J. Org. Chem. **2001,** *66,* 1517−1522

Effect of Supramolecular Inclusion on the Selectivity of 3-Nortricyclanylidene[†]

Murray G. Rosenberg[‡] and Udo H. Brinker*

Institut für Organische Chemie, Universität Wien,
Währinger Strasse 38, A-1090 Wien, Austria

E-mail: Udo.Brinker@univie.ac.at

Received October 31, 2000

Introduction

3-Nortricyclanylidene(tricyclo[2.2.1.0^{2,6}]heptan-3-ylidene) (**2**) was originally generated via the Bamford−Stevens reaction of the 3-nortricyclanone *p*-tosylhydrazone sodium salt (**10**) (Scheme 1).[1] The formation of quadricyclane (tetracyclo[2.2.1.0.^{2,6}0^{3,5}]heptane) (**8**) was anticipated, from an intramolecular 1,3 C−H insertion of the carbene, but was not observed. This is intriguing because 2-norbornanylidene (bicyclo[2.2.1]heptan-2-ylidene) (**5**), which merely lacks the C2−C6 bridge in **2**, undergoes 1,3 C−H insertion to form nortricyclane (tricyclo[2.2.1.0^{2,6}]heptane) (**3**) in over 95% yield.[2] Instead, 4-ethynylcyclopentene (**9**) was formed via cyclopropylcarbene fragmentation,[3] a process similar to the well-known Eschenmoser fragmentation.[4] This carbene rearrangement is believed to proceed through a coarctate TS that requires strict orbital alignment of the divalent carbon with the cyclopropane ring; a bilateral symmetry and an endocyclic configuration are required—both of which are perfectly exemplified by **2**.[5]

Recent advances in carbene chemistry demonstrate that constrictive hosts, like cyclodextrins (CyD's)[6] and faujasite zeolites (FAU's),[7] are able to modify the selectivity of the high-energy reaction intermediate.[8] Thus, we hypothesized that the confinement of **2** within the nanoscopic cavities of CyD's (Figure 1) and FAU's (Figure 2) would inhibit the fragmentation reaction and foster the 1,3 C−H insertion. Our reasoning was 2-fold: (1) there may not be enough space within the hosts' cavities for the unraveling process, **2**→**9**, and (2) distortion of the carbene's topology might concomitantly disfavor the coarctate TS and allow the 1,3 C−H insertion, **2**→**8**, to finally occur.

The main challenge was to imbue the CyD's and FAU's with a carbene precursor that is compatible with the hosts and the standard inclusion complex (IC) preparation. The sodium salt **10** must be kept moisture-free and, therefore, is incompatible with CyD's and FAU's, since both contain adventitious water molecules. Besides, cyclodextrin IC's (CyD IC's) are prepared from aqueous solutions! Likewise, faujasite zeolite IC's (FAU IC's) are prepared by loading the zeolite with a pentane solution of the guest; salt **10** is insoluble in pentane. Therefore, a 3*H*-diazirine,[9] 3-azinortricyclane (**1**), was needed as a precursor[10] in lieu of the Bamford−Stevens reagent **10**. Yet, the synthesis and properties of this compound were unreported.

Results and Discussion

The preparation of diazirine **1** was successful, albeit in only 6% yield from 3-nortricyclanone (**16**).[11] The α-cyclodextrin (α-CyD) and *β*-cyclodextrin (*β*-CyD) IC's

---

[†] Carbenes in Constrained Systems. 7. For part 6, see: Krois, D.; Bobek, M. M.; Werner, A.; Kählig, H.; Brinker, U. H. *Org. Lett.* **2000**, *2*, 315-318. Carbene Rearrangements. 55. For part 54, see: Bobek, M. M.; Brinker, U. H. *J. Am. Chem. Soc.* **2000**, *122*, 7430-7431.

* Corresponding author. Phone: +43-1-4277-52121. Fax: +43-1-4277-52140, U.S.A.

[‡] Department of Chemistry, State University of New York, Binghamton, NY 13902-6016.

(1) (a) Cristol, S. J.; Harrington, J. K. *J. Org. Chem.* **1963**, *28*, 1413−1415. (b) Lemal, D. M.; Fry, A. J. *J. Org. Chem.* **1964**, *29*, 1673−1676. (c) Arct, J.; Brinker, U. H. In *Methoden der Organischen Chemie (Houben-Weyl)*; Regitz, M., Ed.; Thieme: Stuttgart, 1989; Vol. E19b, pp 337−375. (d) Sydnes, L. K.; Brinker, U. H. In *Methoden der Organischen Chemie (Houben-Weyl)*; Regitz, M., Ed.; Thieme: Stuttgart, 1989; Vol. E19b, pp 542−576. (e) Shapiro, R. H. *Org. React. (NY)* **1976**, *23*, 405−507. (f) Freeman, P. K.; George, D. E.; Rao, V. N. M. *J. Org. Chem.* **1963**, *28*, 3234−3237. (g) Kirmse, W.; Knöpfel, N. *J. Am. Chem. Soc.* **1976**, *98*, 4672−4674.

(2) (a) Friedman, L.; Shechter, H. *J. Am. Chem. Soc.* **1961**, *83*, 3159−3160. (b) Freeman, P. K.; George, D. E.; Rao, V. N. M. *J. Org. Chem.* **1964**, *29*, 1682−1684. (c) Kirmse, W.; Meinert, T.; Modarelli, D. A.; Platz, M. S. *J. Am. Chem. Soc.* **1993**, *115*, 8918−8927.

(3) (a) Shevlin, P. B.; McKee, M. L. *J. Am. Chem. Soc.* **1989**, *111*, 519−524. (b) Moss, R. A.; Liu, W.; Krogh-Jespersen, K. *J. Phys. Chem.* **1993**, *97*, 13413−13418. (c) Moss, R. A. *Pure Appl. Chem.* **1995**, *67*, 741−747. (d) Huang, H.; Platz, M. S. *J. Am. Chem. Soc.* **1998**, *120*, 5990−5999. (e) Ammann, J. R.; Subramanian, R.; Sheridan, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 7592−7594. (f) Levashova, T. V.; Semeikin, O. V.; Balenkova, E. S. *J. Org. Chem. USSR* **1980**, *16*, 53−56. (g) Murray, R. K., Jr.; Ford, T. M. *J. Org. Chem.* **1977**, *42*, 1806−1808. (h) Freeman, P. K.; Pugh, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 2269−2273. (i) Bergman, R. G.; Rajadhyaksha, V. J. *J. Am. Chem. Soc.* **1970**, *92*, 2163-2164. (j) Wills, M. S. B.; Danheiser, R. L. *J. Am. Chem. Soc.* **1998**, *120*, 9378−9379.

(4) (a) *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; p 1037. (b) Hassner, A.; Stumer, C. *Organic Syntheses Based on Name Reactions and Unnamed Reactions*; Pergamon: Tarrytown, NY, 1994; p 110. (c) Mundy, B. P.; Ellerd, M. G. *Name Reactions and Reagents in Organic Synthesis*; Wiley: New York, 1988; pp 72−73.

(5) (a) Herges, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 255−276. (b) For a related example of coarctate fragmentation of 2-furfurylcarbenes, see: Khasanova, T.; Sheridan, R. S. *J. Am. Chem. Soc.* **1998**, *120*, 233−234.

(6) (a) *Comprehensive Supramolecular Chemistry*; Lehn, J.-M., Ed.; Pergamon: New York, 1995; Vol. 3. (b) Szejtli, J. *Chem. Intell.* **1999**, *5* (3), 38−45. (c) Pagington, J. S. *Chem. Br.* **1987**, *23*, 455−458. (d) Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344−362. (e) Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803−822. (f) Maheswaran, M. M.; Divakar, S. *J. Sci. Ind. Res.* **1994**, *53*, 924−932.

(7) (a) Rouhi, A. M. *Chem. Eng. News* **2000**, *78* (34), 40−47. (b) Ramamurthy, V. In *Photochemistry in Organized and Constrained Media*; Ramamurthy, V., Ed.; VCH: New York, 1991; pp 432−435. (c) Alvaro, M.; Corma, A.; García, H.; Miranda, M. A.; Primo, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1041−1042.

(8) (a) Brinker, U. H.; Buchkremer, R.; Kolodziejczyk, M.; Kupfer, R.; Rosenberg, M.; Poliks, M. D.; Orlando, M.; Gross, M. L. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1344−1345. (b) Kupfer, R.; Poliks, M. D.; Brinker, U. H. *J. Am. Chem. Soc.* **1994**, *116*, 7393−7398. (c) Kupfer, R.; Brinker, U. H. *Liebigs Ann.* **1995**, 1721−1725. (d) Rosenberg, M. G.; Kam, S. M.; Brinker, U. H. *Tetrahedron Lett.* **1996**, *37*, 3235−3238. (e) Brinker, U. H.; Rosenberg, M. G. *Adv. Carbene Chem.* **1998**, *2*, 29−44.

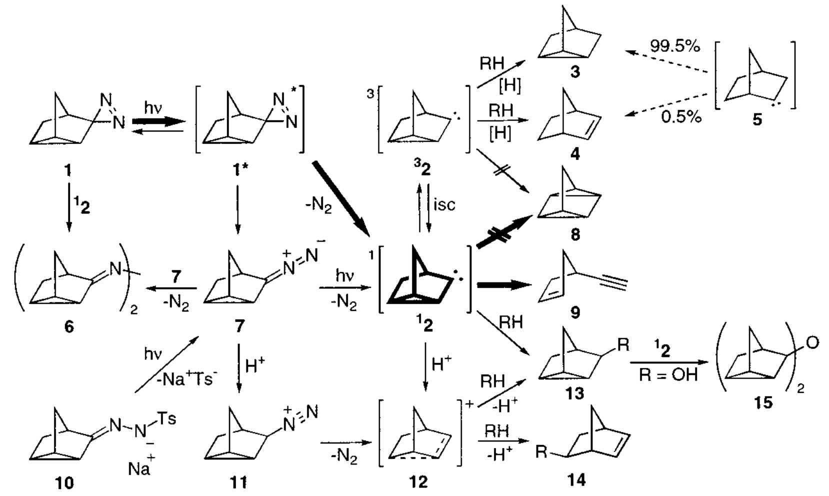
(9) (a) *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC: Boca Raton, FL, 1987; 2 vols. (b) Schmitz, E. *Adv. Heterocycl. Chem.* **1963**, *2*, 83−130. (c) Schmitz, E. *Adv. Heterocycl. Chem.* **1979**, *24*, 63−107. (d) Schmitz, E. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 333−341. (e) Schmitz, E. In *Methoden der Organischen Chemie (Houben-Weyl)*; Klamann, D., Ed.; Thieme: Stuttgart, 1992; Vol. E16c, pp 678−728.

(10) (a) Schmitz, E.; Habisch, D.; Stark, A. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 548. (b) Dürr, H.; Abdel-Wahab, A.-M. A. In *Organic Photochemistry and Photobiology*; Horspool, W. M., Ed.; CRC: Boca Raton, FL, 1995; pp 954−983.

(11) (a) Meinwald, J.; Crandall, J. K. *J. Am. Chem. Soc.* **1966**, *88*, 1292−1301. (b) Meinwald, J.; Crandall, J.; Hymans, W. E. *Org. Synth. Coll.* **1973**, *5*, 866−868. (c) Hall, H. K., Jr. *J. Am. Chem. Soc.* **1960**, *82*, 1209−1215. (d) Upadek, H. Ph.D. Dissertation, Ruhr-Universität Bochum, Germany, 1977; pp 156−159.

10.1021/jo005713e CCC: $20.00

Scheme 1. Generation of 3-Nortricyclanylidene (2) and Its Subsequent Reactions[a]



[a] RH = (a) α-CyD, (b) β-CyD, (c) MeOH, (d) ^{i}PrOH, (e) AcOH, (f) H_2O, (g) c-C_6H_{12}; Ts = p-$SO_2C_6H_4CH_3$.

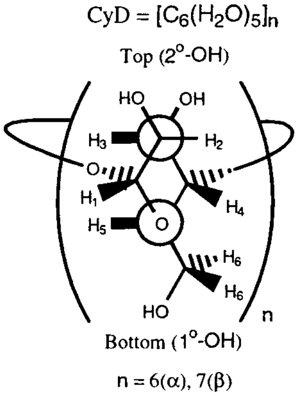


Figure 1. Structure of cyclodextrin (CyD) cyclic oligosaccharides depicting the O1−C4 α-linkage of D-glucose monomers. (Newman projection used to highlight inward pointing H3 and H5 atoms).

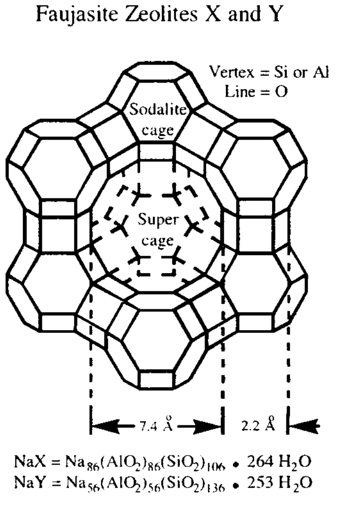


Figure 2. Structure of faujasite zeolite (FAU) depicting 13 Å diameter supercage and tetrahedral arrangement of 7.4 Å apertures (cf. diamond fcc structure).

were analyzed using ^{1}H NMR,[12] including 2-D ROESY;[13] induced circular dichroism (ICD);[14] and microanalysis. The structures of the CyD IC's were concluded to be **1**@(α-CyD)$_2$ and (**1**@β-CyD)$_2$. This denotes that **1** is sandwiched between two α-CyD units but that it forms a 2-fold 1:1 complex with β-CyD.[15] It has been demonstrated that a guest must have an electronegative group, like −F or −OH,[13,15] to effect an opposite inclusion orientation within cyclodextrins in the aqueous versus solid phase. Hence, it is likely that hydrophobic **1** adopts the same orientation within CyD in both phases. The FAU IC was prepared from **1** and thermally activated NaY so as to give a loading factor (⟨*s*⟩) of ca. 0.25, which corresponds to one filled supercage surrounded by four empty ones.[16]

Supramolecular photolyses of the aforementioned IC's of **1** were carried out for at least 24 h each. Of the two possible intramolecular products, **8** and **9**, only **9** was observed. Control experiments were performed on CyD's and FAU's, both bearing **8**, to determine whether **8** is stable toward the reaction conditions. Indeed, it is. Thus, no **8** was formed from the solid-state photolyses of the **1** IC's.

The results are in accord with the proposed supramolecular structures of diazirine **1** and its hosts (vide supra). No azine, di(3-nortricyclanylidene)hydrazine (**6**), was formed upon photolysis of the dimeric **1**@(α-CyD)$_2$ complex because of a complete encapsulation of the reactive guest. Bimolecular reaction of the guests within the (**1**@β-CyD)$_2$ dimer should, of course, produce azine **6** by virtue of their geminated assemblage. Yet, the affinity of carbene **2** for the O−H bonds present in both CyD's *predominated*, giving *O*-substituted CyD's (**13a**, **13b**, **14a**,

---

(12) (a) Casu, B.; Reggiani, M.; Gallo, G. G.; Vigevani, A. *Tetrahedron* **1966**, *22*, 3061−3083. (b) Demarco, P. V.; Thakkar, A. L. *J. Chem. Soc. D* **1970**, 2−4. (c) MacNicol, D. D. *Tetrahedron Lett.* **1975**, 3325−3326. (d) Chung, W.-S.; Turro, N. J.; Silver, J.; le Noble, W. J. *J. Am. Chem. Soc.* **1990**, *112*, 1202−1205. (e) Qi, Z. H.; Mak, V.; Diaz, L.; Grant, D. M.; Chang, C.-j. *J. Org. Chem.* **1991**, *56*, 1537−1542. (f) Salvatierra, D.; Jaime, C.; Virgili, A.; Sánchez-Ferrando, F. *J. Org. Chem.* **1996**, *61*, 9578−9581.

(13) (a) Alderfer, J. L.; Eliseev, A. V. *J. Org. Chem.* **1997**, *62*, 8225−8226. (b) Ivanov, P. M.; Salvatierra, D.; Jaime, C. *J. Org. Chem.* **1996**, *61*, 7012−7017.

(14) (a) Krois, D.; Brinker, U. H. *J. Am. Chem. Soc.* **1998**, *120*, 11627−11632. (b) Bobek, M. M.; Krois, D.; Brinker, U. H. *Org. Lett.* **2000**, *2*, 1999−2002.

(15) For a related example employing X-ray diffraction upon a crystalline diazirine@CyD IC, see: Bobek, M. M.; Giester, G.; Kählig, H.; Brinker, U. H. *Tetrahedron Lett.* **2000**, *41*, 5663−5667.

(16) The limit of the sequence 1/5, 2/9, 3/13, 4/17, ... $n/(5n - (n - 1)) = n/(4n + 1)$ for infinite n is 0.25.

Table 1. Relative Yields (%) of Products Formed upon Photolysis of 3-Azinortricyclane (1) in Different Reaction Media

medium	κ[a]	**3**	**4**	**6**	**9**	**13**	**14**	**15**	**13f**	**16**	**13/14**
c-C_6H_{12}	2.0	0.8	trace	48.7	18.7	20.0		3.6	1.3	7.0	
MeOH	32.7	1.0	trace		15.6	80.6	2.8				29
w/0.2 M DEF[b,c]		0.9	trace		16.9	69.3	2.0				35
^{i}PrOH	18.3	2.1	2.3	9.9	14.2	70.4			0.6	0.5	
AcOH	6.1	trace	trace		14.2	84.2	1.6		trace		53
α-CyD		14.0	trace		6.0	80.0[d]			trace	trace	N/A
β-CyD		3.8	trace	10.0	11.5	52.0[d]			3.4	19.3	N/A
NaY				6.0	16.3	*e*	1.1[f]	1.1	75.5	trace	69

[a] Dielectric constant. [b] Diethyl fumarate. [c] **7** + DEF → scavenger products (10.8% by GC−MS). [d] Sum of **13** and **14**. [e] **13f**. [f] **14f**.

and **14b**), via innermolecular reactions,[17] that were detected using FAB MS analysis (Table 1).

Clearly, the presence of azine **6** and di-3-nortricyclyl ether (**15**) after photolysis of the **1**@NaY FAU IC demonstrates that some bimolecular reactions occurred. The diffusion of ephemeral carbene **2** within the multicameral lattice was thus indicated. The principal formation of 3-nortricyclanol (**13f**) validates that a significant amount of water still remains inside NaY even after thermal activation.[18]

Since products other than the "sole-reported" enyne **9** [1a,19] were formed within the host vessels, control experiments on **1** in relevant solvents were warranted (Table 1).

These trials showed a reluctance of carbene **2** to undergo intramolecular fragmentation to **9** also in the condensed phase. The hydrolysis reaction of **2** with trace amounts of H_2O, giving **13f**, was evident in each medium. Yet, the formation of 5-norbornen-2-yl-substituted products **14** in protic media is noteworthy. Unsaturated **14** cannot directly stem from carbene **2** (i.e., no **2→14**); it derives from carbocation **12**. Thus, carbene protonation is indicated (**2→12**).[20] However, the typical product ratio that is characteristic of nonclassical carbocation **12** (i.e., **13**/**14** = ca. 3.5) was not observed, even in the presence of diethyl fumarate (DEF).[21,22] Thus, the paucity of **14** implies a deviation due to ion pairing of **12** with its counterion.[23]

DEF is a potent 1,3-dipolarophile that precludes the diazonium cation route (**7→11→12**) by intercepting diazo compound **7**. Indeed, the addition of DEF produced ca. 10% scavenger product, which suggests that some diazo compound **7** was formed upon irradiation of diazirine **1**.[24] Barring this route should have reduced the **13**/**14** ratio because **12** generated via pathway **10→7→11** gives an uncharacteristically[25] high ratio (**13f**/**14f** = 24).[1g,26] That is, protonation pathway **2→12** should give the characteristic **13**/**14** ratio in the presence of DEF *and* in the absence of ion pairing. It appears that carbene **2** is as Brønsted basic as its constitutional isomer 5-norbornen-2-ylidene (**17**), which has been shown to be protonated to **12** completely under similar conditions.[27,28] The absence of unsaturated isomers of ether **15** stemming from 5-norbornen-2-ol (**14f**) may be due to limits of detection. Alcohol **13f** has previously been shown to be stable within NaY (i.e., no **13f→12**).[29]

Notwithstanding, the presence of typical H-abstraction products **3** and **4** may indicate intersystem crossing (isc) of carbene **2** from the singlet to the triplet state.[30] In CyD's and cyclohexane, the concomitant oxidation of the surrounding nonpolar media rendered minor amounts of didehydro-CyD's[31] (likely via end-on abstraction of H3 within the nonpolar cavity) and bicyclohexyl,[32] respectively. The comparatively large molar mass of the CyD could provide a collisional mechanism for the isc of **2**.[33] Nevertheless, it is surprising that the triplet state of **2** could be relatively low-lying since angle restraints[34] within the polycyclic structure and homoconjugation between the Walsh orbitals of the cyclopropane ring with the vacant p-orbital of the carbene (or carbocation)[35] center greatly favor the singlet state. Indeed, it is this interaction of the vacant p-orbital with proximal π-bonds

---

[17] (a) Warmuth, R. *Chem. Commun. (Cambridge)* **1998**, 59−60. (b) Bradley, D. *Chem. Br.* **1998**, *34* (3), 16.

[18] NaY·$253H_2O$ is 26.3% (w/w) H_2O; only 22.4 wt % was lost.

[19] After vacuum pyrolysis of salt **10**, compounds **3**, **4**, and the allenic dimer, 3-[2-(3-cyclopentenyl)ethenylidene]nortricyclane (**S1**), were found in addition to **9**; see Supporting Information.

[20] (a) Kirmse, W. *Adv. Carbene Chem.* **2001**, *3*, in press. (b) Kirmse, W. *Adv. Carbene Chem.* **1994**, *1*, 1−57. (c) Bethell, D.; Newall, A. R.; Stevens, G.; Whittaker, D. *J. Chem. Soc., B* **1969**, 749−751. (d) Bethell, D.; Newall, A. R.; Whittaker, D. *J. Chem. Soc., B* **1971**, 23−31.

[21] (a) Schleyer, P. v. R. *J. Am. Chem. Soc.* **1958**, *80*, 1700−1704. (b) Schmerling, L.; Luvisi, J. P.; Welch, R. W. *J. Am. Chem. Soc.* **1956**, *78*, 2819−2821. (c) Roberts, R. M. G. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1183−1190. (d) Cristol, S. J.; Seifert, W. K.; Johnson, D. W.; Jurale, J. B. *J. Am. Chem. Soc.* **1962**, *84*, 3918−3925.

[22] The electron-deficient radical behaves similarly: (a) Davies, D. I.; Done, J. N.; Hey, D. H. *Chem. Commun. (London)* **1966**, 725−726. (b) Roberts, J. D.; Trumbull, E. R., Jr.; Bennett, W.; Armstrong, R. *J. Am. Chem. Soc.* **1950**, *72*, 3116−3124.

[23] Carbocations stemming from *carbenes* can give deviant product ratios due to ion pairing (see ref 20a).

[24] The putatively formed 1,2-diazacyclopent-1-ene derivative decomposes to spiro[1,2-bis(ethoxycarbonyl)cyclopropane-3,3′-tricyclo-[2.2.1.0^{2,6}]heptane]: m/z (EI) 219 ([M − OCH_2CH_3]$^+$, 8), 191 ([M − $C(O)OCH_2CH_3$]$^+$, 100), 163 (11), 145 (7), 125 (11), 117 (32), 97 (13), 91 (15).

[25] Carbocations stemming from *diazonium cations*, such as **11**, often give spurious product ratios: In *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; p 355.

[26] For the related 5-norbornen-2-yl route, see: Kirmse, W.; Knöpfel, N.; Loosen, K.; Siegfried, R.; Wroblowsky, H.-J. *Chem. Ber.* **1981**, *114*, 1187−1191.

[27] Photolysis of 2-azi-5-norbornene is reported to give **13c**/**14c** = 1.9. This ratio is slightly lower than usual for **12** and may also indicate some ion pairing: Kirmse, W.; Meinert, T. *J. Chem. Soc., Chem. Commun.* **1994**, 1065−1066.

[28] The **13**/**14** ratios obtained from carbenes **2** and **17** indicate a *product spread* in the direction of the starting compound: *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; p 328.

[29] (a) Azbel', B. I.; Gol'dshleger, N. F.; Isakov, Y. I.; Épel'baum, E. T.; Yampol'skii, Y. Y.; Minachev, K. M. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1986**, *35*, 1122−1125. (b) Azbel', B. I.; Gol'dshleger, N. F.; Isakov, Y. I.; Épel'baum, E. T.; Yampol'skii, Y. Y.; Khidekel', M. L.; Minachev, K. M. *Dokl. Chem. (Transl. of Dokl. Akad. Nauk)* **1984**, *276*, 197−199.

[30] One may postulate that H atom transfer to excited-state diazirine **1*** leads to a diazene, 3-diazenylnortricyclane, that is responsible for the reduction [H].

[31] A carbonyl n→π* electronic transition (λ = ca. 280 nm) is observed with RP HPLC analysis; see Experimental Section.

[32] Wu, G.; Jones, M., Jr.; Walton, R.; Lahti, P. M. *J. Org. Chem.* **1998**, *63*, 5368−5371.

[33] Wentrup, C. *Reactive Molecules*; Wiley: New York, 1984; pp 182−183.

[34] Hoffmann, R.; Zeiss, G. D.; Van Dine, G. W. *J. Am. Chem. Soc.* **1968**, *90*, 1485−1499.

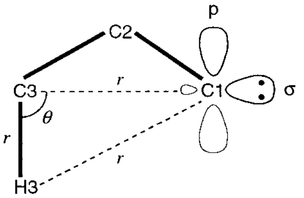


Figure 3. Geometry of carbene 1,3 C−H insertion.

Table 2. Pertinent Interatomic Distances within 2-Norbornanylidene (5), 3-Nortricyclanylidene (2), and 2-Adamantanylidene (18) Measured after Geometry Optimization with the AM1 Hamiltonian (cf. Figure 3)

carbene	r(C1−C3) (Å)	r(C3−H3) (Å)	r(C1−H3) (Å)	θ(C1−C3−H3) (deg)
5	2.411	1.115	2.571	85.3
2	2.378	1.113	2.687	93.5
18	2.457	1.120	2.730	102.9

Table 3. Relevant Enthalpies (kcal/mol) Measured after Geometry Optimization with the AM1 Hamiltonian

carbene	$\Delta_fH°$	product	$\Delta_fH°$	$\Delta H°$
2	+133.2	**8**	+104.3	−28.9
18	+54.3	**19**	+9.3	−45.0
5	+82.8	**3**	+33.8	−48.5

(e.g., Walsh orbitals) that enhances the nucleophilicity of the carbene.

Theoretical chemistry was engaged to provide information about the propensities of carbenes to undergo exothermic 1,3 C−H insertions. The transformation of **2** into **8** could be geometrically inhibited. The carbene center C1, C3, and H3 atoms describe a scalene triangle, whereby cyclopropane ring formation results from incipient C1−C3 bonding during the closely related TS (Figure 3).

The results of AM1 calculations[36] on carbene intermediates **5**, **2**, and 2-adamantanylidene (**18**) are summarized in Table 2. These semiempirical SCF methods indicate the feasibility of 1,3 C−H insertion of carbene **2**. Clearly, both the C1−H3 distance (r) and C1−C3−H3 angle (θ) values for **2** are intermediary, lying between those of **5** and **18**. It has previously been shown that **5** undergoes 1,3 C−H insertion almost exclusively.[2] Yet, **18** mostly undergoes other types of reactions in solution.[8a,37] It can, however, be compelled to undergo 1,3 C−H insertion giving 2,4-didehydroadamantane (**19**) either exclusively in the gas phase[38] or appreciably in the supramolecular phase.[8a,b] This mixed behavior is noteworthy. So further calculations were warranted.

The Bell−Evans−Polanyi principle states that there is a proportionality between the energy of activation (E_a) and the heat of reaction ($\Delta H°$). That is, as a given reaction type becomes more exothermic, the E_a decreases.[39] Hence, from the Eyring equation, the rate (constant) must increase. Table 3 lists the AM1 heats of formation ($\Delta_fH°$) of carbenes **2**, **18**, and **5** with those of their respective 1,3 C−H insertion products, **8**,[40] **19**, and **3**. The values of $\Delta H°$ clearly show that **2**→**8** is the least exothermic and must therefore have the highest E_a. Indeed, it must be so high that other processes, like cyclopropylcarbene fragmentation and innermolecular O−H insertion, happen more readily. Moreover, this dormant reaction of **2** should also be viewed as a 1,4 C−H insertion, which is altogether uncommon—presumably due to improper orbital alignment.[2a,41] In particular, this 1,4 C−H insertion would also form a cyclobutane, embedded within **8**, that is flat!

Even so, it appears that **2** should also be coerced to undergo 1,3 (or 1,4) C−H insertion if an appropriate constraint is imposed. Our experiments show, however, that this is not the case in the relatively spacious α-CyD dimer, in β-CyD, or in NaY supercages—all of which also have many available O−H moieties that intercept the carbene. Besides O−H insertion, the problem may be that the fragmentation,[42] whose rate likely exceeds that of 1,3 C−H insertion,[43] needs less free volume (ΔV) for the unraveling process than we thought. That is, when the standard equation for the free energy of activation $\Delta G^‡ = \Delta H^‡ - T\Delta S^‡$ is rewritten as

$$\Delta G^‡ = \Delta H^‡ - RT\ln\left(\frac{V^‡}{V}\right)$$

it becomes obvious that the host vessel must decrease the volume ($V^‡$) available to the (coarctate) TS to increase $\Delta G^‡$ and concomitantly inhibit the rate of **2**→**9**. We have shown, however, that carbene **2** is somewhat more stable than normal dialkylcarbenes. It undergoes some intramolecular rearrangement to **9** in MeOH, and it forms some azine **6** in lightly loaded FAU zeolites. Therefore, we believe that it is still possible to subdue fragmentation and enhance 1,3 C−H insertion under *more confining* conditions.

In conclusion, we have observed the first inter- and innermolecular reactions of carbene **2** by photolyzing a new and suitable precursor, diazirine **1**. The constraint imposed upon carbene **2** within CyD's and FAU's was not enough to prevent its fragmentation into the thermodynamically favored enyne **9**, nor could inclusion enhance 1,3 C−H insertion, forcing **2** into the highly strained **8**. Undoubtedly, the C2−C6 bridge in **2** markedly alters the chemistry of carbene **2** as compared with that of carbene **5**. Bearing in mind that carbenes can be generated within argon matrixes[44] and crystalline media,[45] we envision that the selectivity of carbene **2** will one day be controlled.

Experimental Section

General Information. 3-Nortricyclanone (**16**) was prepared according to the literature.[11b,21b] Hydroxylamine-*O*-sulfonic acid (HOSA, 95%, Fluka) was used as purchased. Ag_2O was prepared

---

[35] *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; p 169.

[36] Austin Model 1: Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902−3909.

[37] Isaev, S. D.; Yurchenko, A. G.; Stepanov, F. N.; Kolyada, G. G.; Novikov, S. S.; Karpenko, N. F. *J. Org. Chem. USSR* **1973**, *9*, 745−748.

[38] Isaev, S. D.; Yurchenko, A. G.; Stepanov, F. N.; Kolyada, G. G.; Novikov, S. S. *J. Org. Chem. USSR* **1973**, *9*, 436.

[39] Wentrup, C. *Reactive Molecules*; Wiley: New York, 1984; pp 10−12.

[40] Experimental $\Delta_fH°$(**8**) = +81.0 kcal/mol: Steele, W. V. *J. Chem. Thermodyn.* **1978**, *10*, 919−927.

[41] Bradley, G. F.; Evans, W. B. L.; Stevens, I. D. R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1214−1220.

[42] $\Delta_fH°$(**9**) = +66.3 kcal/mol as calcd by Benson group additivity method: Benson, S. W.; Cruickshank, F. R.; Golden, D. M.; Haugen, G. R.; O'Neal, H. E.; Rodgers, A. S.; Shaw, R.; Walsh, R. *Chem. Rev.* **1969**, *69*, 279−324.

[43] Barring quantum mechanical tunneling.

[44] (a) Sheridan, R. S. In *Organic Photochemistry and Photobiology*; Horspool, W. M., Ed.; CRC: Boca Raton, FL, 1995; pp 999−1006. (b) Tomioka, H.; Ozaki, Y.; Koyabu, Y.; Izawa, Y. *Tetrahedron Lett.* **1982**, *23*, 1917−1920.

[45] (a) Shin, S. H.; Keating, A. E.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 7626−7627. (b) Shin, S. H.; Cizmeciyan, D.; Keating, A. E.; Khan, S. I.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 1859−1868.

immediately prior to use.[46] α-CyD and β-CyD were recrystallized from H_2O and found to be 90.0% (w/w) and 86.5% (w/w), respectively, by microanalysis. NaY and bicyclohexyl were purchased from Aldrich. Photolyses were performed using a Heraeus TQ 718 Z4 700-W medium-pressure Hg-arc lamp doped with FeI_2 ($\lambda_{max} = 370$ nm) at $T_{sample} = 15$ °C. Solution photolyses of **1** (concn = 0.02 M) were performed in Schlenk tubes after three freeze−pump−thaw cycles with argon purging. FT NMR spectra were recorded on a Bruker Avance DPX-250 spectrometer ($B_o = 5.875$ T) at the following Larmor frequencies: $\nu_o(^1H) = 250.1$ MHz and $\nu_o(^{13}C) = 62.9$ MHz. 2-D ROESY spectra of the dilute D_2O solutions of $\mathbf{1}@(\alpha\text{-CyD})_2$ and $(\mathbf{1}@\beta\text{-CyD})_2$ were obtained using 0.60 and 0.45 s mixing times, respectively, with solvent peak presaturation. IR absorption spectra were recorded on a Perkin-Elmer 1600 FT IR spectrometer by applying samples as neat liquids onto a Si wafer or by pressing dilute KBr pellets. UV/vis absorption spectra were recorded on a Perkin-Elmer Lambda 7 UV/vis spectrometer. CD spectra were obtained using a CD 6 circular dichrograph (I.S.A. Jobin Yvon) spectrometer. Analytical GC analyses were conducted using a Fisons 8000 series GC instrument outfitted with a 30 m poly(dimethylsiloxane) capillary column (Perkin-Elmer, PE-1, 0.32 mm i.d., and 0.25 μm film-thickness) and a flame-ionization detector. The following conditions and temperature program were used: $T_{oven,i} = 50$ °C (5 min), ramp = +10 °C/min, $T_{oven,f} = 230$ °C (7 min), $T_{injector} = 185$ °C, $T_{FID} = 260$ °C, and flow = 2.1 (mL He)/min. Preparative GC was performed using a Varian Aerograph model 920 instrument equipped with a 3.05 m Al column (6.4 mm i.d.) packed with 20% QF1 on Chromosorb (80−100 mesh, NAW) and a thermal conductivity detector. The following isothermal conditions were used: $T_{oven} = 100$ °C, $T_{injector} = 200$ °C, $T_{TCD} = 200$ °C, and flow = 76 (mL He)/min. The effluent was condensed using a $CO_{2(s)}/^{i}PrOH$ trap. GC−MS analyses were conducted using a Hewlett-Packard 6890 series GC outfitted with a 30 m poly(methylphenylsiloxane) capillary column (Hewlett-Packard, HP-5MS {95% diMe and 5% diPh}, 0.25 mm i.d., and 0.25 μm film-thickness) and a Hewlett-Packard 5973 MSD; a Hewlett-Packard 59864B ionization gauge controller was used for chemical ionization studies. The following GC conditions and temperature programs were used: $T_{oven,i} = 80$ °C (7 min), ramp = +10 °C/min, $T_{oven,f} = 270$ °C (5 min), $T_{injector} = 200$ °C, and initial flow = 0.8 (mL He)/min. Microanalysis was employed to determine the guest@host stoichiometry of the CyD IC's as well as their water content. Analytical RP HPLC was performed using a Hewlett-Packard HP 1090 liquid chromatograph with a Hewlett-Packard 35900E interface, equipped with a Nucleosil 300-5 C8 5 μm column (290 × 4 mm, FZ Seibersdorf, Austria). Isocratic elution giving a 70% H_2O and 30% MeOH mixture was employed at 0.5 mL/min. Product signals were observed using an UV detector ($\lambda = 211$, 281 nm) and a HP 1047A RI detector, consecutively, and compared with those from α-CyD and β-CyD standards. FAB MS assays were performed on a Finnigan MAT 900 spectrometer by bombarding the photolyzed CyD IC's, in a 1-thioglycerol matrix, with a 20 keV beam of Cs atoms at 70 °C.

3-Azinortricyclane (1). CAUTION! Within an efficient fume hood, 100 mL of $NH_{3(l)}$ were condensed by passing $NH_{3(g)}$ through a column of $KOH_{(s)}$ drying agent, then through the rubber septum of a dry, graduated 250 mL Schlenk flask that was submerged in a $CO_{2(s)}/^{i}PrOH$ bath.[47] A hand bellows and a large-bore double-ended needle were used to cannulate the $NH_{3(l)}$ through the rubber septum of a 500 mL three-necked round-bottom (r.b.) flask that was also equipped with a low-T thermometer, a large stirbar, and a 1 L suspended condenser, or coldfinger, which was filled (and periodically refilled) with pulverized dry ice and whose outlet included a silicone oil bubbler. With moderate stirring, neat ketone **16** (5.407 g, 50 mmol) was slowly injected via syringe and rinsed with 1 mL of MeOH.[48] The mixture was refluxed at ca. −33 °C for 1.5 h before addition of the aminating agent. Meanwhile, HOSA (6.071 g, 51 mmol) was dissolved in 50 mL of anhydrous MeOH and sealed in an Erlenmeyer flask with a rubber septum. After cooling this solution in an ice bath, the stirring speed was increased and aliquots of this solution were injected via syringe every 10 min according to the following schedule: 6 × 3.33 mL during the first hour, 6 × 2.50 mL during the second hour, 6 × 1.67 mL during the third hour, and 6 × 0.83 mL during the fourth hour, by which time the reaction T had climbed to −28 °C. The stirring speed was reduced and the $NH_{3(g)}$ was allowed to slowly evaporate overnight in the hood. Both ends of the cool mixture were stoppered, and the remaining NH_3 and MeOH were rotary-evaporated using water aspiration. The white residue was transferred into a sinter funnel (Por. 4) and triturated with CH_2Cl_2 (6 × 50 mL). Each portion was suction-filtered into a receiving flask. The combined, faintly purple filtrates were poured into a 500 mL r.b. flask, and the solvent was rotary-evaporated. The residue was dissolved in Et_2O (30 mL) and transferred to a loosely stoppered 50 mL r.b. flask that was equipped with a stirbar and submerged in a room-temperature water bath. Overhead lighting was dimmed. The putative diaziridine[49] was oxidized with freshly prepared Ag_2O by rapidly stirring overnight.[50] The mixture was dried with anhydrous Na_2SO_4, suction-filtered (Por. 4 sinter funnel),[51] and rotary-evaporated, and the residual oil was chromatographed (silica gel 60, 230−400 mesh) using pentane as eluent. The nonpolar diazirine eluted first, giving 0.356 g, 6% yield of a colorless, odorous liquid after careful rotary evaporation:[52] δ_H/ppm ($CDCl_3$) 0.27 (1 H, td J 5.3, J 1.3), 0.93−0.97 (1 H, m), 1.41 (2 H, dm J 10.3), 1.49 (2 H, dm J 5.3), 1.92 (2 H, dm J 10.3); δ_C/ppm ($CDCl_3$) 11.3 (d J 179), 13.0 (d J 177), 32.0 (t J 134), 33.0 (d J 147), 42.7 (s); $\bar{\nu}_{max}/cm^{-1}$ (neat) 3071, 3005, 2947, 2871, 1567, 1446, 1290, 1239, 936, 821, 787; λ_{max}/nm (pentane) 354, 373; m/z (CI, CH_4)[53] 149 ($[M + C_2H_5]^+$, 1), 121 ($[M + H]^+$, 49), 108 (13), 104 (36), 94 (31), 93 (64), 92 (19), 91 (100), 79 (23), 67 (9).

4-Ethynylcyclopentene (9). CAUTION! Injection of diazirine **1** (60 mg, 0.12 mL of $CDCl_3$) into the preparative GC afforded the malodorous enyne in 91% yield: δ_H/ppm ($CDCl_3$) 2.04 (1 H, d J 2.5), 2.38−2.54 (2 H, m), 2.62−2.78 (2 H, m), 2.93−3.08 (1 H, m), 5.64−5.72 (2 H, m); δ_C/ppm ($CDCl_3$) 27.6 (d J 132), 40.2 (t J 130), 67.4 (d J 248), 89.0 (s), 129.3 (d J 168); $\bar{\nu}_{max}/cm^{-1}$ (neat) 3307, 3061, 2940, 2856, 2118, 1615; m/z (EI) 92 (M^+, 28), 91 ($[M - H]^+$, 100), 89 (3), 66 (3), 65 (10), 63 (6).

Preparation and Photolysis of $\mathbf{1@(\alpha\text{-CyD})_2}$ and $\mathbf{(1@\beta\text{-CyD})_2}$. Filtered solutions of α-CyD (0.811 g, 0.750 mmol, 12.0 mL of H_2O) and β-CyD (0.492 g, 0.375 mmol, 36.5 mL of H_2O) were rapidly stirred in a room-temperature water bath under the exclusion of light. Neat diazirine **1** (30 mg, 0.25 mmol) was injected into each solution and stirred overnight. The white suspensions were transferred to tared centrifuge tubes and centrifuged (2.2K rpm, $T = 18$ °C, 25 min), and the supernatants were decanted. Each precipitate was triturated with 3 mL of H_2O and recentrifuged. After decanting the washings, the samples were placed in a vacuum desiccator, preevacuated by a diaphragm pump, and evacuated by a high-vacuum oil pump to ca. 0.2 mmHg for 4 h, giving 0.331 g of α-CyD IC (Found: C, 42.46; H, 6.58; N, 0.97, corresponding to $\mathbf{1}@2.6\alpha\text{-CyD}\cdot11H_2O$, 46% yield) and 0.180 g of β-CyD IC (Found: C, 44.00; H, 6.48; N, 1.88, corresponding to $\mathbf{1}@1.1\beta\text{-CyD}\cdot4H_2O$, 50% yield). The 2-D ROESY spectrum of the α-CyD IC showed cross-peaks between all protons of **1** with only H3 of α-CyD; that of the β-CyD IC

---

[46] Silver oxide: (wear gloves) 16.5 mL of 2.0 M NaOH was diluted to 45 mL, then slowly poured into a stirred solution of $AgNO_3$ (5.096 g, 30 mmol) in 45 mL of H_2O. The brown precipitate was suction-filtered (Por. 4 sinter funnel), washed with H_2O until the drippings were of neutral pH, and rinsed with acetone and then Et_2O, to dry it, yielding 3.430 g, 14.8 mmol.

[47] A slowly inflating balloon attached to the flask outlet indicates that a slight positive pressure is being maintained.

[48] A peach color develops that is soon followed by the gradual formation of a white precipitate.

[49] 3-Hydrazinortricyclane: $\bar{\nu}_{max}/cm^{-1}$ (KBr) 3204; m/z (EI) 122 (M^+, 20), 121 ($[M - H]^+$, 36), 107 ($[M - NH]^+$, 71), 106 (61), 104 (9), 95 (33), 91 (49), 80 (60), 79 (100), 77 (55), 67 (28), 66 (29).

[50] Although expected, a silver mirror may not form due to a low yield.

[51] The silver residues can be digested by 50% (w/w) aqueous HNO_3.

[52] Diazirine **1** may be preserved for several weeks in the freezer (−22 °C).

[53] For a related MS analysis of 3*H*-diazirines using isobutane as the reagent gas, see: Isaev, S. D.; Karpenko, N. F.; Yurchenko, A. G.; Vodička, L.; Kadentsev, V. I.; Zachař, P. *Collect. Czech. Chem. Commun.* **1989**, *54*, 691−698.

showed cross-peaks between protons of **1** with H3 and H5 of β-CyD. Next, the CyD IC's (50 mg each) were transferred to Schlenk tubes, sealed with rubber septa, and alternately evacuated and purged with argon three times. The CyD IC's were photolyzed for 1 day. A 5 mg portion of each photolyzed CyD IC was set aside for NMR (DMSO-d_6) and FAB MS analyses. **13a** and **14a**: m/z (-νe FAB, thioglycerol) 1063.5 ($[M - H]^-$). **13b** and **14b**: m/z (-νe FAB, thioglycerol) 1225.3 ($[M - H]^-$).[54] The remaining samples were each dissolved in 100 mL of H_2O and continuously extracted overnight with 100 mL of refluxing anhydrous CH_2Cl_2, which was subsequently analyzed by GC. Each aqueous layer was collected and subjected to rotary evaporation ($T = 50$ °C) to recover the CyD's. Hence, analytical RP HPLC was also employed to observe and quantify the modified CyD's.

Preparation and Photolysis of 1@NaY. Zeolite NaY·253H_2O (0.451 g) was dried overnight according to the following oven program: 1 h ramp until $T_{oven} = 100$ °C (1 h), 2 h ramp until $T_{oven} = 500$ °C (12 h), reduce to $T_{oven} = 150$ °C (hold).[55] It was then cooled to room temperature in an anhydrous $CaCl_2$ desiccator. The sample was quickly transferred into a dry, stirbar-containing, tared centrifuge tube with rubber septum and weighed, giving 0.350 g of NaY·$x$$H_2O$.[56] Diazirine **1** (6.6 mg, 55 μmol) was dissolved in 4.6 mL of anhydrous pentane,[57] a 1.0 μL aliquot was analyzed by GC ($T_{injector} = 140$ °C), and the rest was poured into the centrifuge tube, which was quickly resealed. The suspension was slowly stirred for 3 h in a room-temperature water bath. After removing the stirbar, the sample was centrifuged (2.2K rpm, $T = 18$ °C, 20 min) and the supernatant was decanted. Analysis by GC showed that no **1** remained in solution. The FAU IC was triturated with 2 mL of anhydrous pentane and recentrifuged. After decanting the washing, the FAU IC was placed in a vacuum desiccator, preevacuated by a diaphragm pump, and evacuated by a high-vacuum oil pump to ca. 0.2 mmHg for 15 min. The sample was slowly repressurized using an argon-filled balloon and resealed. The FAU IC was photolyzed for 2 days with constant rotation. The photolyzed sample was transferred to a Soxhlet-type extractor and continuously extracted overnight with 40 mL of refluxing anhydrous CH_2Cl_2, which was subsequently analyzed by GC.

Acknowledgment. We thank the Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (Project P12533-CHE) for financial support and both Cerestar USA, Inc., and Wacker Chemie, Germany, for providing the cyclodextrins used in this study. We are also grateful to Dr. D. Krois and Ing. U. Haslinger for their assistance. Helpful consultations with Prof. W. Kirmse, Ruhr-Universität Bochum, Germany, Prof. B. K. Carpenter, Cornell University, U.S.A., and H. W. G. van Herwijnen, Universität Wien, Austria, are greatly appreciated.

Supporting Information Available: Vacuum pyrolysis of **10**. Z-Matrixes for **2**, **3**, **5**, **8**, **18**, and **19** with computed total energies. 2-D ROESY spectra of **1**@(α-CyD)$_2$ and (**1**@β-CyD)$_2$. ICD spectrum of **1**@(α-CyD)$_2$. Formula for **13**/**14** ratio as a function of the extent of ion pairing with accompanying graph. This material is available free of charge via the Internet at http://pubs.acs.org

JO005713E

---

(54) Also observed m/z (-νe FAB, thioglycerol) 1317.5 ($[M - H]^-$). This corresponds to an innermolecular insertion product of *two* carbenes **2** with one β-CyD, which may be expected from dimeric (**1**@β-CyD)$_2$.

(55) Slowly heating the FAU prevents the possible formation of Lewis acidic sites within the zeolite lattice that might decompose a 3*H*-diazirine: van Herwijnen, H. W. G., Universität Wien, personal communication, 1999.

(56) $x =$ ca. 38; see ref 18.

(57) $\langle s \rangle = \{(17319.66 \text{ g/mol NaY·253H}_2\text{O})(1 \text{ mol NaY·253H}_2\text{O})(55\ \mu\text{mol } \mathbf{1})\}/\{(0.451 \text{ g})(8 \text{ mol supercage})\} = 0.26\ \mathbf{1}/\text{supercage}$.