

Controllable Selective Functionalization of a Cavitand via Solid State Photolysis of an Encapsulated Phenyl Azide

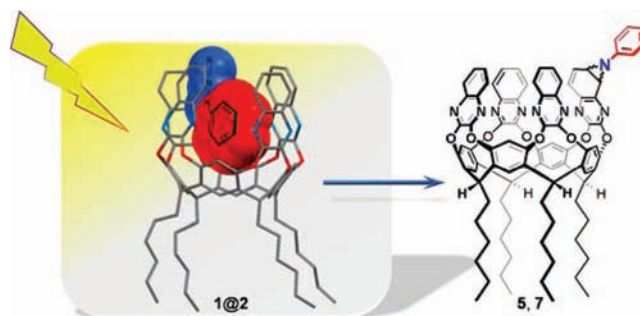
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ABSTRACT



Phenyl azide (1) has been encapsulated within cavitand 2 to form a 1:1 complex of 1@2 in the solid state. Subsequent irradiation affords two diastereomeric nitrene addition products 5 and 7. The ratio of 5 and 7 can be reversed by thermally induced valence isomerization to 1H-azepine 8 followed by photolysis. In sharp contrast, phenylnitrene generation by photolysis of the corresponding 1.5:1 complex results mainly in the regioselective formation of C–H insertion product 4. The supramolecular approach to phenylnitrene chemistry provides good yields, in contrast to the generally low yield reactions of this species in solution.

During the last decades, significant advances have been achieved in understanding the photochemistry of phenyl azide (1) in solution. UV irradiation of phenyl azide generates singlet phenylnitrene, which above 165 K rearranges to 1-azacyclohepta-1,2,4,6-tetraene.¹ At temperatures below 165 K, relaxation to triplet phenylnitrene is favored. However,

little is known about the reactivity of nitrenes in a crystalline environment.²

It is well-known that the encapsulation of reactive intermediates within the nanoscopic cavity of suitable host molecules can increase their lifetime and enhance their selectivity.^{1a,3}

Herein, we report the preparation and characterization of the supramolecular solid state complex of phenyl azide (1)

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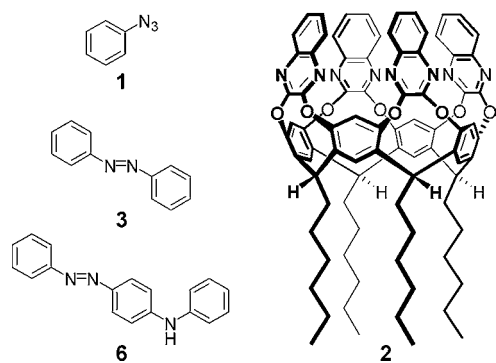


Figure 1

with resorcin[4]arene-based cavitand **2** (Figure 1).⁴ The structure of the complex between **1** and **2** can be changed by thermal treatment. Furthermore, the modified reaction behavior of the photolytically generated phenylnitrene was used to functionalize **2** regioselectively at different positions. Cavitand **2** possesses a large lipophilic preorganized cavity and forms complexes in the solid state as well as in solution with a strong preference for aromatic guests.^{5,6}

The inclusion complex **1**@**2** was formed by crystallization from a saturated solution of cavitand **2** in PhN₃ **1** (51% yield). The molecular structure was confirmed by single-crystal X-ray diffraction (Figure 2).⁷ The phenyl ring of **1** is arranged between

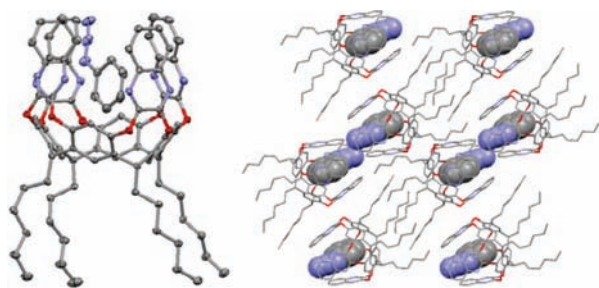


Figure 2. X-ray molecular structure of **1**@**2**: side view and detail of crystal lattice.

two quinoxaline rings of cavitand **2**. A statistical analysis of the Cambridge Structural Database shows that optimal π – π

stacking interactions are realized when the interacting rings are parallel to each other. In **1**@**2**, the dihedral angles between the plane of the phenyl ring of **1** and two opposite quinoxaline rings are 11.4 and 20.2°, respectively, indicating that π – π interactions are disfavored. Such a position of PhN₃ is probably due to van der Waals rather than classical offset stacked face-to-face interactions.⁸ In the crystal, the complexes show an alternating head-to-head and tail-to-tail arrangement.

1@**2** is formed in a 1.5:1 stoichiometry after drying (0.4 Torr; ca. 18 h at 25 °C). This was verified via thermogravimetry (TG; total mass loss: 12.0%) and NMR analysis. TG (Figure 3) shows that the decomposition of the complex

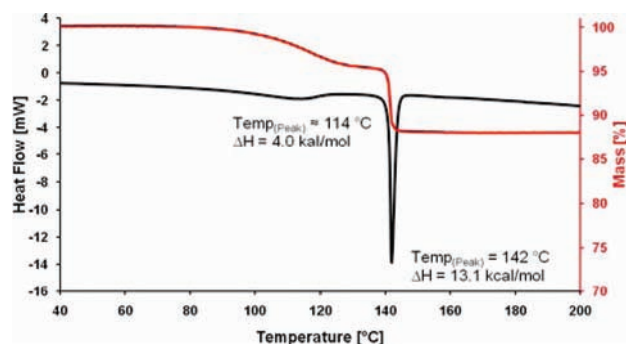


Figure 3. DSC diagram (black graph) and thermogravimetric analysis (red line) of **1**@**2**.

occurs as a two-step process. First, the excess of phenyl azide is released between 70 and 130 °C (weight loss: 4.5%). The remaining 1:1 complex then dissociates at 138 °C. NMR analysis after TG provides evidence for the complete absence of **1**.

DSC (differential scanning calorimetry) analysis (Figure 3) of the 1.5:1 complex shows two endothermic peaks assigned to two dissociation processes. The first broad but flat peak between 70 and 125 °C corresponds to the loss of excess phenyl azide with $\Delta H = 4.0$ kcal/mol. The broad energy distribution supports the excess of **1** to be located in an interstitial volume space in different orientations. The remaining 1:1 complex dissociates at 142 °C with $\Delta H = 13.1$ kcal/mol, a value in good agreement with the 11.1 kcal/mol, we obtained from MPWB1K/6-31G(d) calculations.

Broadband irradiation ($\lambda > 300$ nm, 24 h) of the 1.5:1 complex **1**@**2** in the solid-state at 283 K yields as major products azobenzene (**3**) and the intermolecularly formed *N*-alkylaniline **4**. Additionally, aziridine **5** and 4-(phenylazo)diphenylamine (**6**) are formed as minor products (Scheme 1).⁹ The high yield of azobenzene, when compared with the photolysis of PhN₃ in benzene, can be rationalized by the favorable spatial arrangement of molecules of phenylnitrene for dimerization in the crystal packing of **1**@**2** (Figure 2).

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(9) All yields reported in this paper were ascertained by HPLC measurements of the crude product mixtures (nitrobenzene as internal standard). Isolated yields are listed in the Supporting Information.

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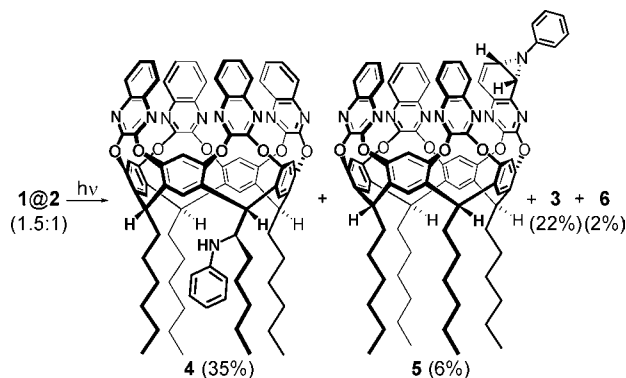
(4) We ascertained that phenyl azide (**1**) forms a 1:1 complex with cavitand **2** with an association constant of $K = 60$ M^{−1} in acetone-*d*₆.

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(7) Enlarged images of the X-ray structure and the crystal packing are given in the Supporting Information.

Scheme 1

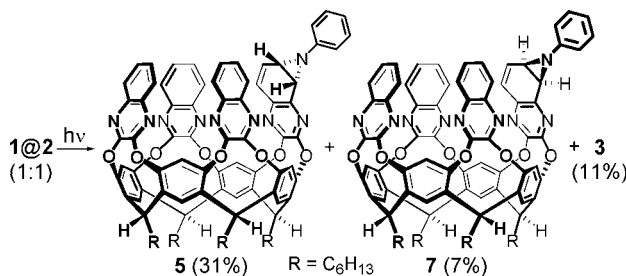


Compound **4** derives from a highly regioselective C–H insertion of phenylnitrene into one of the C–H bonds of the alkyl chains of the cavitaand. Most probably, it is formed by azide **1** embedded either in the interstitial volume of the lattice or within the alkyl chains of **2** with the N₃ moiety pointing toward the resorcinarene skeleton.^{5b} The remarkable yield of **4** demonstrates the higher regioselectivity of solid-state photoreactions compared to their solution counterparts.

Thermal treatment (112 °C for 35 min at 1 atm) of the 1.5:1 complex gives the 1:1 complex.¹⁰

Photolysis of the 1:1 complex **1@2** under the same conditions as above affords the diastereomeric aziridines **5** and **7** in a combined yield of 38% as well as azobenzene (**3**) (Scheme 2).

Scheme 2



The structures **5** and **7** were assigned based on 2D NMR studies. The fact that one of the aziridine protons (H-17) of **5** shows a NOE signal to H-20 (see the Supporting Information, Table S2, column D) suggests that the three-membered ring protons H-17 and H-18 are pointing inward the cavity. This signal is absent for **7** implying that the aziridine protons are pointing outward the cavity. We excluded the isomeric 1-phenyl-3a,7b-dihydropyrrolo[3',2':3,4]cyclobuta[1,2-b]pyrazine¹¹ substructure

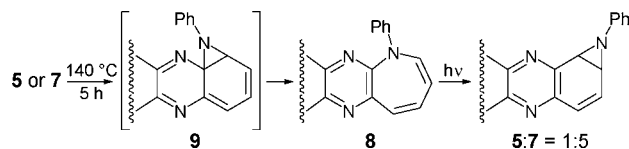
(10) Again, the DSC analysis provides evidence for a two-step dissociation process. Two-thirds of **1** are released at 145 °C with $\Delta H = 16.6$ kcal/mol. This process is significantly more endothermic than the dissociation of the 1:1 complex before heating the probe. Most probably, the thermal treatment leads to a thermodynamically more favorable modification of the crystal lattice. The remaining phenyl azide (**1**) is released at 169 °C ($\Delta H = 2.2$ kcal/mol).

by ¹³C NMR shift correlation and ¹J(C,H) measurements.¹² No insertion product **4** is found.

Compounds **5** and **7** are formed by addition of phenylnitrene to the benzene ring of one of the four quinoxalines. Alternative reaction pathways of the nitrene obviously are blocked due to the lack of diffusion inherent to the solid state. The observed addition is unique, as phenylnitrene generated photolytically from phenyl azide fails to add to benzene, aside from intramolecular additions.¹³ We ascertained that quinoxaline (10 equiv) is not attacked by phenylnitrene during irradiation of phenyl azide (42×10^{-3} M, $\lambda > 300$ nm, 18 h, 283 K) in benzene. Instead aniline and azobenzene are formed in 17 and 9% yield, respectively.

Upon heating, the two “azanorcaradiene” subunits in **5** and **7** undergo a rearrangement to 1*H*-azepine **8** in the solid state, probably via 1,5-sigmatropic nitrogen migration to **9** and subsequent valence isomerization (Scheme 3).¹⁴ Solid phase

Scheme 3



photolysis of **8** ($\lambda > 300$ nm, 5 h) affords back the two aziridines **5** and **7** in quantitative yield in a ratio of 1:5, presumably following a nonconcerted mechanism.

In summary, utilizing the improved reaction behavior of phenylnitrene in the solid state, we are able to offer an alternative to the multistep building of functionalized resorcin[4]arene cavitaands.¹⁵ The regioselective modification of cavitaand **2** is controlled via thermal treatment before UV irradiation of the solid-state complex **1@2**. *N*-Alkylaniline **4** and aziridines **5** and **7**, respectively, are accessible in good yield, in contrast to the generally low yield reactions of phenylnitrene in solution. The ratio of **5** to **7** can be reversed by valence isomerization to 1*H*-azepine **8** and subsequent UV irradiation.

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Supporting Information Available: Experimental procedures and details of NMR and X-ray diffraction (CIF) studies. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(12) ¹J(C,H) = 152, 163 and 155, 163 Hz for the aziridine rings in **5** and **7**, respectively. For further details, see the Supporting Information.

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