** and **2**, as well as the reactivity of the corresponding carbenes formed upon photoelimination of nitrogen. Although the photochemical reactivity of **2** has been studied previously,[16-21] we first conducted irradiations of **2** under different conditions in order to compare our experimental results with literature precedent and establish the dependence of product distribution on photolysis conditions. Irradiations of **1** and **2**



Scheme 1. Photochemistry of **2** in cyclohexane.



Scheme 2. Photochemistry of **2** in CH_3OH.

were performed in benzene, cyclohexane and CH_3OH and the irradiated mixtures were analyzed by GC, GC-MS, ^1H NMR spectroscopy and chromatographed on silica gel to isolate the photoproducts. The isolated fractions enriched in products were reanalyzed by GC, GC-MS, and ^1H NMR spectroscopy to determine the reaction yields (Tables 2 and 3); structures of photoproducts are shown in Schemes 1-5. In the photolysis of **2** all products (Schemes 1 and 2) were isolated from the mixtures or identified by comparison with authentic samples that were synthesized or purchased. The only exception was the very volatile dehydroadamantane **11** which was detected by GC-MS only.

In the irradiation experiments in cyclohexane and benzene we detected ketone **4** and alcohol **10** (Scheme 1). These products are probably formed in the reaction of triplet carbene **8** with O_2 and singlet carbene **8** with H_2O, respectively. Namely, singlet carbenes react with O_2 slowly ($k < 10^8$ $M^{-1}s^{-1}$),[5] whereas the rate constant for triplet carbenes approaches diffusion limits (k = 10^8-10^{10} $M^{-1}s^{-1}$).[5] Therefore, it is more likely that ketone **4** was formed from the triplet carbene **8**, even though the singlet carbene **8** is lower in energy than the corresponding triplet (*vide infra*). However, formation of **4** from singlet carbene **8** *via* a carbonyl oxide[27] cannot be completely disregarded. On the other hand, singlet carbenes react with H_2O or alcohols such as CH_3OH with a rate that is diffusion controlled.[46] Triplet carbenes react with alcohols much slower because the reaction involves H-atom transfer and formation of triplet biradicals.[5] Seeing as the solvent was not dried prior to irradiations, traces of H_2O facilitated formation of alcohol **10**. Furthermore, traces of dissolved O_2 were present in the irradiation experiments, even though the solution was purged with Ar prior to the irradiation, giving ketone **4**. Thus, the irradiation of **2** in air-saturated and O_2-

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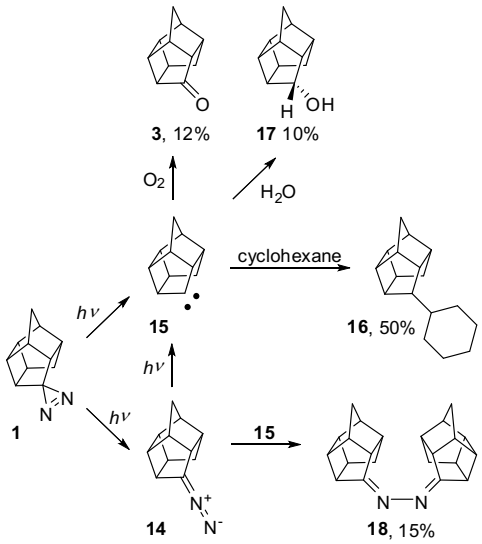
Table 2. Photolysis of **2** under different reaction conditions. Amounts of recovered **2** and the photoproducts are given in %.[a]

Solvent	**2**	**4**	**9**	**10**	**11**	**12**	**13**
cyclohexane	5	25	55	8	traces	7	-
cyclohexane (well dried and deaerated)	0	13	66	0	traces	20	-
C_6H_6	5	17	-	39	10	29	-
C_6H_6 (well dried and deaerated)	0	20	-	0	10	70	-
C_6H_6 + air	4	32	-	48	4	12	-
C_6H_6 + O_2	4	50	-	30	3	13	-
CH_3OH	6	-	-	-	5	25	63
DMSO-H_2O [b]	2	12	-	24	2	60	-
DMSO-H_2O + CB[7] [c]	1	15		30	1	54	-
DMSO-H_2O + β-CD [b, d]	4	2	-	78	3	13	-
DMSO-H_2O + β-CD + CH_3OH [d]	7	1	-	17	3	19	51
DMSO-H_2O + β-CD + O_2 [d]	1	1	-	84	1	13	-
DMSO-H_2O + γ-CD [d]	4	1	-	81	1	13	-
DMSO-H_2O + γ-CD + CH_3OH [d]	3	1	-	63	1	13	17
DMSO-H_2O + γ-CD + O_2 [d]	1	1	-	84	1	13	-

[a] Irradiated **2** (20 mg, 0.12 mmol) in 100 mL of the solvent (c = 1.23 × 10^{-3} M) at 350 nm (5 min, 14 lamps × 8W). The solution was purged with Ar prior to irradiation unless specified otherwise. Yields were determined by combination of GC, ^{1}H NMR and separation on column chromatography and weight of the isolated fractions and their GC and ^{1}H NMR analysis. The estimated error on all values is ± 5-10%, and the difference to 100% corresponds to unidentified products. [b] Photolysis was performed twice and the average value is reported. [c] c (CB[7]) = 1.0 × 10^{-4} M. [d] c (CD) = 1.32 × 10^{-2} M.

purged benzene solution gave a higher yield of ketone **4** (Table 2). Since it is known that traces of H_2O in the solvent system may perturb the equilibrium between the singlet and triplet carbenes, as shown for diphenylcarbene,[47] we performed additional irradiation experiments of **2** in ultra- pure, well dried and deaerated cyclohexane and benzene solutions whereupon cyclohexane adduct **9** was formed predominantly. In addition, **11** and **12** were detected by GC-MS together with some traces of ketone **4** (Table 2). The main cyclohexane adduct **9** was formed by an insertion reaction of carbene **8** into a C-H bond of cyclohexane, whereas irradiation in CH_3OH gave the anticipated ether **13** as the main product (Scheme 2). The amount of azine product **12** is highly dependent on the solvent used and on the substrate concentration, since this product stems from a bimolecular pathway involving two intermediates, diazo compound **7** and carbene **8**. It should be noted that traces of H_2O or dissolved O_2 in the solvent system may affect the relative ratio of products, due to their effect on the equilibrium between the singlet and triplet carbene.[47] However, formation of side-products **4** and **10** gives insight into pathways which would not be detected in ultra-pure solvent systems without any trace of H_2O or O_2.

Upon irradiation of **1** in cyclohexane, we isolated the main product **16** formed from the insertion reaction of carbene **15** into a C-H bond of the cyclohexane (Scheme 3). In addition, we



Scheme 3. Photochemistry of **1** in cyclohexane.

detected alcohol **17** and ketone **3**, formed due to the presence of traces of H_2O and O_2, respectively. However, in ultra-pure, well dried and deaerated cyclohexane the main photoproduct was **16**. Azine **18** is formed in a bimolecular reaction from carbene **15** and diazo compound **14**. After the irradiation of **1**

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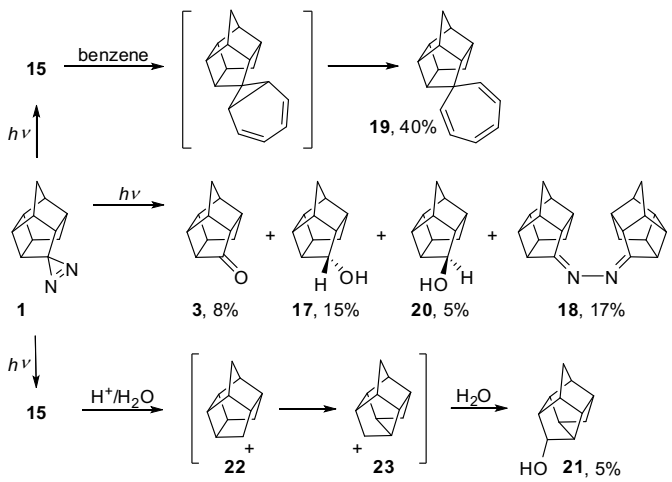
Table 3. Photolysis of **1** under different reaction conditions. Amounts of recovered **1** and the photoproducts are given in %.[a]

Solvent	**1**	**3**	**16**	**17**	**18**	**19**	**20**	**21**	**24**	**25**	**26**
Cyclohexane [b]	0	12	50	10	15	-	-	-	-	-	-
cyclohexane (well dried and deaerated)	10	1	85	0	4	-	-	-	-	-	-
C_6H_6[b]	0	8	-	15	17	40	5	5	-	-	-
CH_3OH [b]	10	-	-	-	-	-	-		50	13	18
DMSO-H_2O [b]	7	5	-	6	50	-	4	9	-	-	-
DMSO-H_2O + CB[7] [c]	16	2	-	2	70	-	2	7	-	-	-
DMSO-H_2O + β-CD [d]	5	2	-	7	63	-	4	14	-	-	-
DMSO-H_2O + γ-CD [d]	8	-	-	15	26	-	23	46	-	-	-

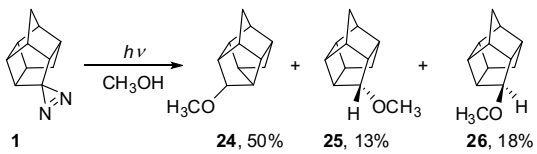
[a] Irradiated **1** (20 mg, 0.11 mmol) in 100 mL of the solvent (c = 1.23 × 10^{-3} M) at 350 nm (2 min, 14 lamps × 8W). The solution was purged with Ar prior to irradiation unless specified otherwise. Yields were determined by combination of GC, ^{1}H NMR and separation on column chromatography and weight of the isolated fractions and their GC and ^{1}H NMR analysis. The estimated error on all values is ± 5-10%, and the difference to 100% corresponds to unidentified products. [b] Data corresponds to the average of several experiments (number of photolyses is reported in the experimental section). [c] c (CB[7]) = 1.0 × 10^{-4} M. [d] c (CD) = 1.32 × 10^{-2} M.



Scheme 4. Photochemistry of **1** in benzene.

in benzene, we isolated benzene adduct **19** and the rearranged alcohol **21**, whereas other products (Scheme 4) were detected and compared with the authentic samples synthesized by other methods (see Scheme S3 in the ESI). Formation of the benzene adduct can be explained by a carbene addition to a benzene double bond and formation of a cyclopropyl intermediate that undergoes ring expansion to the isolated compound **19**. Alcohol **21** is probably formed due to the protonation of carbene by H_2O that was present in trace amounts in the solvent. Formation of carbocation **22** may have taken place by protonation and decomposition of diazo compound **14**.[48] However, the decomposition of **14** is a less likely pathway since it is slow (taking place over hours), and rearranged alcohols were observed immediately after the irradiation. In any case, the protonation of carbene **15** gives **22** which is a nonspecific cation undergoing rearrangement and ultimately delivering alcohol **21** which was isolated. Similarly, upon irradiation of **1** in CH_3OH, the main product was the rearranged ether **24**, whereas non-rearranged PCU ethers **25** and **26** were minor products (Scheme 5).

Photochemical products **16**, **19**, **21**, and **24** were isolated from the irradiation mixtures, whereas other products formed in small quantities were independently synthesized to enable full spectroscopic characterization (see Scheme S3 in the ESI). It was especially important to prepare PCU alcohols and ethers that had not yet been discovered as products in photoreactions and to determine their structure by 2D NMR in



Scheme 5. Photochemistry of **1** in CH_3OH.

order to elucidate the spatial orientation of the OH and OCH_3 groups and compare these spectra and the GC retention times with the products obtained in the photolysis experiments.

The overall reaction efficiencies in different solvents were determined by measuring photochemical quantum yields (Φ_R) using the ferrioxalate actinometer (Φ_{355} = 1.25).[49] The samples were irradiated at 350 nm and the progress of the reaction was monitored by the decrease of absorbance at this wavelength (Table 4).

Table 4. Quantum yields (Φ_R) for the photoelimination of nitrogen from diazirines **1** and **2**.[a]

Solvent	Φ_R (**1**) [b]	Φ_R (**2**) [b]
cyclohexane	0.5 ± 0.1	0.8 ± 0.1
benzene	0.7 ± 0.1	0.8 ± 0.1
CH_3OH	0.6 ± 0.1	0.6 ± 0.1

[a] Measurement were conducted by irradiating the samples at 350 nm with the use of ferrioxalate actinometer (Φ_{355} = 1.25).[49] Measurements were done in triplicate, the mean value is reported and the errors correspond to maximum absolute deviations. [b] Quantum yields of compound decomposition, Φ_R, was calculated according to Eqs. S4-S6 in the ESI.

Photochemistry in inclusion complexes

Brinker *et al.* and Ramamurthy *et al.* reported on the influence of supramolecular hosts on the partition between different photochemical pathways of **2**.[34,45,46] With the aim to study such supramolecular effects further, we performed irradiations of **1** and **2** in DMSO-H_2O (1:9) with and without host molecules (CB[7], β-CD, and γ-CD). The necessary concentration of hosts was calculated from the stability constants (Table 1), to ensure that >90% of the guest was complexed. However, in the irradiation experiments with CB[7], due to its low solubility (< 1 mM), the percentage of the free guest was ≈ 90%. All our irradiation experiments for the inclusion complexes point to somewhat different results than previously reported.[34,45,46] We have not observed the reaction of carbenes with β-CD and γ-CD as reported by Brinker *et al*.[45,46] However, the results are not directly comparable since Brinker *et al*. performed their irradiations in the solid state. As anticipated, irradiations of solutions containing the inclusion complexes of **2** generally gave lower yields of azine dimeric products. However, we did not observed higher yields of dehydroadamantane upon irradiation of **2**@CB[7], **2**@β-CD, and **2**@γ-CD. Irradiations instead gave higher yields of alcohol **8** compared to ketone **4** (Table 3). The irradiation of the inclusion complex **2**@β-CD in a solution that was O_2-purged gave approximately the same distribution of products as an Ar-purged solution. These results indicate that the β-CD host prevents diazirine **2** or the corresponding carbene from interacting or reacting with O_2 (*vide infra*). However, the irradiation of **2**@β-CD in the presence of CH_3OH gave ether **13** in a three times higher yield than alcohol **10**, indicating that β-CD cannot prevent the carbene from reacting with CH_3OH. The result can be explained by preferential solvation of the CD cavities by CH_3OH, or formation of ternary complexes, as found by Bohne *et al*.[50] Furthermore, the changes of the solvation around carbene intermediates were shown to lead to different equilibration between the singlet and triplet carbene.[47] A similar but less pronounced trend was observed upon irradiation of the complexes with **1**. Thus, upon irradiation of **1**@γ-CD a significantly higher yield of the rearranged alcohol **21** was obtained when compared to irradiations without the host molecule.

Laser flash photolysis

LFP experiments were conducted to characterize carbenes and other plausible intermediates formed in the photochemistry of **1** and **2** (for additional LFP data see Figs. S29-S46 in the ESI). LFP experiments were first performed in benzene where the corresponding carbenes should have the longest lifetime due to the chemically inert nature of this solvent. Prior to the measurement, the solutions were purged with N_2 or O_2 since differences were anticipated due to the reactivity of carbenes with O_2. It is generally known that singlet carbenes react with O_2 slowly and are usually not quenched by O_2, whereas triplet carbenes react with rates that are diffusion controlled.[5]

In the N_2-purged benzene solution of **2** a negative signal was observed at 350-450 nm at short delays after the laser flash due to fluorescence from precursor **2** and irreversible bleaching of the precursor absorption caused by light absorption of the laser pulse (Fig. S30 in the ESI). A positive signal at < 330 nm was detected and its formation was very fast, almost within the laser pulse ($k_{obs} \approx 4 \times 10^7$ s^{-1} for the N_2-purged solution and $k_{obs} \approx 2 \times 10^7$ s^{-1} for the O_2-purged solution). This signal, which did not decay, corresponded to the formation of a stable product since the same absorption was detected after the LFP measurements by UV-vis spectroscopy (Fig. S29 in the ESI). A candidate for the assignment of this transient is the diazo intermediate **7** that is known to be formed from diazirines in a high quantum yield.[22] However, **7** has a maximum absorption at 240 nm and it does not absorb at 300 nm,[22] eliminating **7** as the assignment for the transient with an absorption at 300 nm. We assigned the signal at 300 nm to azine **12**, the only photoproduct that has a chromophore. This assignment is based on literature precedent,[26,27] and the fact that the absorbance measured at 300 nm after the LFP experiment does not decay; it corresponds to a product, not a transient species. Purging the solution with O_2 did not change the appearance of the absorption spectra in the LFP experiment. Thus, in a benzene solution at rt the carbene formed from **2** or other plausible intermediates such as radicals or triplets were not detected. Furthermore, the detection of diazo compound **7** that absorbs light at wavelengths < 280 nm was not possible in our experiment due to the absorption of benzene and low intensity of the Xe-lamp at these wavelengths.

LFP experiments were conducted in the presence of pyridine (Fig. S31 in the ESI), an ubiquitous quencher of singlet (but not triplet) carbenes.[26,27] Here we detected the characteristic strong transient absorption with a maximum at ≈ 400 nm that was assigned to adamantane ylide. This assignment is based on the reaction of adamantylidene carbene with pyridine (k_q =

(1.5-1.8) × 10^6 $M^{-1}s^{-1}$),[25] giving rise to a strong absorption at 400 nm. The formation of the ylide can be time resolved (pseudo-first order reaction k_{obs} = (1-2) × $10^7 s^{-1}$), as well as its decay (k = 9.1 × 10^2 s^{-1}, τ = 1.1 ± 0.2 ms). Thus, the adamantylidene singlet carbene was indirectly detected by means of its intermolecular reaction with pyridine. Platz *et al.* intercepted the formation of ylides with alcohols giving lower yields but not affecting the ylide formation rate constant.[26] Based on their finding they concluded that an intermediate on the pathway between **2** and the corresponding carbene should exist that can react with alcohols but the structure was not assigned.[26] This transient probably corresponds to diazo intermediate **7**. However, we cannot say if **7** is indeed formed because we cannot probe the required region in the spectrum.

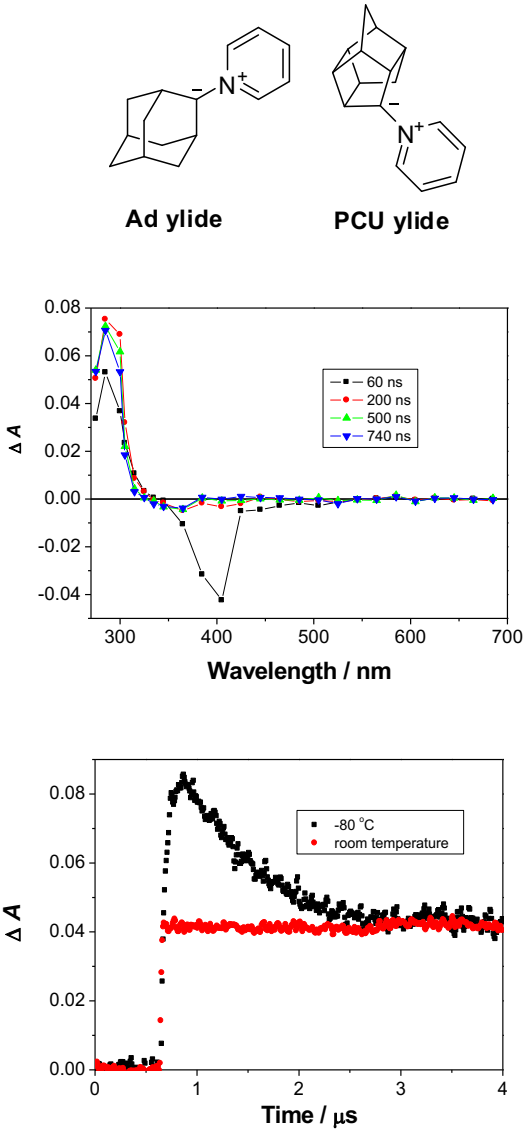


Fig. 3. Transient absorption spectra of a N_2-purged solution of **2** in pentane at -80 °C, where the dots presented in the spectra are average values of Δ*A* in the time window of 40-80 ns, 150-200 ns, 440-560 ns or 700-780 ns after the laser pulse (top); and decay of transient absorption for **2** at 300 nm in N_2-purged pentane solution at ≈ -80 °C and at rt (bottom).

Platz *et al.*[26] and Wirz *et al.*[27] estimated the lifetimes of the singlet carbene from the growth kinetics of azine or ylide formation and these lifetimes are generally in the order of 50-700 ns, depending on the solvent and the presence of trace amounts of H_2O. Decreasing the temperature should prolong the carbene lifetimes because of slower unimolecular, and particularly bimolecular reactions. We conducted LFP experiments in a N_2-purged pentane solution at rt and a cooled solution that was kept between -80 and -90 °C (Fig. 3). Contrary to rt, in the cooled solution we detected a transient at 280-300 nm that decayed following unimolecular kinetics with the lifetime of 650 ns. The transient absorption does not decay to the baseline since its absorption overlaps with the one of azine photoproduct **12**. Upon increase of the temperature, the transient was not detected and only formation of **12** was observed. The same LFP experiments were performed for **1** in a pentane solution at -80 °C and at rt, where we detected the analogous transient only in the cold solution that decayed with the lifetime of 480 ns (Figs. S36-S38 in the ESI). The transients were tentatively assigned to carbenes **8** and **15**.

The assignment of the transients detected in cold pentane to **15** and **8** was corroborated by computations and quenching experiments. The computed absorption spectra of **15** and **8** have the strongest absorption band at ≈ 300 nm (Fig. S47 in the ESI), corresponding to the excitation to S_5 and S_4, respectively. The absorption band corresponding to the $S_0 \rightarrow S_1$ transition for carbenes is in the visible region, but its oscillator strength is very small (*vide infra*). We attempted to quench the transient absorbing at 300 nm in the cold pentane solution with O_2. However, we obtained similar decay kinetics for both the N_2- and the O_2-purged pentane solution of **1** at -90 °C (Fig. S38 in the SI), meaning that O_2 did not quench the transient. This finding agrees with the assignment of the transient to a singlet carbene. Taking into account the slow reactivity of singlet carbenes with O_2,[5] the solubility of O_2 in pentane (c = 17.7 mM at 20 °C and 1 atm),[51] and the fast decay kinetics, the singlet carbene could not be quenched by O_2. On the contrary, for a pentane solution of **1** at -90 °C, in the presence of CH_3OH, the transient at 300 nm was not detected, indicating that CH_3OH quenched the transient (see Fig. S39 in the ESI). Based on the known quenching of singlet carbenes with CH_3OH, the transient at 300 nm detected only in a cold solution can most likely be assigned to singlet **15** and **8**.

In the transient absorption spectra for the N_2-purged benzene solution of **1** at a short delay after the laser pulse, fluorescence from the sample was detected that gave a negative signal covering almost the whole spectrum. However, with a delay of > 100 ns, a transient was detected absorbing in the visible part of the spectrum with a maximum at 450 nm (Fig. 4). The transient decayed with unimolecular kinetics to the baseline with a lifetime of 10 ± 1 μs. This transient was detected also in the solution purged with O_2, but its decay was faster (τ = 125 ± 5 ns, where the shortening of the lifetime corresponds to k_q = 8.8 × 10^8 $M^{-1}s^{-1}$). Based on the quenching with O_2, the transient could be assigned to a triplet excited state, a biradical or a triplet carbene. In particular, the reported quenching

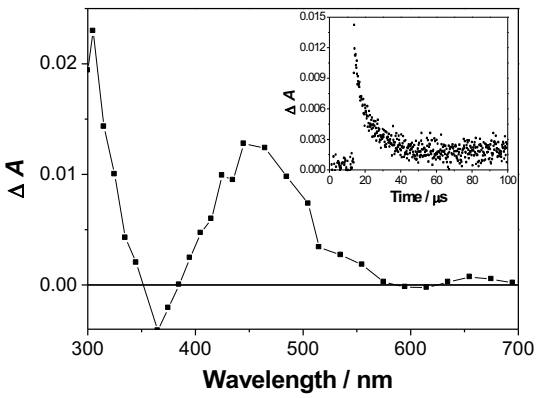


Fig. 4. Transient absorption spectrum of **1** in a N_2-purged benzene with the delay of 170 ns (average value of Δ*A* in the time window of 100-240 ns after the laser pulse), Inset: decay of the transient at 450 nm.

constants for triplet carbenes with O_2 have similar values (k = 10^8-10^{10} $M^{-1}s^{-1}$).[5] To assign the transient, quenching with pyridine and CH_3OH was performed. Whereas pyridine did not quench the transient, CH_3OH did. The slope of the k_{obs} *vs.* CH_3OH concentration gave the k_q = (9 ± 1) × 10^6 $M^{-1}s^{-1}$, which is close to the reported values for hydrogen abstraction by triplet carbenes (k = 10^6-10^7 $M^{-1}s^{-1}$).[5] Consequently, the transient can most likely be assigned to the triplet carbene **15**. Although triplet carbene **15** is higher in energy then the singlet, it could be formed *via* the triplet excited state of diazirine **1**.

In N_2- and O_2-purged benzene solutions of **1**, in addition to the transient absorbing at ≈ 400 nm, formation of azine products **18** can be observed at λ < 350 nm, similar to the spectra of **2**. Azine products **18** are formed much faster (pseudo-first order reaction, k_{obs} ≈ 4 × 10^7 s^{-1}) than the transient at 400 nm assigned to the triplet **15** decays (k = 1 × 10^5 s^{-1}), precluding that the triplet carbene **15** is an intermediate in the formation of **18**. The reaction probably involves singlet carbene **15**.

Addition of pyridine to the solution of **1** gave a characteristic transient absorbing at 400 nm, assigned to PCU ylide (Fig. S34 in the ESI) that was formed with the approximate pseudo-first order rate constant of k_{obs} ≈ (3-5) × 10^7 s^{-1}. The ylide was formed more efficiently from **1** when compared to the ylide from **2** (based on the stronger signal of the optically matched solutions and assumption that transients have similar molar absorption coefficients) and was longer lived with a lifetime of 8.5 ± 0.5 ms. In the presence of pyridine, the transient assigned to triplet **15** was not quenched.

LFP studies were also conducted for **2** in DMSO-H_2O in the absence and presence of CB[7] or β-CD (Figs. S42-S46 in the ESI). We anticipated that inclusion complexes may prevent carbenes to react with H_2O, thus making them longer-lived and detectable by LFP. The main obstacle for these experiments was the low solubility of compounds **1** and **2** in aqueous solvents. In the transient absorption spectra of **2** no positive signal was observed in the presence of CB[7] or β-CD, indicating that **8** was not detected. This result agrees with the preparative irradiations of the inclusion complexes where we observed increased yields of alcohol **10** and not of dehydroadamantane **11**. Therefore, both preparative irradiations and LFP experiments indicate that these supramolecular hosts do not prevent carbene **8** from reacting with water. It is known that singlet carbenes react with H_2O with a rate constant that is diffusion controlled.[4,5] Thus, in the transient absorption spectra of **2** in DMSO-H_2O (1:9) in the presence of pyridine (without any host) no ylide formation could be detected due to a faster reaction of **8** with H_2O than with pyridine.

Computations

In order to further rationalize the observed experimental results, we performed theoretical studies dealing with the properties of diazirines **1** and **2** as well as the corresponding diazo intermediates **14** and **7** and carbenes **15** and **8**. Since choosing a suitable approach for computing carbene structures is not a trivial matter,[52] we decided on a recently developed DFT method that was already used for polycyclic carbenes.[21] More specifically, we chose a MN12-SX/6-311+G(d) level of theory that was successfully applied for describing 2-adamantylidene (**8**) reactivity and its nucleophilic character toward alkenes.[21] The DFT approach was selected due to its time cost efficiency and the possibility of later expansion to comparable TD-DFT computations necessary for obtaining the simulated UV-vis spectra (*vide infra*). After optimizing the singlet and triplet structures of carbenes **15** and **8** in the gas phase and in selected solvents using the CPCM solvation model and confirming the obtained minima by frequency analysis, we compared their respective ground state triplet-singlet gaps. The obtained results are shown in Table 5. Previously it was shown both experimentally[31] and computationally[30] that the singlet ground state is preferential for 2-adamantylidene (**8**). It is known that the triplet-singlet gap for **8** amounts in the gas phase to Δ*G* = 3.4 kcal mol^{-1} (computed at the MP2/cc-pVTZ//CCSD(T)/cc-pVTZ level of theory) and in alkane solvents it ranges from 4 to 5 kcal mol^{-1}.[30] Consequently, less than 0.001 of carbene molecules are present in the triplet ground state at 298 K at equilibrium conditions, making the singlet the dominant species.[25]

Table 5. Triplet-singlet gaps for polycyclic carbenes **15** and **8** computed at the MN12-SX/6-311+G(d) level of theory with a CPCM solvation model used. Values in parentheses correspond to the difference in electronic energies (Δ*E*) in kcal mol^{-1}.

T-S	$\Delta G_{298.15K}$ / kcal mol^{-1}						
	gas phase	water	DMSO	benzene	cyclohexane	hexane	pentane
15	7.8 (7.9)	11.1 (11.4)	11.1 (11.3)	9.5 (9.7)	9.3 (9.5)	9.2 (9.4)	9.2 (9.3)
8	5.6 (5.2)	8.9 (8.7)	8.9 (8.7)	7.3 (7.0)	7.1 (6.8)	7.0 (6.7)	6.9 (6.7)

Table 6. Energy difference between singlet S_1 and triplet T_1 state for diazirines **2** and **1** and diazo compounds **7** and **14** computed at the TD-MN12-SX/6-311+G(d) level of theory with a CPCM solvation model used.

	$\Delta E(S_1\text{-}T_1)$ / kcal mol^{-1}			
compounds	gas phase	water	DMSO	pentane
2	16.0	16.3	16.2	15.9
1	15.9	16.4	16.3	15.9
7	10.4	11.5	11.5	10.8
14	10.3	11.4	11.4	10.7

Our computational results are in complete agreement with previous reports[21,30] and, what is more, the triplet-singlet gaps of **15** and **8** are also comparable. Similar gap energies were anticipated since both carbenes are integrated into the framework of the respective polycyclic skeleton. Accordingly, the singlets are in all cases more stable than the corresponding triplets, with **15** having a slightly larger gap (*e.g.*, 7.8 *vs.* 5.6 kcal mol^{-1} in the gas phase, Table 5). Since singlet 2-adamantylidene (**8**) has a somewhat larger dipole moment than the triplet (2.7 *vs*. 1.0 D in the gas phase),[30] its preferential stabilization is expected in more polar solvent, as observed (Table 5). The same trend holds true for **15**. We have not performed QM/MM computations to investigate the influence of solvent mixtures to relative energies of singlet and triplet carbenes, as it was performed for diphenylcarbene.[47] However, the ground state in diphenylcarbene is a triplet and the singlet carbene becomes more stable upon interaction with two H_2O molecules.[47] In our case, singlet carbenes **8** and **15** are more stable than the corresponding triplets in all solvents and we do not have any indication that preferential solvation in some solvent mixture may lead to triplet carbenes becoming more stable. We also computed vertical excitation energies (VEE)[53] of carbenes **15** and **8** at the TD-MN12-SX/6-311+G(d) level of theory in the gas phase and in pentane using the CPCM solvation model. The resulting simulated UV-vis spectra in pentane (Fig. S47 in the ESI) are in good agreement with the experimental absorption spectra obtained by LFP (*vide supra*). We tentatively ascribed the strongest absorption bands for **15** and **8** at ≈ 300 nm to the excitation to S_5 and S_4, respectively. The molecular orbitals involved in the transitions are shown in Fig. S50 in the ESI.

Using the same level of theory as for the computation of carbenes, we also computed vertical excitations for singlet and triplet excited states of diazirines **1** and **2** in several solvents and compared the energetic difference between the S_1 and the T_1 state (Table 6) as well as for several higher T_n states (Table S16 and Fig. S53 in the ESI). A relatively large energy difference between the S_1 and the T_1 indicates that intersystem crossing (ISC) between these states is not highly probable but it may take place if it involves the $n\pi^* \rightarrow \pi\pi^*$ transition, according to the El-Sayed rules.[54] Furthermore, higher excited triplet states are all significantly higher in energy then S_1, precluding their population. However, the formation of ketones **3** and **4** can be explained by the population of diazirine triplet excited state which undergoes elimination of nitrogen and gives carbenes in the triplet manifold. To get an insight into the probability of ISC, in addition to higher excited state energy levels computed for **1** and **2**, molecular orbitals (MOs) were used to evaluate the type of the transition. The MOs that are involved in the transition corresponding to the S_1 excitation (HOMO→LUMO+1, see Fig. S51 in the ESI) suggest that this state can mostly be described as a $n\pi^*$ configuration, although it is an approximation since the HOMO orbital has significant charge density along the σ bonds of the polycyclic skeleton. Similarly, the T_1 state can also mostly be described as a $n\pi^*$ configuration with the n orbital significantly delocalized along the σ bonds of the polycyclic skeleton (Fig. S52 in the SI) The configuration of the excited state does not change with solvent polarity. A relatively large energy difference between the S_1 and T_1 and the same type of orbitals involved in the transition suggest that ISC would be slow and, due to a very short singlet excited state lifetimes, inefficient. Nevertheless, although the population of the T_1 state for **1** and **2** upon direct excitation without the use of triplet sensitizers is unlikely, it cannot be disregarded since we did isolate ketone photoproducts, which were probably formed from triplet carbenes.

Optimizations of possible diazo intermediates **14** and **7** were also performed and we computed vertical excitation energies for the population of their singlet and triplet states in several solvents using a CPCM solvation model (see Fig. S49 and Tables S7 and S14-S16 in the ESI). The energy differences between the S_1 and the T_1 are somewhat lower compared to the corresponding diazirines, suggesting that ISC in the excited state of diazo molecules may take place more efficiently than for the diazirines **1** and **2**. However, formation of photoproducts *via* diazo compounds requires two photons of different energy. The first photochemical step is the formation of the diazo compound from a diazirine (350 nm), whereas carbenes **15** and **8** would be formed in the second photochemical reaction after the absorption of light by **14** and **7** (240 nm). This pathway can be excluded for preparative irradiations and LFP experiments since we used the 355 nm light, which **14** and **7** do not absorb.

Discussion

Formation of carbenes

A thorough understanding of the photochemical reactivity of diazirines is important for their application in synthesis. Our comprehensive study involving preparative irradiations and spectroscopy unraveled some pathways that were hitherto not considered as plausible. The excitation of diazirines **1** and **2** at 350 nm populates very short-lived S_1 states (≈ 100 ps) that are not emissive (Φ_F < 0.01) and do not undergo ISC efficiently. Instead, molecules deactivate from S_1 by very efficient photoelimination of nitrogen (Φ_R = 0.5-0.8), delivering carbenes **15** and **8** in the singlet manifold that were most probably detected in a cold pentane solution at -80 to -90 °C. In addition, we detected a transient that was tentatively assigned to triplet carbene **15**. However, based on

computational results, reactions from triplet carbenes are not anticipated since triplet carbenes are higher in energy than singlet carbenes.

Irradiations of **1** and **2** in different solvents gave a different distribution of products that can be grouped as those from singlet carbene intramolecular reactions (*e.g.*, **11**), singlet carbene intermolecular reactions (primarily with the solvent, *e.g.*, cyclohexyl products **9** and **16**, benzene adduct **19**, and methoxy products **13**, and **24**-**26**), the typical triplet carbene products (ketones **3** and **4**), and the azine dimers **18** and **12** which were formed *via* carbenes and diazo compounds **14** and **7**. Thus, both preparative irradiations and the LFP measurements indicate that triplet carbenes were indeed formed. Since the population of diazirine triplet excited states is anticipated to be inefficient (but still plausible), we also considered the possibility for triplet carbenes formation *via* the ISC from singlet carbenes, which is generally known to be a fast process since it involves a $sp^2 \rightarrow \pi$ transition.[55-57] However, our computations as well as those from the literature[25,30] demonstrate that singlet carbene is more stable. The observed higher stability of the singlet electronic state was rationalized by the occurrence of hyperconjugation acting inside the adamantane cage.[28] Hyperconjugation of the empty carbene p orbital with the vicinal C–C σ bond causes a slight tilt of the carbene C, resulting in the bending of the carbene bridge and a C_s symmetry for the molecule. Although singlet **15** and **8** are more stable, the ketone products derived from the triplet carbenes were still observed in all solvents except for CH_3OH (Tables 2 and 3). Consequently, based on computational results we propose that triplet carbenes were formed *via* diazirine triplet excited states. Wirz *et al*. also reported formation of small amounts of triplet adamantylidene **8**.[27]

Protonation of carbenes by CH_3OH

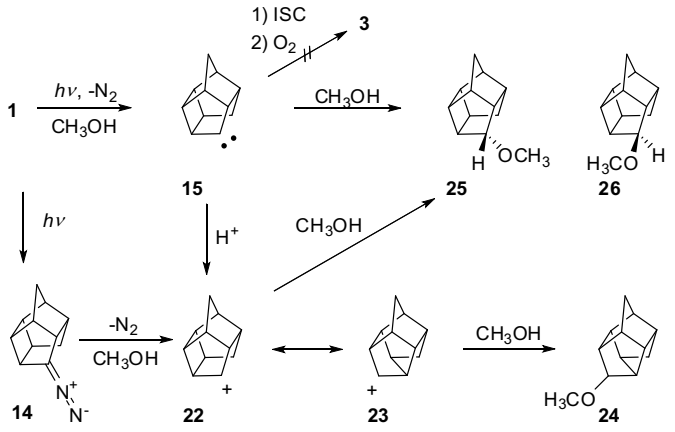
It is known that **8** has a nucleophilic character leading to the facile protonation with strong acids.[20,21,25,28] Relatively high proton affinity of **8** is a consequence of hyperconjugative stabilization that is also present in the protonated form. Note, however, that 2-adamantylidene actually has an ambiphilic character since hyperconjugative interaction is not sufficient to completely quench the electron deficiency of the carbene that results in its electrophilic behavior.[28] Our preparative irradiation results of **1** and **2** in CH_3OH are interesting in this context, particularly with **1**. Neither diazirine gave ketones in CH_3OH, suggesting that triplet carbenes were not formed. Instead, very fast protonation of singlet carbenes probably took place that lead to carbocations. It should be noted that protonation of dialkylcarbenes by CH_3OH or H_2O is rare.[19,38] Formation of the methoxy products or alcohols has usually been explained by insertion of the carbene into the O-H bond.[3,4] However, formation of rearranged products **21** and **24** derived from **1** indicates the formation of a nonclassical PCU carbocation **22** (Scheme 6). Although ethers **25** and **26** can be formed from both carbene **15** and cation **22**, ether **24** that is the main photoproduct can only be derived from **22**, since these carbenes do not undergo a 1,2-alkyl shift.[3,4] Another plausible, but less likely pathway for the formation of cation **22** is protonation and elimination of N_2 from diazo compound **14**.

Effects of inclusion complexes on the reaction selectivity

Preparative irradiations of both **1** and **2** in the presence of CB[7], β-CD, γ-CD, or without the host molecules gave different product distributions when compared to the reactivity in solution. In the presence of the hosts, one generally observes lower yields of dimeric structures **18** and **12**, which is anticipated since the hosts inhibit bimolecular reactions of intermediates **15** and **8** with diazo intermediates **14** and **7**, respectively. However, the anticipated intramolecular singlet carbene product **11** was not detected upon irradiation of **2**@β-CD and **2**@γ-CD. Instead, the major product was alcohol **10**. This finding may be rationalized by considering that **8** formed inside the inclusion complex is not fully protected from H_2O.

Due to similar lipophilic character of **2** and the corresponding carbene **8**, the exit kinetics of the carbene from the inclusion complex is anticipated to be slow. The exit of the carbene will not take place due to a short lifetime of **8** (< ns). The reaction of **8** with the host molecule upon irradiation of **2** in the solid state, reported by Brinker *et al.*,[45,46] was not observed in our case since the photolysis was performed with a large excess of H_2O surrounding the inclusion complexes. Furthermore, as indicated by the NOESY experiments, and MDS from the Brinker's group,[45,46] the diazirine moiety in **2**@β-CD and **2**@γ-CD is not fully inside the cavity and is partially exposed to H_2O. Thus, the formed **8** reacts faster with H_2O than with the host or by an intramolecular reaction that would give the strained compound **11**.

Despite the lack of reactivity with the host, our results indicate that the inclusion complexes change the ratio of the reactions taking place *via* the singlet and triplet carbenes. In the inclusion complexes products from triplet carbenes (ketones **3** and **4**) were formed in lower yields (Tables 2 and 3). Namely, the alcohols can only be formed from singlet carbenes, whereas the ketones are mostly products of triplet carbenes. The formation of ketones **3** and **4** may in principle take place by the carbene abstraction of oxygen from DMSO. However, ketones **3** and **4** were also formed in other solvents where



Scheme 6. Photochemical formation of PCU ethers.

DMSO was not present. Thus, we assign the difference in the ketone *vs*. alcohol formation as being due to different efficiencies for the singlet and triplet carbene population. This effect is particularly pronounced for **2**, where the ratio of singlet *vs.* triplet pathways changes from 2:1 in DMSO-H_2O to ≈ 80:1 in the presence of β-CD and γ-CD. In the presence of CB[7], the concentration of the host was not sufficient for a formation of the complex in high concentration and the product distribution is almost identical to the one in DMSO-H_2O. Upon irradiation of **1**@β-CD and **1**@γ-CD, the relative ratio of singlet *vs.* triplet pathways (expressed as the ratio of ketone **3** *vs.* all alcohols **17**, **20**, and **21**) is less pronounced for **1**@β-CD, where it changes from 5:19 in DMSO-H_2O to 1:13. On the contrary, upon irradiation of **1**@γ-CD, the ketone was not detected and the alcohols were isolated in a total yield of 77%. Note that in **1**@γ-CD the major product is alcohol **21** formed *via* the carbocation from the singlet carbene **15**. Consequently, our results indicate that formation of inclusion complexes for both **1** and **2** leads predominantly to singlet carbene products.

The cavities of β-CD and γ-CD hosts are known to be less polar than the solvent. However, the change in polarity cannot rationalize the less efficient population of triplet carbenes in the complexes since the energy gap between singlet and triplet carbene is not significantly larger in nonpolar solvents. Furthermore, we imply that higher yields of alcohols upon irradiation of inclusion complexes with carbenes are not due to higher reactivity of singlet carbene under such conditions. Alcohols are formed in the reaction with H_2O, which involves a bimolecular reaction and it does not seem plausible that the host molecule would enhance this rate constant. On the contrary, it is probable that the host molecule protects the diazirine precursors or their corresponding carbenes from the contact with other species (O_2, DMSO) that can induce ISC. A plausible explanation for the formation of triplet carbenes might be the interaction of the diazirine singlet excited state or less likely singlet carbene with traces of O_2 that acts as a spin catalyst,[58] as reported for biradicals.[59] Once the triplet carbenes are formed, they rapidly react with O_2, giving isolated ketone products **3** and **4**. In line with this reasoning, in inclusion complexes singlet excited states are protected from the interaction with oxygen. Another less likely explanation might be that DMSO (due to the heavy atom effect of sulfur, spin-orbit coupling constant ζ = 365 cm^{-1})[51] acts as a spin catalyst and enhances the ISC in the excited state. Thus, it is plausible that inclusion complexes protect diazirine singlet excited states and singlet carbenes from DMSO. Furthermore, it is known that the changes of carbenes solvation by H_2O or CH_3OH affect the ISC.[47] The host molecules and formation of the inclusion complexes affect the carbene solvation, and may therefore change the equilibrium between the singlet and triplet carbene. Although the exact reasons for the lower efficiency of ISC leading to the ultimate population of triplet carbenes in the inclusion complexes remains unresolved, it is an important finding that should be taken into account when applying supramolecular control to carbene reactivity.

Conclusions

The photochemical reactivity of diazirines **1** and **2** in different solvents and in inclusion complexes was investigated by preparative irradiations, spectroscopy and computations. The studied diazirines undergo very efficient photoelimination of N_2 from the singlet excited state and afford the corresponding singlet carbenes that were probably detected by LFP in a cold pentane solution at -80 °C. However, preparative irradiations gave rise to products from both singlet and triplet carbenes. The formation of triplet carbenes probably take place *via* diazirine triplet excited states. The product studies unraveled a pathway involving the protonation of carbenes and formation of cations, which for dialkylcarbenes was hitherto not usually considered as plausible without the presence of a strong acid. Furthermore, we discovered that formation of inclusion complexes of diazirines with β-CD and γ-CD changes the relative ratio of singlet *vs.* triplet pathways, with singlet carbene products being dominant upon irradiation of the inclusion complexes, that was to date never reported. Our comprehensive experimental and theoretical study may have applications in the future design of different systems where the control of carbene reactivity is of essence, particularly for selective synthesis of desired products controlled by a careful choice of solvent or constrained media.

Experimental

General. The main ^1H and ^{13}C NMR spectra were recorded at 300, or 600 MHz (75 MHz and 150 MHz) at 25 °C using TMS as a reference and chemical shifts were reported in ppm. IR spectra were recorded on a spectrophotometer in KBr, and the characteristic peak values are given in cm^{-1}. HRMS were obtained on a MALDI TOF/TOF instrument. Melting points were determined using a Mikroheiztisch apparatus and are not corrected. Irradiation experiments were performed in a reactor equipped with 10-14 lamps with output at 350 nm (1 lamp 8 W). Solutions were purged with Ar or N_2 for 30 min before irradiation and during irradiation. Solvents for irradiations were of HPLC or spectroscopic grade purity. Cyclohexane and benzene used for the irradiation experiments were dried by use of molecular sieves (4Å) or sodium. Silica gel (0.05–0.2 mm) was used for chromatographic purifications. Chemicals were purchased from the usual commercial sources and were used as received. PCU diketone was prepared according to the published procedure in a photochemical reaction from 1:1 adduct obtained by Diels Alder reaction of *p*-benzoquinone with cyclopentadiene.[59,60] The desired ketone **3** was obtained from the diketone, according to the published procedure.[61] Solvents for chromatographic separations were used as delivered from the supplier (p.a. or HPLC grade) or purified by distillation (CH_2Cl_2). Dry CH_2Cl_2 was obtained after standing of commercial product over anhydrous $MgSO_4$ overnight, then filtered and stored over 4Å molecular sieves. Dry CH_3OH was obtained by standard Mg-methoxide method

and stored over 3Å molecular sieves. GC analyses were performed on an instrument equipped with a DB-1701 or DB-210 column. The injector temperature was held at 150 °C and the program started at 70 °C (held for 10 min) and then the temperature was raised by 10 °C/min up to 200 °C and then held for 10 min. Diaziridines **5** and **6** were prepared according to the known procedure[39] which were oxidized to **1**[40] and **2**[39] according to the published procedure. The NMR spectroscopic data for **1** and **2** are in accord with those in the literature.[39,40] In the NMR and ITC titration experiments with CB[7], the actual concentrations of CB[7] were determined by titration.[63]

Photochemical experiments, general procedure. Diazirine **1** or **2** (20 mg) was dissolved in a solvent (100 mL) including cyclohexane, CH_3OH, benzene, or H_2O-DMSO (9:1), and the solution was purged with argon for 30 min. The solution was irradiated in a photochemical reactor with 11 lamps (350 nm, 1 lamp 8 W) 2 min for PCU diazirine **1** or 5 min for adamantane diazirine **2**. The solvent was evaporated on a rotary evaporator and the residue analyzed by GC and ^{1}H NMR. The retention times of the photoproducts were compared to those of the synthesized or purchased molecules. To isolate the photoproducts, the residue was chromatographed on a column of silica gel using pentane or CH_2Cl_2 as eluent. Photochemical experiments with diazirine **2** are reported in the ESI (see pages S4-S6).

Photochemistry of 1 in cyclohexane. According to the general procedure, the photolysis and chromatographic separation gave, cyclohexyl-PCU **16** (9 mg, 50%), alcohol **17** (3 mg, 17%), ketone **3** (3mg, 17%) and a mixture of azines **18** (2 mg, 11%). Photolysis was performed in triplicate and the average value is reported. For the full characterization of known photoproducts **3**, **17**, and **18** see page S7 in the ESI.

8-Cyclohexylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (16). Colorless oil; IR (KBr) 2951.2, 2925.8, 2852.5, 2362.6, 2333.8, 1448.4, 1093.5; ^{1}H NMR (300 MHz, $CDCl_3$, 20°C): δ = 2.45-2.55 (m, 4H), 2.15-2.25 (m, 4H), 1.55-1.65 (m, 6H), 1.47 (d, *J* = 12.0 Hz, 1H), 1.05-1.30 (m, 6H), 0.94 (d, *J* = 12.1 Hz, 1H), 0.55-0.80 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$, 20°C): δ = 46.6 (d), 44.1 (d), 43.4 (d), 43.3 (d), 42.7 (d), 42.5 (d), 42.2 (d), 38.6 (d), 37.6 (d), 35.8 (d), 33.6 (t), 32.1 (t), 30.1 (t), 26.9 (t), 26.8 (t), 26.6 (t), 26.6 (t) ppm; HRMS (MALDI-TOF) calculated for $C_{17}H_{24}$ + Na^+ 251.1776, found 251.1769.

Photochemistry of 1 in benzene. According to the general procedure, the photolysis and chromatographic separation gave, benzene adduct **19** (4 mg, 21%), ketone **3** (2 mg, 10%), alcohol **17** (2 mg, 10%), alcohol **20** (3 mg, 16%), alcohol **21** (1 mg, 5%), and a mixture of azines **18** (4 mg, 21%). Photolysis was performed six times and the average value is reported. Characterization of known photoproducts and synthetic procedure for alcohols **17** and **20** is reported in the ESI (pages S7-S11).

Benzene adduct 19. Isolated by column chromatography on silica gel using CH_2Cl_2 as eluent. Oily crystals; IR (KBr): *v* = 2958.5, 2362.6, 1718.4, 1654.8, 1508.2, 1458.0, 1089.7 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, 20°C): δ = 5.99-6.02 (m, 2H), 5.79-5.83 (m, 1H), 5.72-5.76 (m, 1H), 5.69-5.72 (m, 2H), 2.89-2.92 (m, 1H), 2.53-2.57 (m, 1H), 2.12-2.15 (m, 1H), 2.02-2.05 (m, 3H), 1.88-1.92 (m, 2H), 1.41 (d, *J* = 10.1 Hz, 1H), 1.28-1.32 (m, 3H), 1.25-1.27 (m, 2H), 1.50 (d, *J* = 10.6 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, 20°C): δ = 135.7 (d), 135.2 (d), 128.7 (d), 128.4 (d), 126.7 (d), 125.1 (d), 55.5 (d), 51.5 (d), 48.2 (d), 47.8 (d), 47.8 (d), 47.3 (d), 44.6 (d), 43.2 (d), 32.7 (t), 31.4 (t) ppm; HRMS (MALDI-TOF) calculated for $C_{17}H_{18}$ + Na^+ 245.1306, found 245.1300.

Photochemistry of 1 in CH_3OH. According to the general procedure, the photolysis and chromatographic separation gave, diazirine **1** (3 mg, 18%), ether **24** (5 mg, 30%), ether **25** (2 mg, 12%) and ether **26** (2 mg, 12%). Photolysis was performed seven times and the average value is reported. For the full characterization ethers **25** and **26** were synthesized in a larger amount (see pages S8-S13 in the ESI).

4-Methoxy-(D_3)-trishomocubane (24). Isolated by column chromatography on silica gel using CH_2Cl_2 as eluent. Colorless oil; IR (KBr or neat): *v* = 2962.7, 2920.9, 2362.6, 2338.5, 1654.8, 1508.2, 1089.7 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, 20°C): δ = 3.70 (br. s, 1H), 3.37 (br.s, 3H), 2.47-2.49 (m, 1H), 2.11-2.13 (m, 1H), 2.02-2.08 (m, 5H), 1.89-1.93 (m, 1H), 1.45 (d, *J* = 9.9 Hz, 1H), 1.28-1.36 (m, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, 20°C): δ = 85.7 (d), 56.7 (q), 50.5 (d), 49.3 (d), 47.4 (d), 47.2 (d), 44.4 (d), 42.9 (d), 41.1 (d), 40.8 (d), 33.7 (t), 33.0 (t) ppm; HRMS (MALDI-TOF calculated for $C_{12}H_{16}O$ + Na^+ 199.1099, found: 199.1096.

Photochemical experiments with the inclusion complexes. Diazirine (20 mg) was dissolved in DMSO (10 mL) and added to the solution of cyclodextrins (c = 1.32 × 10^{-2} M) or cucurbit[7]uril (c = 0.1 × 10^{-3} M) in H_2O. The solution was purged with Ar for 30 min and irradiated in a Rayonet reactor with 11 lamps (350 nm, 1 lamp 8 W) 2 min for PCU diazirine **1** or 5 min for diazirine **2**. After the irradiation, the photolyzed solution was extracted with hexane (3 × 50 mL), followed by CH_2Cl_2 (3 × 50 mL), and the organic extracts were dried over anhydrous $MgSO_4$. The solvent was evaporated on a rotary evaporator. The residue was analyzed by GC and ^{1}H NMR but only pentane solution contained products. The retention times of the photoproducts were compared to those of the synthesized molecules. Separation of photoproducts was accomplished by the chromatography on a column of silica gel using pentane as eluent. Photochemical experiments with diazirine **2** in the inclusion complexes are reported in the ESI (see pages S5 and S6).

Photochemistry of 1 in the presence of β-CD. According to the general procedure, the photolysis, extraction with hexane and GC analysis gave the following yields of the photoproducts: PCU ketone **3** (2%), alcohol **17** (7%), alcohol **20** (4%), alcohol **21** (14%), and a mixture of azines **18** (63%) (Table 3).

Photochemistry of 1 in the presence of γ-CD. According to the general procedure, the photolysis, extraction with hexane and GC analysis gave the following yields of the photoproducts: PCU diazirine **1** (8%), alcohol **17** (15%), alcohol **20** (23%), alcohol **21** (46%), and a mixture of azines **18** (26%) (Table 3).

Photochemistry of 1 in the presence of CB[7]. According to the general procedure, the photolysis, extraction with hexane and GC analysis gave the following yields of the photoproducts: PCU- diazirine **1** (16%), PCU ketone **3** (2%), alcohol **17** (2%), alcohol **20** (2%), alcohol **21** (7%), and a mixture of azines **18** (70%) (Table 3).

Quantum yields for the photoelimination of nitrogen. Quantum yields for the nitrogen elimination were determined by ferrioxalate actinometer, as recently described by us.[64] The measurements were performed in quartz fluorescence cells that were irradiated from the front side only. Solutions of diazirines in different solvents, and the actinometer were freshly prepared and their concentrations adjusted to have absorbances of 0.4–0.8 at 350 nm. After adjustment of the concentrations and measurements of the corresponding UV-vis spectra, 2.5 mL of the solutions were transferred to the cells and the solutions were purged with a stream of N_2 (20 min), and sealed with a cap. The cells were placed in a holder with equal distance from the lamp and were irradiated at the same time in the reactor with 1 lamp at 350 nm for 30 or 60 s, the actinometer was taken out from the reactor and the irradiation of the diazirine solutions was continued 20, 30, 40 or 50 min. To both solutions of ferrioxalate actinometer (irradiated and blank) a solution of phenantroline was added (0.5 mL, 0.1% phenanthroline in buffer containing 1.65 M NaOAc and 0.5 M H_2SO_4) and A_{510} was measured. The concentration of Fe^{II} was determined using ε_{510} = 11100 $M^{-1}cm^{-1}$.[49] After the irradiation, absorption spectra were taken for all solutions. All equations for the calculation of quantum yields are given in the Supporting Information (Eqs. S1-S5). The measurement was performed in triplicate and the mean value was reported.

^{1}H NMR titrations. Diazirines **1** or **2** were dissolved in DMSO-d_6 (60 mM) and an aliquot (1 or 2 µL i.e. 0.1 or 0.2 eq.) of this solution was added to the D_2O solution of host (1 mM, 0.6 mL). The NMR tube with the resulting mixture was shaken for 5 min, and the ^{1}H NMR spectrum was recorded after each addition. The addition of guest was stopped when broadening of the signals was observed or when precipitation started to take place.

Another set of NMR titrations for **1** and **2** with β-CD and γ-CD was performed in DMSO-d_6:D_2O (1:1). The hosts and the guests were dissolved in DMSO-d_6:D_2O (1:1) (c = 6 mM) and mixed in different ratios.

ITC titrations. The titrations where performed on an isothermal titration calorimeter (ITC) with a cell volume of 1.4406 mL. Before the titrations, the samples where degassed at 23 °C, 0.4 atm, with stirring at 120 rpm for 10 min. The titrations where performed at 25 °C, stirring speed 351 rpm, reference power 10 µcal/sec and the filter period 2 s. The guest was added in 30 injections with an initial delay of 1600 s. The host and the guest were dissolved in DMSO:H_2O (1:1), and the reference cell was filled with DMSO:H_2O (1:1). The host concentration in the cell was c = 0.05 mM, and the diazirine (guest) concentration in the syringe was c = 1 mM.

Circular dichroism titrations. Fresh solutions of diazirines (**1** or **2**) in DMSO (5 mM) and cyclodextrins (β-CD or γ-CD) in water (50 mM) were prepared. A set of solutions in DMSO-H_2O (1:1) was prepared according to Tables S2-S5, and the circular dichroism spectra were taken on an instrument using parameters defined in the ESI.

Steady-state and time-resolved fluorescence measurements. Fluorescence measurements were performed on a PTI QM40 fluorometer at 20°C. All slits (excitation and emission) were set to the bandpass of 5 nm. The spectra were corrected for the fluctuations in lamp intensity and transmission of optics. For the measurements of fluorescence quantum yields, quinine sulfate in aqueous 2.0 M H_2SO_4 was used as a reference (Φ = 0.55).[41] For these measurements the slits were set to the bandpass of 2 nm for the excitation monochromator and 5 nm for the emission monochromator. Emission spectra were recorded by exciting samples at 340, 345 and 350 nm, and the emission was detected in the range of 350-650 nm (or 360-650 nm). Excitation spectra were recorded in the range 280-380 (or 390) nm by detecting emission at 380 or 400 nm. Fluorescence decays, collected over 1023 time channels, were obtained on an Edinburgh Instruments OB920 single photon counter using a light emitting diode for excitation at 360 nm or pulsed diode laser at 375 nm. The instrument response function (IRF), using LUDOX as the scatterer, was recorded at the same wavelengths as the excitation wavelength and had a half width of ≈ 0.8 ns for the excitation at 360 nm and ≈ 90 ps for the excitation at 375 nm. The time increment per channel was 0.020 ns. Emission decays for samples were recorded at 380 and 400 nm until they reached 1 × 10^3 counts in the peak channel. For the excitation at 360 nm only one decay at 380 nm was collected. Results obtained by excitation at 360 nm could not be processed by non-linear least-squares fitting. For the decays collected upon excitation at 375 nm, global analysis of two decays was performed by fitting to sums of exponentials using global Gaussian-weighted non-linear least-squares fitting based on Marquardt-Levenberg minimization implemented in the Fast software package from Edinburgh Instruments. The fitting parameters (decay times and pre-exponential factors) were determined by minimizing the reduced chi-square χ^2 and graphical methods were used to judge the quality of the fit that included plots of the weighted residuals *vs*. channel number. However, for all fits the χ^2 remained high due to additional artificial scattering signals (in IRF and sample traces).

Laser flash photolysis (LFP). All LFP studies were performed on a system previously described[50] using as an excitation source a pulsed Nd:YAG laser at 355 nm (<50 mJ per pulse), with a pulse width of 10 ns. Static cells (7 mm × 7 mm) were used and the solutions were purged with N_2 or O_2 for 20 min prior to performing the measurements. A Unisoku USP-203 cryostat placed at the position of the sample holder was used for the low temperature experiments.[65] Absorbances at 355 nm were 0.2-0.5. Details on the sample preparation for the LFP measurements can be found in the supporting information.

Computational details: Geometry optimizations were performed with the GAUSSIAN09 program package[66] using the MN12-SX/6-311+G(d) level of theory[67] and the CPCM solvation model.[68,69] The obtained minima were verified by frequency

computations and the TD-MN12-SX/6-311+G(d) level of theory was used for excited state computations.

Conflicts of interest

There are no conflicts to declare.

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