JOC*Article*

Inter- and Innermolecular Reactions of Chloro(phenyl)carbene†

Murray G. Rosenberg‡ and Udo H. Brinker*

Institut für Organische Chemie, Universität Wien, Währinger Strasse 38, A-1090 Wien, Austria, and Department of Chemistry, State University of New York, Binghamton, New York 13902-6016

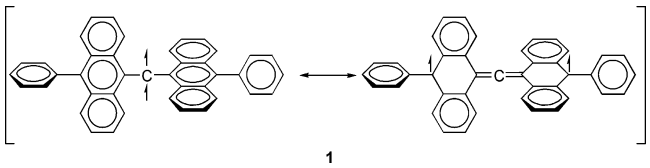
udo.brinker@univie.ac.at

Received October 3, 2002

Supramolecular photolyses of 3-chloro-3-phenyl-3*H*-diazirine (**8**) were performed within cyclodextrin (CyD) hosts to determine whether these toroidal inclusion compounds could alter the reactivity of the ensuing carbene reaction intermediate, chloro(phenyl)carbene (**9**). Remarkably, no *intra*molecular products stemming from carbene **9** could be detected. Instead, modified CyDs were formed via so-called *inner*molecular reactions. Hence, diazirine **8** was photolyzed in various conventional solvents to gauge the *inter*molecular reactivity of carbene **9**. Relevant results were used to rationalize the CyD *inner*molecular reaction products.

Introduction

Much time and effort has been spent in recent years seeking long-lived carbenes.[1] This flurry of activity has met limited success. Tomioka carbenes,[2] such as triplet bis(10-phenylanthracen-9-yl)carbene (**1**) ($t_{1/2}$ = 19 min, D/hc = 0.105 cm^{-1}) (Figure 1),[1a,2a,b,3] are persistent organic reaction "intermediates" and constitute one area of promising research. Ylide-like singlet carbenes, such as Breslow thiazol-2-ylidenes (**2**),[4] Wanzlick imidazolidin-2-ylidenes (**3**),[5] Arduengo imidazolin-2-ylidenes (**4**),[1f,5f,6] and Bertrand phosphinocarbenes (**5**),[1c,7] comprise another (Figure 2).[8] However, supramolecular inclusion of more *typical* carbenes within suitable hosts may offer distinct advantages.



1

FIGURE 1. Is triplet bis(10-phenylanthracen-9-yl)carbene (**1**) really a geminate diradical?

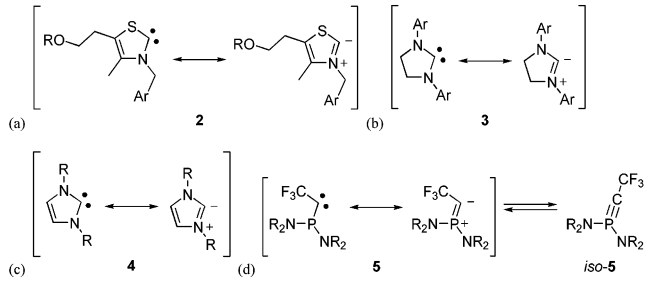


FIGURE 2. Singlet carbene or pnictonium ylide? (a) Breslow, (b) Wanzlick, (c) Arduengo, and (d) Bertrand carbenes.

The rearrangement of phenylcarbene (**6**) to 1,2,4,6-cycloheptatetraene (**7**) has been extensively studied (eq 1).[9] Recently, Warmuth reported the generation of car-

* To whom correspondence should be addressed. Phone: +43-1-4277-52121. Fax: +43-1-4277-52140.

† Carbenes in Constrained Systems. 8. For part 7, see: Rosenberg, M. G.; Brinker, U. H. *J. Org. Chem.* **2001**, *66*, 1517-1522. Carbene Rearrangements. 57. For part 56, see: Knoll, W.; Bobek, M. M.; Giester, G.; Brinker, U. H. *Tetrahedron Lett.* **2001**, *42*, 9161-9165.

‡ State University of New York.

(1) (a) Freemantle, M. *Chem. Eng. News* **2001**, *79* (33), 11. (b) Freemantle, M. *Chem. Eng. News* **1999**, *77* (45), 19. (c) Freemantle, M. *Chem. Eng. News* **2000**, *78* (19), 57. (d) Freemantle, M. *Chem. Eng. News* **2001**, *79* (24), 22. (e) Dagani, R. *Chem. Eng. News* **1994**, *72* (18), 20−22. (f) *Chem. Eng. News* **1991**, *69* (4), 19−20. (g) Krishnamurthy, S. S. *Curr. Sci.* **1991**, *60*, 619−620. (h) Bucher, G.; Winkler, M. *Nachr. Chem.* **2002**, *50*, 289−293. (i) Hopkins, J. M.; Bowdridge, M.; Robertson, K. N.; Cameron, T. S.; Jenkins, H. A.; Clyburne, J. A. C. *J. Org. Chem.* **2001**, *66*, 5713−5716.

(2) (a) Tomioka, H.; Iwamoto, E.; Itakura, H.; Hirai, K. *Nature* **2001**, *412*, 626−628. (b) Tomioka, H.; Nozaki, Y.; Iwamoto, E.; Hirai, K. In *Proceedings of the Conference on Reactive Intermediates and Unusual Molecules*; Bobek, M. M., Ed.; Eigenverlag: Vienna, 2000; p 3. (c) Hirai, K.; Tomioka, H. *J. Am. Chem. Soc.* **1999**, *121*, 10213−10214. (d) Tomioka, H. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, CT, 1998; Vol. 2, pp 175−214. (e) Tomioka, H. *Acc. Chem. Res.* **1997**, *30*, 315−321. (f) Tomioka, H.; Watanabe, T.; Hirai, K.; Furukawa, K.; Takui, T.; Itoh, K. *J. Am. Chem. Soc.* **1995**, *117*, 6376−6377.

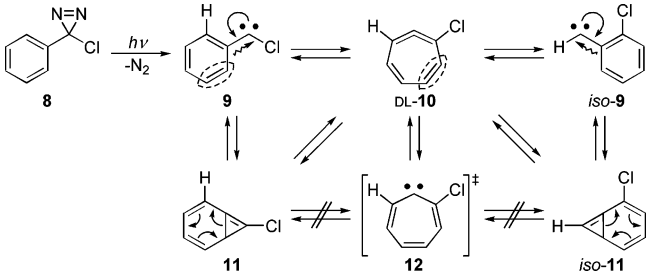
(3) In triplet-state ESR, the zero-field splitting parameter D represents the slight energy difference between the T± and T_0 states, e.g., D(**1**) = 3.0 × 10^{-4} kcal/mol, and is inversely related to the distance of the two unpaired electrons. See: (a) Turro, N. J. *Modern Molecular Photochemistry*; University Science Books: Mill Valley, CA, 1991; pp 551−552. (b) Wentrup, C. *Reactive Molecules*; Wiley: New York, 1984; pp 46−48, 176−180.

(4) (a) Breslow, R. *J. Am. Chem. Soc.* **1957**, *79*, 1762−1763. (b) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719−3726. (c) Wanzlick, H.-W.; Kleiner, H.-J. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 65. (d) Olofson, R. A.; Landesberg, J. M.; Houk, K. N.; Michelman, J. S. *J. Am. Chem. Soc.* **1966**, *88*, 4265−4266. (e) Hoffmann, R. W.; Hagenbruch, B.; Smith, D. M. *Chem. Ber.* **1977**, *110*, 23−36. (f) Sugimoto, H.; Hirai, K. *Tetrahedron Lett.* **1985**, *26*, 883−886. (g) Kluger, R. *Chem. Rev.* **1987**, *87*, 863−876.

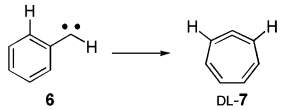
(5) (a) Wanzlick, H.-W.; Kleiner, H.-J. *Angew. Chem.* **1961**, *73*, 493. (b) Wanzlick, H.-W.; Schikora, E. *Chem. Ber.* **1961**, *94*, 2389−2393. (c) Wanzlick, H. W. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 75−80. (d) Wanzlick, H.-W.; Ahrens, H. *Chem. Ber.* **1964**, *97*, 2447−2450. (e) Lemal, D. M.; Lovald, R. A.; Kawano, K. I. *J. Am. Chem. Soc.* **1964**, *86*, 2518−2519. (f) Winberg, H. E.; Carnahan, J. E.; Coffman, D. D.; Brown, M. *J. Am. Chem. Soc.* **1965**, *87*, 2055−2056. (g) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 754−765. (h) Wiberg, N. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 766−779. (i) Lemal, D. M. In *The Chemistry of the Amino Group*; Patai, S., Ed.; Wiley: New York, 1968; Chapter 12. (j) Arduengo, A. J., III; Goerlich, J. R.; Marshall, W. J. *J. Am. Chem. Soc.* **1995**, *117*, 11027−11028.

10.1021/jo026521h CCC: $25.00
Published on Web 05/21/2003

SCHEME 1. Ring Expansion of Chloro(phenyl)carbene (9)



bene **6** within a hemicarcerand (HC).[10] Encapsulated allene **7** was protected from dimerization, so even the ^{1}H 2-D NOESY NMR spectrum of **7**@HC could be measured.



(1)

Photolysis of 3-chloro-3-phenyl-3*H*-diazirine (**8**) in Ar at 10 K generates matrix-isolated chloro(phenyl)carbene (**9**) (Scheme 1),[11] which completely undergoes ring expansion to 1-chloro-1,2,4,6-cycloheptatetraene (**10**) when exposed to short wavelength irradiation (λ > 254 nm).[12] This rearrangement proceeds by either a direct or an indirect 1,2-C shift. Indeed, neither 7-chlorobicyclo[4.1.0]-hepta-2,4,6-triene (**11**) nor 2-chloro-2,4,6-cycloheptatrien-1-ylidene (**12**) was observed during prolonged irradiation (λ > 338 nm) of carbene **9**.[9c,13] Hence, cyclic allene **10** apparently derives from a direct "*vinyl*" migration (**9** → **10**) within the frozen argon matrix.[14−16] However, if 7-chlorobicyclo[4.1.0]hepta-2,4,6-triene (**11**) were to lie in a shallow potential energy well then it would be very fleeting and perhaps unobservable.[9d,e]

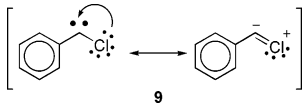
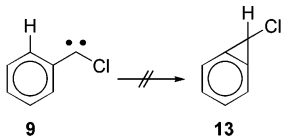


FIGURE 3. Mesomeric forms of chloro(phenyl)carbene (**9**).

Moreover, (2-chlorophenyl)carbene (*iso*-**9**) also rearranges to cyclic allene **10** (Scheme 1).[9c,11] Sander reported that the two carbenes do not interconvert,[11] which could be due to the fact that halo(phenyl)carbene **9** has a singlet ground state (GS) whereas (halophenyl)carbene *iso*-**9** likely has a triplet GS. In contrast, Chapman and coworkers reported that irradiation (λ > 212 nm) of cyclic allene **10** (produced from *iso*-**9**) affords some carbene **9**.[9c] Finally, the 1,3-C−H insertion of carbene **9** to 1-chloro-1*H*-cyclopropabenzene (**13**) was not observed by either research group (eq 2).



(2)

Chloro(phenyl)carbene (**9**) can be drawn as a reversed-electronegativity chloronium ylide possessing a weak $C_{2p}-Cl_{3p}$ π-bond (Figure 3). Electron donation to the divalent carbon of carbene **9** by the chlorine substituent stabilizes the singlet electronic state relative to the triplet. This inner covalent coordination is sufficient enough to make the singlet state the ground state (GS). Hence, carbene **9** shows no ESR signal and adds stereospecifically to alkenes.[17]

To determine whether room-temperature supramolecular constraint of carbene **9** could yield ring-expanded allene **10**, triplet carbene *iso*-**9**, or benzocyclopropene **13**, the carbene precursor 3-chloro-3-phenyl-3*H*-diazirine (**8**) was prepared,[18] and then included within cyclodextrins prior to photolysis. Indeed, recent advances in carbene chemistry[19] demonstrate that constrictive hosts, like cyclodextrins,[20] are able to modify the selectivity of the

(6) (a) Arduengo, A. J., III; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361−363. (b) Arduengo, A. J., III; Dias, H. V. R.; Dixon, D. A.; Harlow, R. L.; Klooster, W. T.; Koetzle, T. F. *J. Am. Chem. Soc.* **1994**, *116*, 6812−6822. (c) Olofson, R. A.; Thompson, W. R.; Michelman, J. S. *J. Am. Chem. Soc.* **1964**, *86*, 1865−1866. (d) Staab, H. A.; Irngartinger, H.; Mannschreck, A.; Wu, M.-T. *Justus Liebigs Ann. Chem.* **1966**, *695*, 55−64. (e) Regitz, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 725−728. (f) Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2162−2187. (g) Arduengo, A. J., III; Krafczyk, R. *Chem. Unserer Zeit* **1998**, *32*, 6−14.

(7) (a) Buron, C.; Gornitzka, H.; Romanenko, V.; Bertrand, G. *Science* **2000**, *288*, 834−836. (b) Dixon, D. A.; Dobbs, K. D.; Arduengo, A. J., III; Bertrand, G. *J. Am. Chem. Soc.* **1991**, *113*, 8782−8785. (c) Bertrand, G. *Heteroat. Chem.* **1991**, *2*, 29−38. (d) Igau, A.; Baceiredo, A.; Trinquier, G.; Bertrand, G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 621−622. (e) Igau, A.; Grutzmacher, H.; Baceiredo, A.; Bertrand, G. *J. Am. Chem. Soc.* **1988**, *110*, 6463−6466.

(8) (a) Chen, P. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, CT, 1998; Vol. 2, pp 45−75. (b) Warkentin, J. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, CT, 1998; Vol. 2, pp 245−295.

(9) (a) Jones, W. M.; Brinker, U. H. In *Pericyclic Reactions*; Marchand, A. P., Lehr, R. E., Eds.; Academic: New York, 1977; Vol. 1, Chapter 3, pp 137−159. (b) Jones, W. M.; Joines, R. C.; Myers, J. A.; Mitsuhashi, T.; Krajca, K. E.; Waali, E. E.; Davis, T. L. Turner, A. B. *J. Am. Chem. Soc.* **1973**, *95*, 826−835. (c) McMahon, R. J.; Abelt, C. J.; Chapman, O. L.; Johnson, J. W.; Kreil, C. L.; LeRoux, J.-P.; Mooring, A. M.; West, P. R. *J. Am. Chem. Soc.* **1987**, *109*, 2456−2469. (d) Wong, M. W.; Wentrup, C. *J. Org. Chem.* **1996**, *61*, 7022−7029. (e) Schreiner, P. R.; Karney, W. L.; Schleyer, P. v. R.; Borden, W. T.; Hamilton, T. P.; Schaefer, H. F., III. *J. Org. Chem.* **1996**, *61*, 7030−7039. (f) Matzinger, S.; Bally, T. *J. Phys. Chem. A* **2000**, *104*, 3544−3552. (g) Geise, C. M.; Hadad, C. M. *J. Org. Chem.* **2002**, *67*, 2532−2540. (h) Bayley, H.; Knowles, J. R. *Biochemistry* **1978**, *17*, 2420−2423.

(10) (a) Warmuth, R.; Marvel, M. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1117−1119. (b) Warmuth, R. In *Proceedings of the Conference on Reactive Intermediates and Unusual Molecules*; Bobek, M. M., Ed.; Eigenverlag: Vienna, 2000; p 28. (c) Warmuth, R. *Eur. J. Org. Chem.* **2001**, 423−437.

(11) Sander, W. W. *Spectrochim. Acta, Part A* **1987**, *43A*, 637−646.

(12) No range is given in ref 11.

(13) Singlet 2-chloro-2,4,6-cycloheptatrien-1-ylidene (**12**) is expected to lie at the transition state (TS) between (*R*)-1-chloro-1,2,4,6-cycloheptatetraene ((*R*)-**10**) and (*S*)-1-chloro-1,2,4,6-cycloheptatetraene ((*S*)-**10**). For an account of the related enantiomerization of DL-**7**, see ref 10c, p 432.

(14) Brinker, U. H.; König, L. *Chem Lett.* **1984**, 45−48.

(15) (a) Jones, W. M. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, Chapter 3. (b) Kirmse, W.; Kopannia, S. *J. Org. Chem.* **1998**, *63*, 1178−1184.

(16) Compare with the rearrangement of phenylnitrene to 1-aza-1,2,4,6-cycloheptatetraene: (a) Platz, M. S.; Gritsan, N. P. *Abstr. Pap. Am. Chem. Soc.* **2001**, *222*, ORGN 242. (b) Platz, M. S. *Acc. Chem. Res.* **1995**, *28*, 487−492. (c) Marcinek, A.; Leyva, E.; Whitt, D.; Platz, M. S. *J. Am. Chem. Soc.* **1993**, *115*, 8609−8612.

(17) (a) Turro, N. J.; Lehr, G. F.; Butcher, J. A., Jr.; Moss, R. A.; Guo, W. *J. Am. Chem. Soc.* **1982**, *104*, 1754−1756. (b) Gould, I. R.; Turro, N. J.; Butcher, J., Jr.; Doubleday: C., Jr.; Hacker, N. P.; Lehr, G. F.; Moss, R. A.; Cox, D. P.; Guo, W.; Munjal, R. C.; Perez, L. A.; Fedorynski, M. *Tetrahedron* **1985**, *41*, 1587−1600. (c) Moss, R. A.; Turro, N. J. In *Kinetics and Spectroscopy of Carbenes and Biradicals*; Platz, M. S., Ed.; Plenum: New York, 1990; pp 213−238.

(18) (a) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396−4397. (b) Padwa, A.; Pulwer, M. J.; Blacklock, T. J. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, pp 203−206.

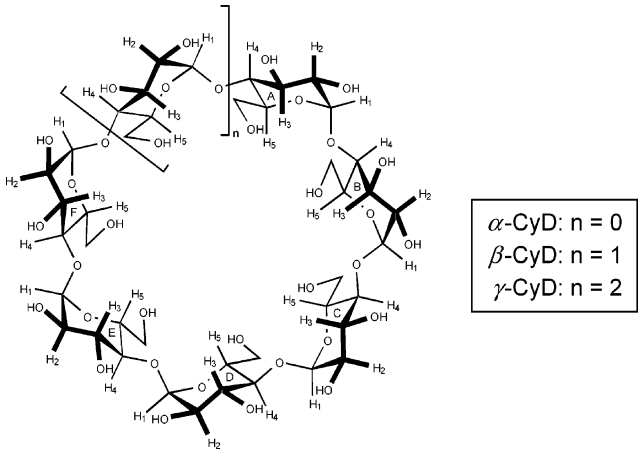


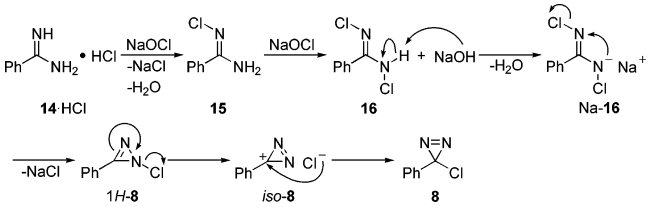
FIGURE 4. Structure of cyclodextrin (CyD) depicting the O1−C4 α-linkage of D-glucopyranose monomers. Note the inward pointing H3 and H5 atoms.

high-energy reaction intermediate.[21] Thus, we hypothesized that the confinement of carbene **9** within the nanoscopic cavities of cyclodextrins (Figure 4) would alter its reactivity.

A cyclodextrin (CyD) is a nonreducing, cyclic oligosaccharide molecule composed of α-D-glucopyranose (α-D-Glc*p*) monomers linked at the 1 and 4 glycosidic positions. The general structure of CyDs is shown in Figure 4. Their prefixes depend on the number of pyranose units present: six (α-CyD), seven (*β*-CyD), eight (*γ*-CyD), and nine (*δ*-CyD).[22]

These torus-shaped[23] hosts can accommodate many sorts of organic molecules that can reside within the nonpolar cavity. The strength of this noncovalent interaction is directly related to the position of the equilibrium for complex formation. This is evaluated by a binding

SCHEME 2. Formation of Graham's Diazirine 3-Chloro-3-phenyl-3*H*-diazirine (8)



constant (*K*)[24] that may be measured in a variety of different ways, e.g., spectrofluorometric methods based on competition experiments.[25] Recently, induced circular dichroism (ICD) has also been used to assess the binding constants of carbene-forming 3*H*-diazirine@CyD inclusion complexes (ICs).[26]

Results and Discussion

3-Chloro-3-phenyl-3*H*-diazirine (**8**) was prepared from benzamidine hydrochloride (**14**·HCl) and sodium hypochlorite (NaOCl) in ca. 70% yield.[18a,27] In addition to diazirine **8**, other more polar compounds were formed in the following relative yields: benzaldehyde (PhCHO, 9%), benzonitrile (PhCN, 16%), *x*-(1-chloro-1-phenylmethyl)-pentanes (**20i**, 4%),[28,29] benzyl benzoate (BzOBn, 54%),[30] 1,2-dichloro-1,2-diphenylethene (**17**, 3%),[31] 2,5-diphenyl-1,3,4-oxadiazole (PPD, trace),[32] and bis(1-chloro-1-phenylmethylidene)hydrazine (**18**, 14%).[33] However, most of these byproducts can be attributed to the decomposition of diazirine **8**.

The original mechanism for diazirine **8** formation, proposed by Graham,[18a] was contested in 1980 when 3-chloro-3-phenyl-3*H*-diaziridine (*N*,*N*′-dihydro-**8**) was suggested as a reaction intermediate (Scheme 2).[34]

(19) (a) Hine, J. *Divalent Carbon*: Ronald: New York, 1964. (b) Kirmse, W. *Carbene, Carbenoide, und Carbenanaloge*; Verlag Chemie: Weinheim, 1969. (c) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic: New York, 1971. (d) *Carbenes*; Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1973; Vol. 1. (e) *Carbenes*; Jones, M., Jr.; Moss, R. A., Eds.; Wiley: New York, 1975; Vol. 2. (f) Jones, M., Jr. *Sci. Am.* **1976**, *234* (2), 101−113. (g) Jones, W. M.; Brinker, U. H. In *Pericyclic Reactions*; Marchand, A. P., Lehr, R. E., Eds.; Academic: New York, 1977; Vol. 1, Chapter 3. (h) *Methoden der Organischen Chemie (Houben-Weyl)*; Regitz, M., Ed.; Thieme: Stuttgart, 1989; Vol. E19b. (i) *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Greenwich, CT, 1994; Vol. 1. (j) *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, CT, 1998; Vol. 2. (k) *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; Elsevier: Amsterdam, 2001; Vol. 3.

(20) (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.

(21) (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. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, CT, 1998; Vol. 2, pp 29−44.

(22) (a) *Cyclodextrins*; D'Souza, V. T., Lipkowitz, K. B., Eds.; Chemical Reviews; American Chemical Society: Washington, DC, 1998; Vol. 98, No. 5, pp 1741-2076. (b) Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803−822. (c) Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344−362. (d) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer: Berlin, 1978.

(23) (a) Compare to a basketball net. (b) *δ*-CyD [85220-53-7] is not toroidal.

(24) Cramer, F.; Henglein, F. M. *Chem. Ber.* **1957**, *90*, 2561−2571.

(25) Tee, O. S.; Gadosy, T. A.; Giorgi, J. B. *Can. J. Chem.* **1996**, *74*, 736−744.

(26) (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.

(27) Galvin, J. M.; Jacobsen, E. N. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 7, pp 4580−4585.

(28) Padwa, A.; Eastman, D. *J. Org. Chem.* **1969**, *34*, 2728−2732.

(29) For details about the statistical distribution of carbene C−H insertion into pentane, see: Doering, W. v. E.; Knox, L. H. *J. Am. Chem. Soc.* **1956**, *78*, 4947−4950.

(30) (a) Kamm, O.; Kamm, W. F. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, pp 104−107. (b) Cannizzaro, S. *Ann. Chem. Pharm.* **1854**, *90*, 252−254.

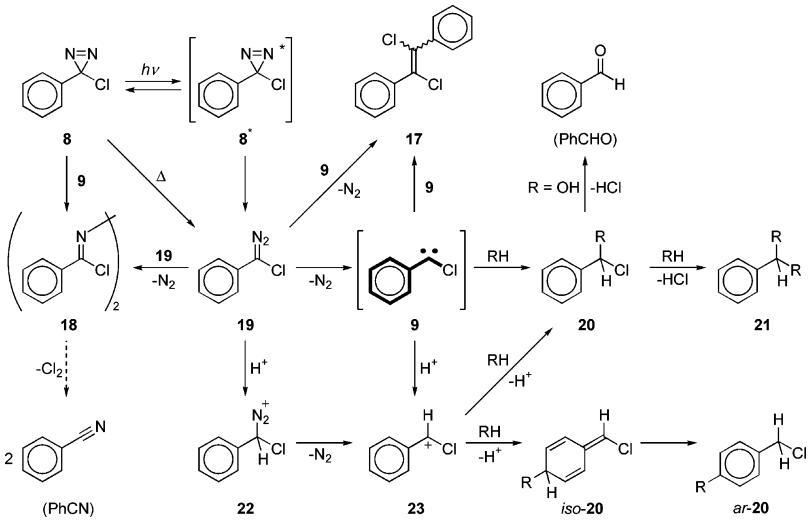
(31) (a) Il'ichev, A. M. *Zh. Obshch. Khim.* **1948**, *18*, 1121−1124; *Chem. Abstr.* **1949**, *43*, 1755. (b) Suzuki, H. *Bull. Chem. Soc. Jpn.* **1960**, *33*, 396−405. (c) Debon, A.; Masson, S.; Thuillier, A. *Bull. Soc. Chim. Fr.* **1975**, 2493−2498. (d) Yates, K.; Go, T. A. *J. Org. Chem.* **1980**, *45*, 2377−2384. (e) Görner, H. *J. Photochem. Photobiol., A* **1995** *90*, 57−63.

(32) (a) Günther, E. *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 516−518. (b) Günther, E. *Justus Liebigs Ann. Chem.* **1889**, *252*, 44−72. (c) Hayes, F. N.; Rogers, B. S.; Ott, D. G. *J. Am. Chem. Soc.* **1955**, *77*, 1850−1852. (d) Nesynov, E. P.; Grekov, A. P. *Russ. Chem. Rev. (Transl. of Usp. Khim.)* **1964**, *33*, 508−514. (e) Belen'kii, L. I.; Brokhovetskii, D. B.; Krayushkin, M. M. *Tetrahedron* **1991**, *47*, 447−456.

(33) (a) Stollé, R. *J. Prakt. Chem.* **1906**, *73*, 277−287. (b) Stollé, R.; Thomä, K. *J. Prakt. Chem.* **1906**, *73*, 288−300. (c) Stollé, R. *J. Prakt. Chem.* **1912**, *85*, 386-390. (d) Lange, J.; Tondys, H. *Dissert. Pharm. Pharmacol.* **1970**, *22*, 217−221. (e) Flowers, W. T.; Taylor, D. R.; Tipping, A. E.; Wright, C. N. *J. Chem. Soc. C* **1971**, 1986−1991. (f) Gautun, O. R.; Carlsen, P. H. J. *Acta Chem. Scand.* **1991**, *45*, 609−615.

(34) Berneth, H.; Hünig, S. *Chem. Ber.* **1980**, *113*, 2040−2042.

SCHEME 3. Generation of Chloro(phenyl)carbene (9) and Its Subsequent Reactions[a]



[a] RH = (a) α-CyD, (b) *β*-CyD, (c) *γ*-CyD, (d) MeOH, (e) *i*-PrOH, (f) *t*-BuOH, (g) H_2O, (h) HCl, (i) C_5H_{12} (j) *c*-C_6H_{12}, (k) PhH, (l) THF, (m) $CHCl_3$, (n) PhCH(OH)CH(OH)Ph (**24**).

TABLE 1. Relative Yields (%) of Products Formed upon Photolysis of 3-Chloro-3-phenyl-3*H*-diazirine (8) in Different Reaction Media

medium (RH)	κ[a]	PhCHO	**17**	**18**	**20**	**20h**	**21**	other
neat				100				
n-C_5H_{12} (0.01 M)	1.8	trace	trace	32	68[b]	trace		
n-C_5H_{12} (0.5 M)	1.8		trace	23	77[b]			
c-C_6H_{12} (0.1 M)	2.0	trace	trace	20	80[c]			trace[d]
c-C_6H_{12} (0.5 M)	2.0			61	39[c]			
benzene	2.3	2	5	83	trace	8		2[e]
$CHCl_3$ (wet)	4.7	21		trace	33[f]	46		
$CDCl_3$		3	4	57	22[g]	11		3[h]
THF	7.3				100[i]			
i-PrOH (0.1 M)	18.3						100[j]	
i-PrOH (0.5 M)	18.3	4				15	81[j]	
MeOH	32.7						100[k]	

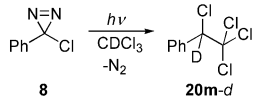
[a] Dielectric constant. [b] *x*-(1-Chloro-1-phenylmethyl)pentanes (**20i**). [c] [Chloro(cyclohexyl)methyl]benzene (**20j**). [d] PPD. [e] Biphenyl (**25**). [f] (1,2,2,2-Tetrachloroethyl)benzene (**20m**). [g] (1,2,2,2-Tetrachloroethyl-1-*d*)benzene (**20m**-*d*). [h] PhCN. [i] 2-(1-Chloro-1-phenylmethyl)-oxolane (**20l**). [j] [Di(1-methylethoxy)methyl]benzene (**21e**). [k] (Dimethoxymethyl)benzene (**21d**).

However, this notion was later shown to be incorrect.[35] Note that the ring closure leading to the diazirine parallels that for the classical Neber rearrangement.[36]

The photolysis of diazirine **8** is expected to form relatively "long-lived" chloro(phenyl)carbene (**9**), which usually decomposes via intermolecular reactions (Scheme 3).

3-Chloro-3-phenyl-3*H*-diazirine (**8**) was photolyzed in various solvents and within CyDs. The solution results are summarized in Table 1. The conventional solvents were used to gauge whatever effects the CyD hosts had on chloro(phenyl)carbene (**9**). Hydrocarbon solvents, like pentane (*n*-C_5H_{12}) and cyclohexane (*c*-C_6H_{12}), were used to mimic the inner cavities of CyDs, which are also nonpolar, hydrophobic environments. Tetrahydrofuran (THF) was employed because the cyclic ether resembles the D-glucopyranose (D-Glc*p*) monomer units of the CyDs. Moreover, since CyDs also possess many hydroxyl (OH) groups, it seemed appropriate to perform control experiments upon alcoholic solutions of diazirine **8**. Finally, chloroform ($CHCl_3$) was used to assess the spin-state of carbene **9**.

Photolysis in Solution Phase. The photolysis of 3-chloro-3-phenyl-3*H*-diazirine (**8**) in chloroform and chloroform-*d* resulted in moderate amounts of (1,2,2,2-tetrachloroethyl)benzene (**20m**)[37] and (1,2,2,2-tetrachloroethyl-*1-d*)benzene (**20m**-*d*), respectively (Table 1). Both of these isotopomers stem from carbene **9** insertions into the C−H(D) bonds of chloroform(-*d*), rather than the expected C−Cl insertions (eq 3; cf. Scheme 7).



(3)

The photolysis results for diazirine **8** in pentane (Table 1)[38] are similar to those already reported for a 19.7 mM solution, i.e., 28% of **18** and 71% of **20i**.[28] Further analysis of the C−H insertion products, i.e., *x*-(1-chloro-1-phenyl-

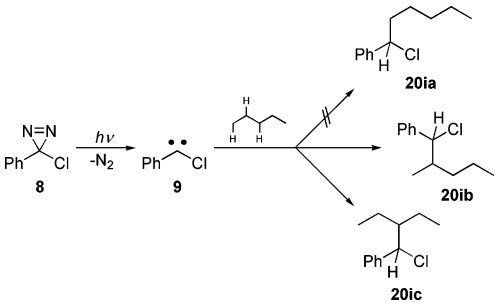
(35) (a) Moss, R. A.; Włostowska, J.; Guo, W.; Fedorynski, M.; Springer, J. P.; Hirshfield, J. M. *J. Org. Chem.* **1981**, *46*, 5048−5050. (b) Moss, R. A. In *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC: Boca Raton, FL, 1987; Vol. 1, pp 99−109.

(36) (a) Neber, P. W.; Burgard, A. *Justus Liebigs Ann. Chem.* **1932**, *493*, 281−294. (b) O'Brien, C. *Chem. Rev.* **1964**, *64*, 81−89. (c) *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; pp 1089−1090. (d) Hassner, A.; Stumer, C. *Organic Syntheses Based on Name Reactions and Unnamed Reactions*; Pergamon: Tarrytown, NY, 1994; p 271.

(37) (a) Ettel, V.; Weichet, J. *Collect. Czech. Chem. Commun.* **1950**, *15*, 520−527. (b) Naidan, V. M.; Dombrovskii, A. V. *J. Org. Chem. USSR* (*Transl.Zh. Org. Khim.*) **1965**, *1*, 2037−2040. (c) Grishchuk, B. D.; Sinchenko, V. G.; Kudrik, E. Y.; Gorbovoi, P. M.; Shandruk, R. N.; Kulaga, O. E. *Pharm. Chem. J.* (*Transl. Khim.-Farm. Zh.*) **1995**, *29*, 406−408.

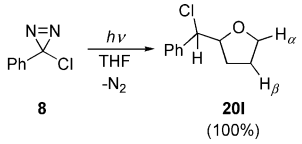
(38) Since azine **18** precipitated from the pentane solutions, the samples were rotary evaporated, and then the residues were dissolved in $CHCl_3$ (0.1 M) for GC analysis.

SCHEME 4. Selective Formation of *x*-(1-Chloro-1-phenylmethyl)Pentanes (20i)



methyl)pentanes (**20i**), revealed that carbene **9** did *not* react with the terminal methyl groups of pentane (Scheme 4). This is in stark contrast with the results reported for (methoxycarbonyl)carbene, which gave methyl heptanoate via C−H insertions of the $-CH_3$ groups of pentane.[29]

Similarly, C−H insertion was observed with THF as solvent, but only with the α-C−H bonds of the cyclic ether,[39] giving 2-(1-chloro-1-phenylmethyl)oxolane (**20l**) exclusively (eq 4; Table 1).

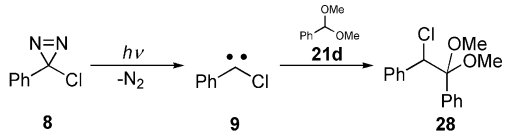


(4)

The photolysis of diazirine **8** in anhydrous methyl alcohol (MeOH) yielded (dimethoxymethyl)benzene (**21d**) (Table 1) and HCl (Scheme 5). Since the product mixture was very sensitive to moisture,[40] it was necessary to quench the photolyzed MeOH solution with anhydrous $NH_{3(g)}$ to inhibit subsequent HCl acid-catalyzed hydrolysis of the benzaldehyde dimethyl acetal **21d** to benzaldehyde (PhCHO). Ammonium chloride (NH_4Cl) mist and heat were observed upon quenching. To gauge the effect of ammonia on carbene **9**, anhydrous $NH_{3(g)}$ was introduced prior to photolysis of the methanolic solution of diazirine **8**. Again, only acetal **21d** was produced. Indeed, addition of anhydrous potassium carbonate ($K_2CO_{3(s)}$) before photolysis also made no difference and was most convenient.

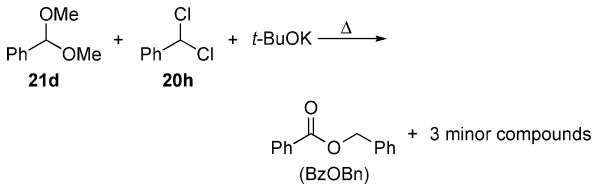
Next, the reaction of 3-chloro-3-phenyl-3*H*-diazirine (**8**) with the primary reaction product (dimethoxymethyl)-benzene (**21d**) was investigated to determine whether the acetal was inert toward chloro(phenyl)carbene (**9**). It was found that photolysis of diazirine **8** in neat benzaldehyde dimethyl acetal **21d** gave (1-chloro-2,2-dimethoxy-2-phenylethyl)benzene (**28**) in low yield (eq 5). Desyl chloride dimethyl acetal **28** likely derives from benzylidene C−H insertion of acetal **21d** by carbene **9**.[41]

In a prior and seemingly conflicting report about this reaction (eq 5), heating (dimethoxymethyl)benzene (**21d**) with (dichloromethyl)benzene (**20h**) and *t*-BuOK, followed by aqueous workup, gave benzyl benzoate (BzOBn, ca.



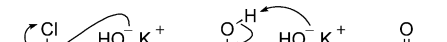
(5)

80% relative yield) and three other undisclosed products (eq 6).[42] However, an unusual mechanism involving chloro(phenyl)carbene (**9**) was formulated to explain BzOBn formation.



(6)

It should be noted, however, that *t*-BuOK is hygroscopic (eq 7). So, any resulting KOH impurities would transform benzal chloride **20h** into benzaldehyde (PhCHO) (eq 8). Therefore, it is more likely that the benzyl ester BzOBn was formed by the action of the alkoxide base upon adventitious PhCHO according to the Tishchenko reaction, i.e., 2PhCHO → BzOBn.[30,43,44]



(7)

(8)

It should also be mentioned that base-induced α-elimination of HCl from (dichloromethyl)benzene (**20h**) does not even necessarily afford chloro(phenyl)carbene (**9**).[45] A carbenoid intermediate **9**·KCl is likely formed. However, this condition could be remedied by using crown ethers, which appear to promote the formation of free carbene **9**, as compared with results obtained from the nitrogenous precursor 3-chloro-3-phenyl-3*H*-diazirine (**8**).[45]

Photolysis of a 0.1 M solution of 3-chloro-3-phenyl-3*H*-diazirine (**8**) in anhydrous isopropyl alcohol (*i*-PrOH), followed by $NH_{3(g)}$ quenching, afforded [di(1-methylethoxy)methyl]benzene (**21e**)[46] as the sole product (Table 1). Photolysis of a 0.5 M solution of diazirine **8** in anhydrous *i*-PrOH, followed by $NH_{3(g)}$ quenching, afforded benzaldehyde diisopropyl acetal **21e**, (dichloromethyl)benzene (**20h**), and benzaldehyde (PhCHO) in 81%, 15%, and 4% yields, respectively (Table 1, eq 9). The formation of benzal chloride **20h** within the concentrated, i.e., 0.5 M, solution of diazirine **8** may be a consequence

(39) For similar examples, see: Lin, G. *Diss. Abstr. Int. B* **1995**, *56* (6), 3203; *Chem. Abstr.* **1996**, *124*, 175117.

(40) Appreciable amounts of benzaldehyde (PhCHO) were formed even within 1 min of exposure to air, as detected via GC.

(41) For a similar example, see: Moss, R. A.; Yan, S. *Tetrahedron Lett.* **1998**, *39*, 9381−9384.

(42) Dement'eva, L. P.; Kostikov, R. R. *J. Org. Chem. USSR* (*Transl. Zh. Org. Khim.*) **1990**, *26*, 117−118.

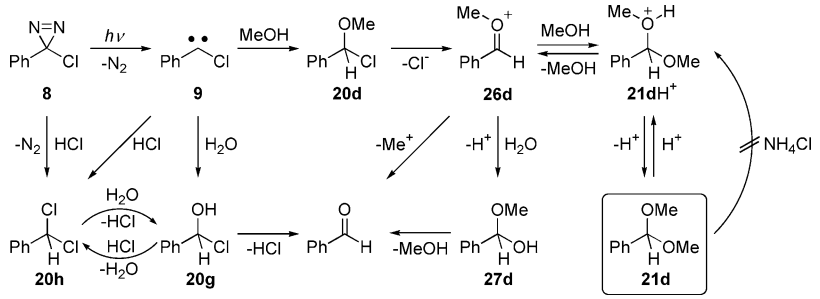
(43) (a) *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; p 1235. (b) Hassner, A.; Stumer, C. *Organic Syntheses Based on Name Reactions and Unnamed Reactions*; Pergamon: Tarrytown, NY, 1994; p 384.

(44) Rosenberg, M. G. Ph.D. Dissertation, State University of New York at Binghamton, 2002.

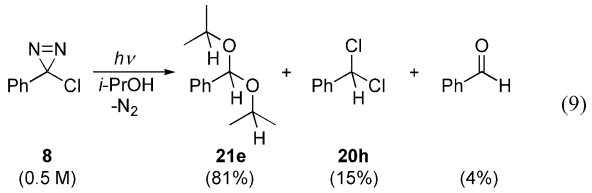
(45) Moss, R. A.; Pilkiewicz, F. G. *J. Am. Chem. Soc.* **1974**, *96*, 5632−5633.

(46) Roelofsen, D. P.; van Bekkum, H. *Synthesis* **1972**, 419−420.

SCHEME 5. Photolysis of 3-Chloro-3-phenyl-3*H*-diazirine (8) in MeOH



of the relatively low acidity of *i*-PrOH.[47] The subdued reactivity of *i*-PrOH with carbene **9** decreases the usually diffusion-limited rate of carbene O−H insertion and concomitantly fosters HCl insertion. However, the existence of benzal chloride **20h** within the product solution may also reflect a diminished ability of the bulkier alcohol to solvolyze the *gem*-dichloride byproduct.



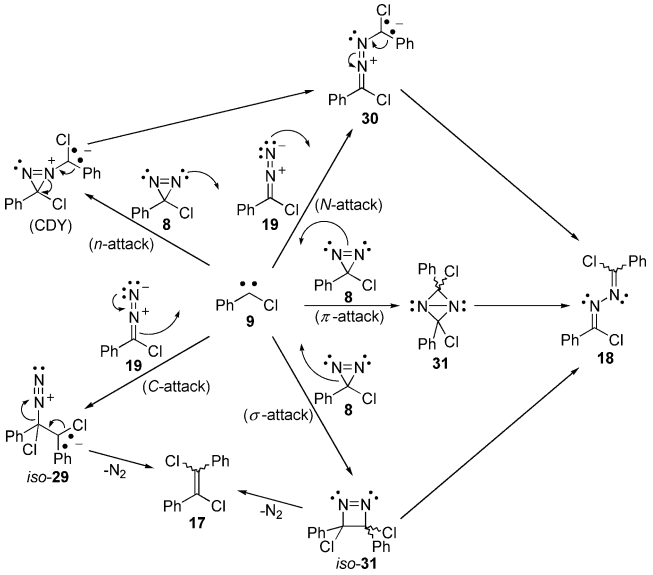
(9)

Further analysis of the reactions of chloro(phenyl)carbene (**8**) with relevant oxygen-containing functional groups (alcohols, such as *t*-BuOH, MeOH, and DL-hydrobenzoin (DL-**24**), aldehydes, and ethers) can be found elsewhere.[48]

Condensed-phase carbenes will often react with the surrounding solvent medium, but they can also combine with other solute molecules. Indeed, these intermolecular reactions commonly occur at rates that are limited only by diffusion. Consequently, such carbenes are just short-lived intermediates. Nevertheless, arylhalocarbenes tend to have much longer lifetimes than typical alkylhalocarbenes, e.g., 3 orders of magnitude longer, because the latter also undergo rapid 1,2-H shift to form alkenes.[49,50] Indeed, the lifetime (τ) of singlet chloro(phenyl)carbene (**9**) ($\lambda_{max} = 310$ nm)[51] in 2,2,4-trimethylpentane (isooctane) is reported to be ca. 3.6 μs, as determined via laser flash photolysis (LFP) of 3-chloro-3-phenyl-3*H*-diazirine (**8**).[52]

Under thermal conditions, diazirine **8** decomposes unimolecularly to give N_2 and carbene **9**.[53] The free carbene can subsequently react with the ubiquitous solvent to form insertion products (Table 1). Moreover,

SCHEME 6. Mechanistic Pathways Leading to the Formation of Azine 18 and Carbene Dimer 17



carbene **9** appears to react with its nitrogenous precursor(s). Indeed, the thermolysis of diazirine **8** in benzene, an "inert" solvent,[54] yields bis(1-chloro-1-phenylmethylidene)hydrazine (**18**).[28] It was observed during this study that the photolysis of neat diazirine **8** at room temperature afforded azine **18** in high yield and purity. Therefore, the diazirine route to **18** could become the leading alternative to Stollé's classical reaction involving chlorination of benzaldehyde azine (**29**).[28,33]

It has been suggested that intermolecular reaction of chloro(phenyl)carbene (**9**) with 3-chloro-3-phenyl-3*H*-diazirine (**8**) yields the azine bis(1-chloro-1-phenylmethylidene)hydrazine (**18**) (Scheme 3).[28] 2,4-Dichloro-2,4-diphenyl-1,3-diazabicyclobutane (**31**) was postulated as an intermediate in the formation of azine **18** (Scheme 6).[28] It would stem from π-attack of diazirine precursor **8** by carbene **9**. Recently though, the carbene−diazirine ylide (CDY) was postulated as an intermediate in the formation of azine **18**.[55] It would stem from *n*-attack (of a N atom) of diazirine precursor **8** by carbene **9**. However, the **9**−**8** CDY could not be observed. Therefore, it was concluded that *if* the **9**−**8** CDY did form then it rapidly rearranged to azine **18**, which is photostable.[55]

(47) The pK_a of *i*-PrOH is 17.1, whereas that for MeOH is 15.5. See: Miller, A.; Solomon, P. H. *Writing Reaction Mechanisms in Organic Chemistry*, 2nd ed.; Academic: San Diego, 2000; pp 461−462.

(48) See the Supporting Information.

(49) Liu, M. T. H. *Acc. Chem. Res.* **1994**, *27*, 287−294.

(50) (a) Bonneau, R.; Liu, M. T. H. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, CT, 1998; Vol. 2, pp 1−28. (b) Liu, M. T. H.; Bonneau, R. *J. Am. Chem. Soc.* **1996**, *118*, 8098−8101.

(51) For the $\pi \rightarrow \pi^*$ transition. For the $\sigma \rightarrow$ p transition ($\lambda_{max} = 750$ nm), see: (a) Zuev, P. S.; Sheridan, R. S. *J. Org. Chem.* **1994**, *59*, 2267−2269. (b) Sheridan, R. S. *Inter-Am. Photochem. Soc. News.* **2000**, *23* (1), 39−48.

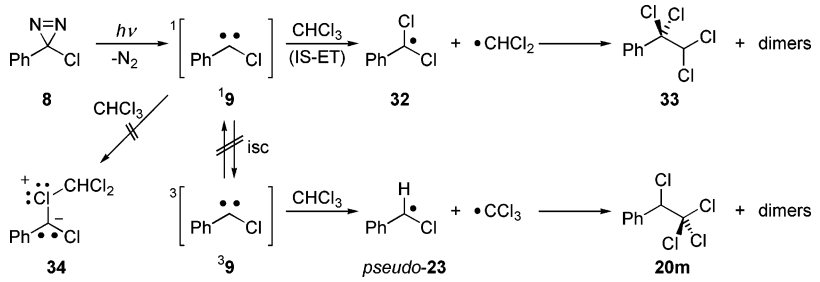
(52) (a) Turro, N. J.; Butcher, J. A., Jr.; Moss, R. A.; Guo, W.; Munjal, R. C.; Fedorynski, M. *J. Am. Chem. Soc.* **1980**, *102*, 7576−7578. (b) Naito, I.; Oku, A.; Otani, N.; Fujiwara, Y.; Tanimoto, Y. *J. Chem. Soc., Perkin Trans. 2* **1996**, 725−729.

(53) Liu, M. T. H.; Toriyama, K. *J. Phys. Chem.* **1972**, *76*, 797−801.

(54) Benzene may not be totally inert since it may form a charge-transfer complex with arylhalocarbenes. See: Çelebi, S.; Platz, M. S. In *Proceedings of the Conference on Reactive Intermediates and Unusual Molecules*; Bobek, M. M., Ed.; Eigenverlag: Vienna, 2000; p 31.

(55) Bonneau, R.; Liu, M. T. H. *J. Phys. Chem. A* **2000**, *104*, 4115−4120.

SCHEME 7. Expected Reaction of Chloro(phenyl)carbene (9) with Chloroform



In contrast, the formation of Δ^1-1,2-diazetines from σ-attack of 3*H*-diazirines appears to have never been considered. If formed, 3,4-dichloro-3,4-diphenyl-Δ^1-1,2-diazetine (*iso*-**31**) might be expected to yield (irreversibly) *both* the azine **18**, via C−C cleavage, and the alkene 1,2-dichloro-1,2-diphenylethene (**17**), via N_2 extrusion.[56,57] The formation of alkene **17** from the direct dimerization of two short-lived carbenes **9** in dilute solution is highly improbable. Therefore, the presence of trace amounts of dimer **17** found after the photolysis of a 0.01 M pentane solution of diazirine **8** (Table 1) suggests that either diazo compound **19** or Δ^1-1,2-diazetine *iso*-**31** may have been involved. Indeed, much of the electron density within the highest occupied *n*-orbital of diazirines is coincident with the C−N σ-orbital.[58] Hence, the formation of Δ^1-1,2-diazetine *iso*-**31**, via formal carbene C−N insertion, is not implausible.

The reaction of chloro(phenyl)carbene (**9**) with ethers has already been examined.[48] However, the reactions of carbenes with aldehydes has been studied only to a limited extent.[59,60] Therefore. the reactivity of carbene **9** within benzaldehyde (PhCHO) was investigated in order to learn more about the reaction mechanism and its intermediates.[48]

Finally, the spin-state results from the photolyses of 3-chloro-3-phenyl-3*H*-diazirine (**8**) in both chloroform and chloroform-*d*, reported herein (eq 3; Table 1), are *not* consistent with those expected from singlet chloro(phenyl)carbene (^{1}**9**) (Scheme 7).

Insertions by singlet carbene **9** into the C−Cl bonds of chloroform and chloroform-*d*, yielding (1,1,2,2-tetrachloroethyl)benzene (**33**) and (1,1,2,2-tetrachloroethyl-2-*d*)-benzene (**33**-*d*), respectively, were expected. In contrast,

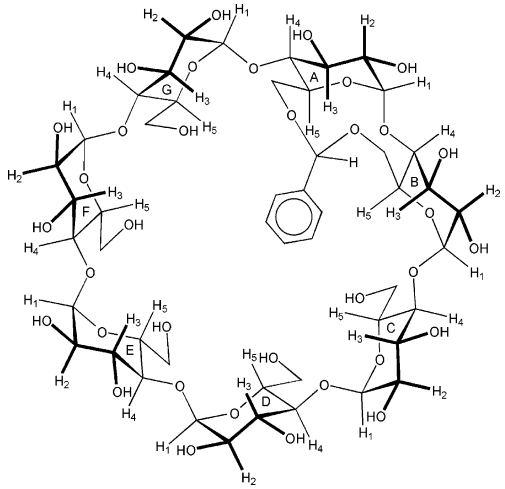


FIGURE 5. Structure of 6^A,6^B-*O*-(benzylidene)β-cyclodextrin (**21b**).

the NMR and MS data indicate the formation of (1,2,2,2-tetrachloroethyl)benzene (**20m**) and (1,2,2,2-tetrachloroethyl-1-*d*)benzene (**20m**-*d*),[61] respectively. However, the unanticipated C−H(D) insertion products **20m** and **20m**-*d* most likely derive from a concerted C−H(D) insertion by singlet carbene **9** because the preponderance of other evidence (vide supra) challenges the existence of triplet chloro(phenyl)carbene (^{3}**9**).

Photolysis in the Supramolecular Phase. The addition of benzaldehyde (PhCHO) and acetic acid (AcOH) to an *aqueous* solution of β-CyD allegedly gives 6^A,6^B-*O*-(benzylidene)β-cyclodextrin (**21b**) in 45% yield (Figure 5).[62] However, that result could not be reproduced in this study. Moreover, the microanalysis, mass spectrometry, and NMR spectroscopy data that were used to characterize acetal **21b** were not made available in the patent.[62] Therefore, its formation should be regarded with skepticism. Surely, the OH groups of the hydroxylic solvent, i.e., water, would compete with those of β-CyD for PhCHO. Indeed, acidified water is typically used to catabolize acetals.[63] Moreover, the preparation of benzylidene acetals from nonreducing glucopyranosides typically gives the 4,6-*O*-benzylidene isomers.[64] Only 2,3-*O*-benzylidenation of *intact* cyclodextrins should occur since they are 1,4-linked.

(56) (a) Timberlake, J. W.; Elder, E. S. In *Comprehensive Heterocyclic Chemistry*; Lwowski, W., Ed.; Pergamon: Oxford, 1984; Vol. 7; pp 456−457, 483. (b) White, D. K.; Greene, F. D. *J. Am. Chem. Soc.* **1978**, *100*, 6760−6761. (c) Wildi, E. A.; Carpenter, B. K. *Tetrahedron Lett.* **1978**, 2469−2472. (d) Vereshchinskii, I. V.; Podkhalyuzin, A. T. *Dokl. Chem.* (*Transl. Dokl. Akad. Nauk SSSR, Ser. Khim.*) **1965**, *165*, 1065−1067. (e) Ebsworth, E. A. V.; Hurst, G. L. *J. Chem. Soc.* **1962**, 4840−4843.

(57) Compare to cyclobutene electrocyclic ring opening vs cycloreversion: (a) Cook, B. H.; Leigh, W. J.; Michael, C. L.; Squillacote, M. *Abstr. Pap. Am. Chem. Soc.* **1997**, *214*, CHED 121. (b) Leigh, W. J.; Postigo, J. A. *J. Am. Chem. Soc.* **1995**, *117*, 1688−1694.

(58) (a) Baird, N. C. In *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC: Boca Raton, FL, 1987; Vol. 1, pp 1−17. (b) Jorgensen, W. L.; Salem, L. *The Organic Chemist's Book of Orbitals*; Academic: New York, 1973; pp 40−42, 135−136. (c) Shustov, G. V.; Varlamov, S. V.; Rauk, A.; Kostyanovsky, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 3403−3408. (d) Bobek, M. M.; Krois, D.; Brehmer, T. H.; Giester, G.; Wiberg, K. B.; Brinker, U. H. *J. Org. Chem.* **2003**, *68*, 2129−2134.

(59) Gutsche, C. D. *Org. React. N.Y.* **1954**, *8*, 364−429.

(60) (a) L'Esperance, R. P.; Ford, T. M.; Jones, M., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 209−213. (b) de March, P.; Huisgen, R. *J. Am. Chem. Soc.* **1982**, *104*, 4952. (c) Huisgen, R.; de March, P. *J. Am. Chem. Soc.* **1982**, *104*, 4953−4954.

(61) See the Supporting Information, Scheme S9.

(62) Yoshinaga, M. Jpn. Patent 05 32 704, 1993; *Chem. Abstr.* **1993**, *119*, 10738.

(63) Meskens, F. A. J. *Synthesis* **1981**, 501−522.

(64) (a) Evans, M. E. *Carbohydr. Res.* **1972**, *21*, 473−475. (b) Horton, D.; Weckerle, W. *Carbohydr. Res.* **1975**, *44*, 227−240.

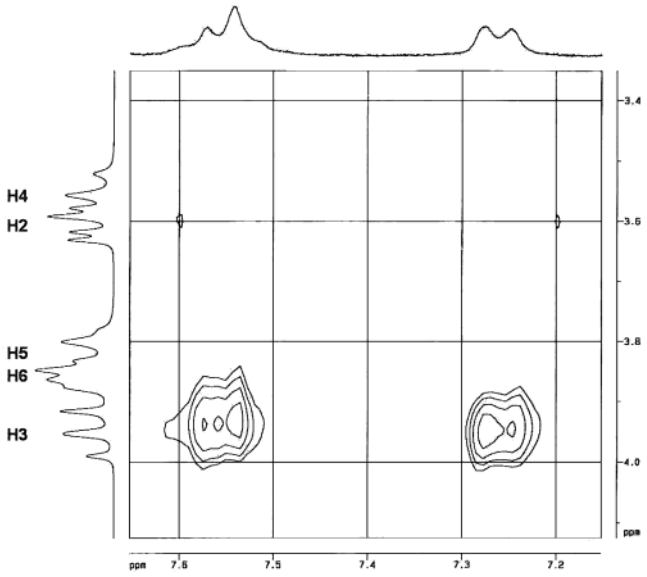


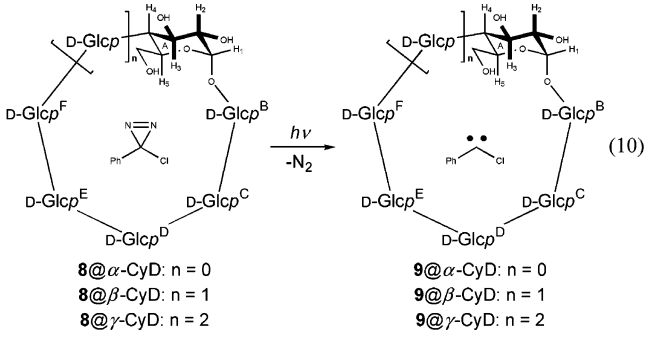
FIGURE 6. 250 MHz 2-D ROESY spectrum of the diazirine CyD IC **8**@(α-CyD)$_2$.

Cyclodextrin inclusion complexes (CyD ICs) of 3-chloro-3-phenyl-3*H*-diazirine (**8**) were prepared to determine the effect of supramolecular inclusion upon chloro(phenyl)carbene (**9**). The α-cyclodextrin (α-CyD) and *β*-cyclodextrin (*β*-CyD) ICs were analyzed using ^{1}H NMR,[65] including 2-D ROESY,[66] induced circular dichroism (ICD),[26] and microanalysis. The integral structures of the CyD ICs were concluded to be **8**@(α-CyD)$_2$ and (**8**@*β*-CyD)$_2$, based on their physical and chemical characteristics (vide infra). These stoichiometries denote that diazirine **8** is sandwiched between two α-CyD units, but that it forms a 2-fold 1:1 complex with *β*-CyD.[67] It has been demonstrated that a guest must have a substituent capable of hydrogen bonding, like −F or −OH,[66,67] to effect an opposite inclusion orientation within cyclodextrins in the aqueous versus solid phase. Hence, it is likely that hydrophobic diazirine **8** adopted the same orientation within its CyD host during photolyses in both phases that were employed.

The 2-D ROESY spectrum of **8**@(α-CyD)$_2$ showed cross-peaks between the phenyl ring protons of diazirine **8** with only the H3 protons of one α-CyD (Figure 6). The absence of cross-peaks with the H5 protons of α-CyD suggests that diazirine **8** does not fit entirely within one α-CyD and, therefore, requires two hosts to ensnare it. Moreover, a tight fit between the diazirine **8** guest and either α-CyD host is not indicated since neither H3 nor H5 are shifted upfield to any considerable degree, with deference to the spectrum of empty α-CyD.[65f] In contrast to the 2-D ROESY spectrum for the **8**@(α-CyD)$_2$ inclusion complex (IC), no cross-peaks were observed for the (**8**@*β*-CyD)$_2$ IC.

The induced circular dichroism (ICD) spectrum of aqueous **8**@(α-CyD)$_2$ was also obtained.[68] Asymmetric induction by chiral α-CyD upon the chromophore of achiral diazirine **8** was made evident by the weak negative circular dichroism exhibited at $\lambda_{max} = 372$ nm. In contrast, an ICD spectrum for the (**8**@*β*-CyD)$_2$ complex could not be observed. However, this absence is not unexpected after considering the lack of cross-peaks in its 2-D ROESY spectrum.

Photolysis of 3-chloro-3-phenyl-3*H*-diazirine (**8**) included within the cavities of CyDs presumably formed chloro(phenyl)carbene (**9**) CyD ICs, i.e., **9**@CyD (eq 10). The lifetime (*τ*) of carbene **9** was expected to be prolonged due to the preclusion of intermolecular reactions (Scheme 3), such as azine **18** formation and solvent insertion, i.e., **9** → **20**. However, interfering *innermolecular* reactions[10c,69] between the host and guest were indicated (vide infra). Therefore, the latent intramolecular rearrangement of carbene **9** to cyclic allene **10**, a rare transformation seen under the forbidding, low-temperature conditions of argon matrixes,[9c,11] was not observed.



(10)

The **8**@CyD ICs were photolyzed initially in the solid state under inert atmosphere. Principally, carbene **9** appears to have reacted with adventitious H_2O, which likely resides near the perimeters of the CyDs, to give PhCHO and HCl (eq 11; cf. Scheme 3). Of course, these hydrolysis products may also stem from **9**·CyDs, which are daughter isomers of **9**@CyDs, that derive from innermolecular reactions (eq 12). Therefore, such descendants were sought. Indeed, fast atom bombardment (FAB) mass spectrometry of the products revealed the presence of new signals with masses greater than those of the unfilled CyD hosts.[70] However, the main $[M - H]^-$ signals are not attributable to **9**·CyDs, but rather to CyD hydrochlorides that could be either noncovalently bound HCl@CyD ICs or their covalently bound, constitutional isomers CyD·HCl.

$$\mathbf{9} + H_2O \rightarrow PhCHO + HCl \quad (11)$$

$$\mathbf{9}\cdot CyD + H_2O \rightarrow PhCHO + HCl + CyD \quad (12)$$

Since H_2O molecules appear to remain chemisorbed onto the "dried" CyD ICs, it was decided that photolyzing

(65) (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.

(66) (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.

(67) 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.

(68) See the Supporting Information, Figure S5.

(69) Warmuth, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1347−1350. (b) Warmuth, R. *Chem. Commun.* (*Cambridge*) **1998**, 59−60. (c) Bradley, D. *Chem. Br.* **1998**, *34* (3), 16. (d) Warmuth, R. *J. Inclusion Phenom. Macrocycl. Chem.* **2000**, *37*, 1−38.

(70) See the Supporting Information, Figure S7.

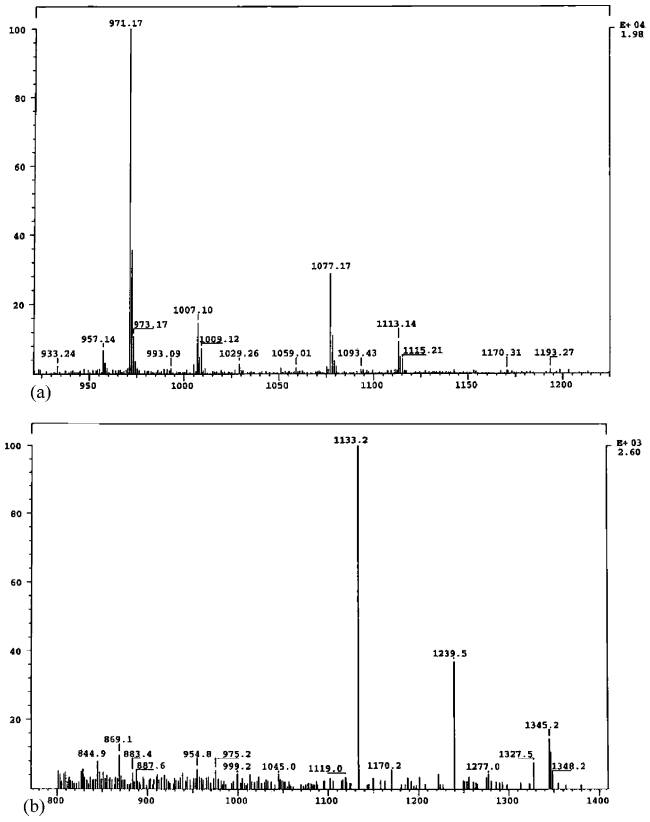


FIGURE 7. FAB MS spectra of the innermolecular products formed by photolysis of diazirine **8** within (a) α-CyD and (b) *β*-CyD in the presence of *alkaline buffer*.

an aqueous suspension of **8**@CyD could do no further harm and might even present an advantage. In deference to the instructive MeOH and *i*-PrOH results (eq 9; Scheme 5), the **8**@CyD ICs were suspended in an *alkaline buffer* (to neutralize the HCl byproduct)[71] during subsequent photolysis experiments. Hence, the HCl acid-catalyzed hydrolysis of any CyD benzylidene acetals, e.g., **21b** (Figure 5),[62] that may have formed would be thwarted. Indeed, such detrimental effects were remedied by conducting the photolyses in aqueous alkaline buffer (vide infra).

The ability of the CyDs to insulate carbene **9** from the bulk aqueous medium while still allowing HCl neutralization appears to have been realized to some extent, according to the FAB MS spectra of the **8**@CyD alkaline buffer photolysis products (Figure 7). Still, the main $[M - H]^-$ signals are not attributable to **9**·CyDs. Instead, the spectra clearly show appreciable amounts of PhCHO·CyD (*not* PhCHO@CyD) and only traces of HCl@CyD (or CyD·HCl) byproducts. Note that the covalently bound character of each modified PhCHO·CyD was confirmed by control experiments and reversed-phase high-pressure liquid chromatography (RP HPLC).

Control FAB MS spectra of the independently prepared PhCHO@$(\alpha\text{-CyD})_2$ and (PhCHO@β-CyD)$_2$ ICs were obtained to verify that these noncovalently bound PhCHO@CyD ICs do not register a supramolecular signal.[72] Indeed, only signals from the empty CyD hosts were observed.[73] Evidently, loosely bound PhCHO is expelled from the PhCHO@CyD ICs during FAB MS analyses, leaving behind the empty CyDs.[74] This result lends support to the notion that covalently bound CyD·HCl species, rather than loosely bound HCl@CyD ICs, are responsible for the signals that were observed after unbuffered, solid-state photolyses.[70]

The FAB MS spectra of the alkaline buffer photolysis products indicated that innermolecular reactions took place between the carbene **9** guest and the CyD hosts (Figure 7). Such supramolecular processes might entail carbene **9** insertions into the C−H bonds of the CyDs, but more likely they involve insertions into the host's O−H bonds (Scheme 8). However, no **9**·CyD primary insertion products, e.g., **35**, were detected. Instead, such daughter isomers appear to have reacted further by conceptual replacement of an HCl formula unit by H_2O. To clarify the FAB MS results, a summary of exact mass calculations is given in Table 2.

Carbene C−H insertion products within CyDs have never been observed.[21,75] Instead, formal O−H insertion appears to be preferred and can even be chemospecific.[76] Therefore, one could envision an insertion into the O2−H bond by carbene **9** (Scheme 8), because the −OH groups on the C2 atoms of the smaller CyDs also point toward the apolar cavities. The resulting O−H insertion product **35** is an α-chloroether that could undergo CyD ring expansion to **38** or scission to *seco*-**38**. Cyclic **38** and acyclic *seco*-**38** might account for the observed FAB MS signal (Figure 7, Table 2).

In summary, chloro(phenyl)carbene (**9**) was generated within the supramolecular phase and control experiments were conducted in several organic solvents, so that the supramolecular effects upon carbene **9** could be ascertained. The question to be answered was whether CyD hosts modify the guest or vice versa? The latter process appears to be true for chloro(phenyl)carbene (**9**). The true structure of the innermolecular product that was formed in alkaline buffer, and then observed via FAB MS and RP HPLC, has not yet been determined. But the covalently bound, modified cyclodextrin is definitely not the acetal $6^A,6^B$-*O*-(benzylidene)*β*-cyclodextrin (**21b**) (Figure 5).[62] The ability of the basic medium to preserve the innermolecular product and reduce the amount of PhCHO formed seems to indicate that the latter stems from the former, e.g., O−H insertion product **38**. However, the

(71) Photolyses of the **8**@CyD ICs under an atmosphere of $NH_{3(g)}$ or within a vacuum line equipped with a trap containing $NaH_{(s)}$ were also considered. However, both of these strategies were rejected in favor of using an aqueous alkaline buffer to neutralize the HCl byproduct.

(72) PhCHO@CyDs have been studied in the solid state using ^{13}C CP/MAS NMR: (a) Ripmeester, J. A. *J. Inclusion Phenom.* **1988**, *6*, 31−40. (b) Garces, F. O.; Rao, V. P.; Garcia-Garibay, M. A.; Turro, N. J. *Supramol. Chem.* **1992**, *1*, 65−72.

(73) See the Supporting Information, Figure S9.

(74) The association constants (*K*) for PhCHO@CyDs have been determined: $K(\text{PhCHO@}\alpha\text{-CyD}) = 1.02(4) \times 10^2\ M^{-1}$ and $K(\text{PhCHO@}\beta\text{-CyD}) = 1.50(7) \times 10^2\ M^{-1}$. See: Guo, Q.-X.; Luo, S.-H.; Liu, Y.-C. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1998**, *30*, 173−182; *Chem. Abstr.* **1998**, *128*, 270367.

(75) (a) Abelt, C. J.; Pleier, J. M. *J. Org. Chem.* **1988**, *53*, 2159−2162. (b) Abelt, C. J.; Lokey, J. S.; Smith, S. H. *Carbohydr. Res.* **1989**, *192*, 119−130. (c) Smith, S. H.; Forrest, S. M.; Williams, D. C., Jr.; Cabell, M. F.; Acquavella, M. F.; Abelt, C. J. *Carbohydr. Res.* **1992**, *230*, 289−297. (d) Abelt, C. J. *Insertion Reactions of Cyclodextrin-Bound Carbenes*; final report to the Petroleum Research Fund on Grant 22092-B4; College of William and Mary; Williamsburg, VA, 1992. (e) Abelt, C. J. *Minutes Int. Symp. Cyclodextrins, 6th* **1992**, 649−654; *Chem. Abstr.* **1994**, *121*, 83794.

(76) Krois, D.; Bobek, M. M.; Werner, A.; Kählig, H.; Brinker, U. H. *Org. Lett.* **2000**, *2*, 315−318.

SCHEME 8. Hydrolysis of O2−H Inserted-CyD 35 Should Give FAB MS Candidates 38 and/or *seco*-38

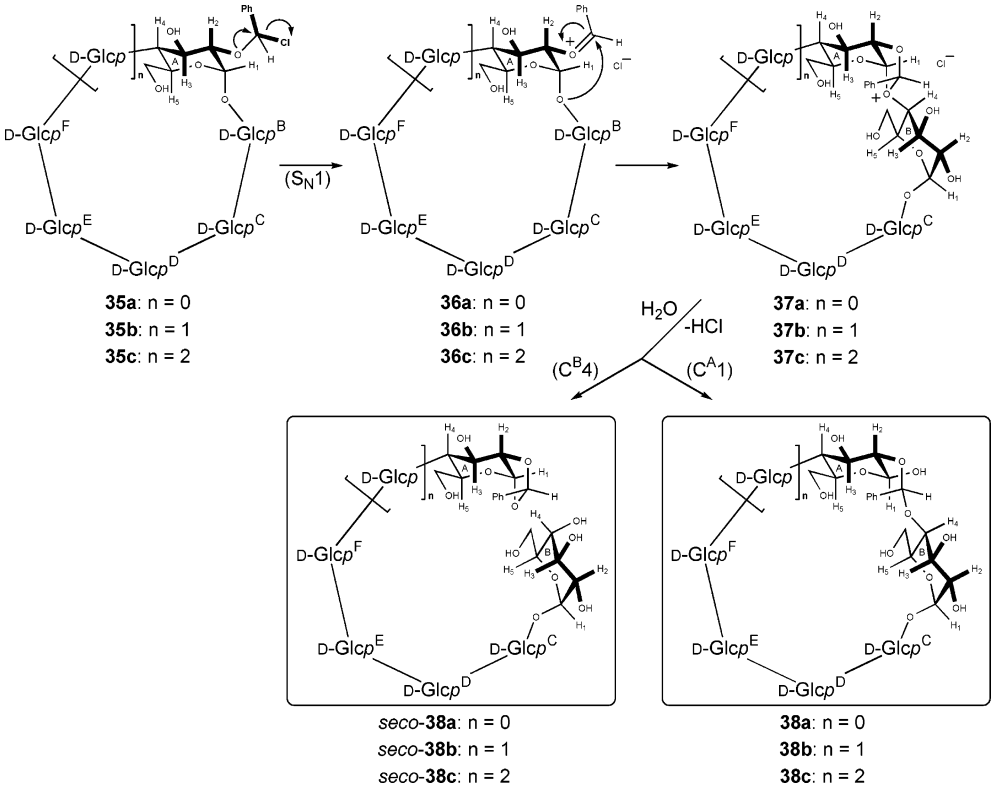


TABLE 2. Calculated Exact Masses for CyD Innermolecular Products[a]

	n =		
	6 (α-CyD)	7 (*β*-CyD)[b]	8 (*γ*-CyD)
$[C_6(H_2O)_5]_n$	$C_{36}H_{60}O_{30}$	$C_{42}H_{70}O_{35}$	$C_{48}H_{80}O_{40}$
	972.3169	1134.3698	1296.4226
9@$[C_6(H_2O)_5]_n$, **9**·$[C_6(H_2O)_5]_n$, **35**	$C_{43}H_{65}ClO_{30}$	$C_{49}H_{75}ClO_{35}$	$C_{55}H_{85}ClO_{40}$
	1096.3249	1258.3777	1420.4306
PhCHO@$[C_6(H_2O)_5]_n$, **38**, *seco*-**38**	$C_{43}H_{66}O_{31}$	$C_{49}H_{76}O_{36}$	$C_{55}H_{86}O_{41}$
	1078.3588	1240.4116	1402.4645
HCl@$[C_6(H_2O)_5]_n$, $[C_6(H_2O)_5]_n$·HCl	$C_{36}H_{61}ClO_{30}$	$C_{42}H_{71}ClO_{35}$	$C_{48}H_{81}ClO_{40}$
	1008.2936	1170.3464	1332.3993

[a] (a) $^{12}C = 12$ amu; (b) $^{1}H = 1.007825035$ amu; (c) $^{35}Cl = 34.96885272$ amu; (d) $^{16}O = 15.99491463$ amu. [b] For comparison, the exact mass of **21b** is 1222.4011 Da.

exact mechanism of PhCHO formation within the CyD ICs could not be pinpointed.

Experimental Section

General Information. 3-Chloro-3-phenyl-3*H*-diazirine (**8**) [CAS Registry No. 4460-46-2 (registry numbers supplied by author)] was prepared according to the literature,[18a] with slight variations. Common household chlorine bleach solutions were used as sources of sodium hypochlorite (NaOCl).[27] The concentration (*C*) of NaOCl was determined via redox titration and was unchanged after several weeks of refrigeration (ca. 2 °C). Benzaldehyde (PhCHO) was purified prior to use by washing an Et_2O solution of the aldehyde with 10% aqueous Na_2CO_3 and then H_2O. After predrying with saturated NaCl, the PhCHO solution was fully dried over anhydrous $MgSO_4$. After suction filtration, the Et_2O was removed via rotary evaporation and the residue was vacuum distilled using a diaphragm pump (ca. 15 mmHg) and a hot water bath.[77] Benzaldehyde azine (**29**) [28867-76-7] was prepared according to the literature.[78] 1,2-Diphenylethyne (tolan) [501-65-5] was recrystallized (3 mL of EtOH/1 g of tolan) prior to use.[79] Desyl chloride (DsCl)[80] [447-31-4], benzil (**39**) [134-81-6], benzoin (DsOH) [579-44-2], LiCl [7447-41-8], *i*-PrOH [67-63-0], benzaldehyde dimethyl acetal (**21d**) [1125-88-8], and (±)-hydrobenzoin (DL-**24**) [655-48-1] were used without further purification. Chlorine [7782-50-5] was dried by bubbling the gas through a trap containing concentrated H_2SO_4 [7664-93-9]. An aqueous "scrubber" was attached to the outlet of the reaction vessel. Methanol (MeOH) [67-56-1] was dried over magnesium and then stored over active 3 Å molecular sieves.[81] α-CyD [10016-20-3] and *β*-CyD [7585-39-9] were recrystallized from H_2O and found to be 90.0% (w/w) and 86.5% (w/w), respectively, by microanalysis. Centrifugation was necessary

(77) Leonard, J.; Lygo, B.; Procter, G. *Advanced Practical Organic Chemistry*, 2nd ed.; Chapman & Hall: London, 1995; p 73.

(78) (a) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R.; Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Longman: Essex, 1989; p 1260. (b) Hatt, H. H. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, pp 395−397.

(79) Smith, L. I.; Falkof, M. M. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, pp 350−351.

(80) Ward, A. M. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, pp 159−160.

(81) See ref 77, p 64.

TABLE 3. FTNMR Spectrometers Used in This Study

Bruker spectrometer	magnetic field strength B_0 (T)	^{1}H Larmor frequency $\nu_0(^1H)$ (MHz)	^{13}C Larmor frequency $\nu_0(^{13}C)$ (MHz)
AVANCE DPX-250	5.875	250.1	62.9
AC-300	7.049	300.1	75.5
AM-360	8.458	360.1	90.6
AVANCE DRX-400	9.398	400.1	100.6

when precipitates, e.g., CyD ICs, were too fine to collect via suction filtration with a sintered funnel (Porosity 4 frit); turbid solutions were centrifuged. The pH of aqueous solutions, e.g., $NaHCO_3/Na_2CO_3$ buffer, were measured using a pH meter that was calibrated using pH 7.00 buffer. Photolyses were performed using a Hanovia 450-W medium-pressure Hg-arc lamp. Both solid and liquid samples were agitated using a vortexer and cooled by an electric fan. Photolyses were also performed using a Heraeus TQ 718 Z4 700-W medium-pressure Hg-arc lamp doped with FeI_2 (λ_{max} = 370 nm) at T_{sample} = ca. 15 °C (water bath). Although made from quartz, i.e., SiO_2, the lamps were placed in water-cooled jackets that were made of borosilicate glass, which essentially filtered out light below λ = 300 nm. Precautions must be taken to prevent exposure to the skin and eyes.[82] Solution photolyses of 3*H*-diazirine **8** (concn = 0.01−0.50 M) were performed in Schlenk tubes after three freeze−pump−thaw cycles with argon purging.[83] Sometimes, however, samples were placed in sealed test tubes and submerged in a water bath, and argon was slowly bubbled in for 10 min with the aid of a second vent needle. The solid samples were placed in either Schlenk tubes or round-bottom flasks, sealed with rubber septa, and alternately evacuated and purged with argon three times. Larger samples were partially submerged in a continuously cooled water bath and slowly spun at an angle using a modified mechanical stirrer. The times required for complete photolysis of the 3*H*-diazirine guest were occasionally short, e.g., 2 h, but usually exceeded 1 day of exposure. The CyD ICs of 3-chloro-3-phenyl-3*H*-diazirine (**8**) were also suspended in an alkaline buffer solution. FTNMR spectra were recorded on various spectrometers (Table 3). *J* values are reported in Hz. 2-D ROESY spectra of the dilute D_2O solutions of **8**@(α-CyD)$_2$ and (**8**@*β*-CyD)$_2$ were obtained using a mixing time of 0.60 s, with solvent peak presaturation.

For IR absorption spectroscopy, solid samples were analyzed by pressing dilute, e.g., 1−4% (w/w), KBr pellets or by applying a concentrated solution onto a silicon wafer and evaporating the volatile solvent; liquid samples were analyzed as dilute CCl_4 solutions or by applying neat, viscous samples onto a silicon wafer. UV/vis absorption spectra were recorded using quartz cuvettes. CD spectra of aqueous solutions were obtained using an I. S. A. Jobin Yvon CD 6 circular dichrograph spectrometer and quartz cuvettes. Analytical GC assays were conducted using a Sichromat 1−4 series GC instrument outfitted with a 26-m poly(dimethylsiloxane) capillary (glass) column (silicone OV-101), a flame-ionization detector (T_{FID} = 250 °C), and a split-injector system (splitter-vent flow = 1.5 (mL of He)/min). The following conditions and temperature program were used: $T_{oven,i}$ = 100 °C (16 min), ramp = +30 °C/min, $T_{oven,f}$ = 220 °C (40 min), and $T_{injector}$ = 150 °C. Analytical GC assays were also conducted using a Fisons 8000 series GC instrument outfitted with a 30-m poly(dimethylsiloxane) capillary (copper) column (PE-1, 0.32-mm i.d., and 0.25-*μ*m film-thickness), a flame-ionization detector (T_{FID} = 260 °C), and a split injection system (splitter-vent flow = 2.1 (mL of He)/min). 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), and $T_{injector}$ = 185 °C. Preparative GC was performed using a Varian Aerograph model 920 instrument equipped with a 3.05-m poly(methyltrifluoropropylsiloxane) packed (aluminum) column (Alltech, 20 wt % of silicone DC-QF1 (50% trifluoropropyl and 50% methyl) on Chromosorb (80−100 mesh, NAW, 6.4-mm i.d.), and a thermal conductivity detector (T_{TCD} = 200 °C). The following isothermal conditions were used: T_{oven} = 100 °C, $T_{injector}$ = 200 °C, and carrier flow = 76 (mL of 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 (HP-5MS (95% dimethyl and 5% diphenyl), 0.25-mm i.d., and 0.25-*μ*m film-thickness), a Hewlett-Packard 5973 mass selective detector (T_{MSD} = 280 °C), and an auto split-injection system (splitter-vent flow = 8.0 (mL of He)/min). 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), and $T_{injector}$ = 200 °C; $T_{oven,i}$ = 140 °C (10 min), ramp = +30 °C/min, $T_{oven,f}$ = 220 °C (20 min), and $T_{injector}$ = 180 °C. Microanalysis and a manual fitting procedure using a spreadsheet program were employed to determine the guest@host stoichiometry of the CyD ICs as well as their crystal-water content. Microanalyses were performed by the Mikroanalytisches Laboratorium am Institut für Physikalische Chemie der Universität Wien, Vienna, Austria. 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-*μ*m 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 (λ = 211 and 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 ICs, in either a 1-thioglycerol (3-mercapto-1,2-propanediol) or a diethanolamine (2,2′-iminodiethanol) matrix, with a 20 keV beam of Cs atoms at 70 °C.

3-Chloro-3-phenyl-3*H*-diazirine (8) [4460-46-2]. CAUTION! (Perform behind a safety shield under dim lighting.) A solution of LiCl (5.30 g, 0.125 mol) in DMSO (87 mL) was rapidly stirred within a 1-L Erlenmeyer flask bearing a ground joint. Meanwhile, NaCl (31.7 g, 0.542 mol) was dissolved in cold 0.56 M NaOCl (296 mL, 0.166 mol) in another 1-L Erlenmeyer flask. The salty chlorine bleach solution was transferred to a 500-mL dropping funnel equipped with an equilibrating sidearm and ground joints. Benzamidine hydrochloride hydrate (**14**·HCl·H_2O, 4.365 g,[84] ca. 23.7 mmol) was added to the 1-L Erlenmeyer reaction flask, and then pentane (50 mL) was poured in. The reaction flask was submerged into an ice−salt bath, and rapid stirring was continued. The NaOCl/NaCl solution was dripped in within 15 min. The reaction mixture was stirred for an additional 30 min in the ice−salt bath. The pentane layer was collected using a 1-L separatory funnel. Next, the aqueous DMSO layer was extracted with Et_2O (4 × 25 mL). The combined organic extracts were washed with H_2O (5 × 20 mL) and then predried with saturated aqueous NaCl (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and then suction-filtered through a sintered funnel (Porosity 4 frit) into a tared 250-mL round-bottom flask. A diluted aliquot was analyzed via GC and GC−MS. The entire sample was carefully rotary-evaporated affording 3.117 g of an odorous yellow oil. The residual oil was chromatographed (15 g of silica gel 60, 230−400 mesh) using pentane as eluant. The nonpolar diazirine eluted first giving 2.496 g, 69% yield of a yellow, odorous liquid after 30 min of careful rotary evaporation.^{1}H NMR integration showed only traces of pentane eluant. The neat diazirine **8** could be stored for up to four months in the freezer (−22 °C) without

(82) Note that UV-A (λ = 320−400 nm) penetrates more deeply into the skin than UV-B (λ = 280−320 nm); see: Reisch, M. *Chem. Eng. News* **2002**, *80* (25), 38.

(83) CAUTION! Take care not to condense $Ar_{(g)}$ in $N_{2(l)}$ trap!

(84) Calculated from 3.71 g anhydrous basis.

decomposition: δ_H/ppm (360.1 MHz, $CDCl_3$) 7.08−7.15 (2 H, m), 7.35−7.41 (3 H, m); δ_C/ppm (90.6 MHz, $CDCl_3$) 47.1, 126.0, 128.5, 129.3, 135.8; $\bar{\nu}_{max}$/cm^{-1} (pentane) 1570; λ_{max}/nm (pentane) 368 ($\epsilon = 2.3 \times 10^2$ M^{-1} cm^{-1}); λ_{max}/nm (EtOH) 371 ($\epsilon = 2.1 \times 10^2$ M^{-1} cm^{-1}).

1,2-Dichloro-1,2-diphenylethene (17) [13700-82-8].[31] CAUTION! (Perform within a well-ventilated fume hood.) Dry $Cl_{2(g)}$ was bubbled through a solution of 1,2-diphenylethyne (tolan) (10.0 g, 56.1 mmol) in CCl_4 (100 mL) for 5 min until no more heat was evolved. The green solution was stirred overnight whereupon a white precipitate had formed. The mixture was refrigerated to induce more precipitation and then suction-filtered through a sintered funnel. (A second crop of oily material could be obtained after rotary evaporation of the CCl_4 filtrate.) Analysis by GC showed a 3:1 ratio of the tolan dichlorides **17** in addition to tolan tetrachloride (**40**) and traces of tolan. A portion of the first crop was chromatographed (silica gel 60, 230−400 mesh) using pentane as eluant yielding fractions of various purity, R_f 0.32 (UV; pentane). It was found that impure samples of dichloride **17** could be separated from tetrachloride **40** via preparative GC or via vacuum sublimation. $\bar{\nu}_{max}$/cm^{-1} (KBr) 866.

(*Z*)-**17** (76%) [5216-32-0]: mp 58 °C; δ_H/ppm (360.1 MHz, $CDCl_3$) 7.13−7.23 (10 H, m); δ_C/ppm (90.6 MHz, $CDCl_3$) 128.1 (CH), 128.6 (CH), 129.7 (CH), 130.8 (C), 137.3 (CCl); *m*/*z* (EI) 248 (M^+, 67), 213 (41), 178 (100), 151 (17), 106 (14), 88 (24), 76 (13), 63 (5), 51 (5).

(*E*)-**17** (24%) [951-86-0]: mp 148 °C; δ_H/ppm (360.1 MHz, $CDCl_3$) 7.36−7.46 (6 H, m), 7.61 (4 H, dm *J* 7.6); δ_C/ppm (90.6 MHz, $CDCl_3$) 128.2 (CH), 129.0 (CH), 129.1 (CH), 129.7 (C), 137.6 (CCl); *m*/*z* (EI) 248 (M^+, 40), 213 (20), 178 (100), 151 (9), 106 (7), 88 (9), 76 (7), 63 (3), 51 (3).

Bis(1-chloro-1-phenylmethylidene)hydrazine (18).[33c−e] **Method 1.** CAUTION! (Perform within a well-ventilated fume hood.) Dry $Cl_{2(g)}$ was *rapidly* bubbled for 3 h through a solution of benzaldehyde azine (4.639 g, 22.3 mmol)[78] in CCl_4 (65 mL) that also contained anhydrous $K_2CO_{3(s)}$ (5.0 g, 36.2 mmol). The product mixture was suction-filtered through a sintered funnel, and the collected filtrate was rotary-evaporated to give a yellow oil that solidified in the freezer (−22 °C). The product was recrystallized from Et_2O and cooled in the freezer to induce precipitation. The crystals were suction-filtered and washed with cold Et_2O affording 0.395 g of a mixture that was analyzed by GC: azine **18** (62%) and PPD (38%). More azine **18** was sought by analyzing the Et_2O filtrate, which contained the following compounds: PhCHO (30%), PhCN (trace), benzal dichloride **20h** (3%), (trichloromethyl)benzene (**41**) (33%), PPD (31%) and azine **18** (2%).

Method 2. CAUTION! (Perform behind a safety shield.) A small amount of neat diazirine **8** was photolyzed (Hanovia 450-W) for 1−2 h. The solid product was triturated in pentane and then suction-filtered using a Büchner funnel. The off-white residue was washed with more pentane yielding a substantial amount of pure azine **18**: mp 120−122 °C; δ_H/ppm (360.1 MHz, $CDCl_3$) 7.44−7.61 (6 H, m), 8.10−8.22 (4 H, dm *J* 7.7); δ_C/ppm (90.6 MHz, $CDCl_3$) 128.5, 128.6, 131.8, 133.7, 144.1; $\bar{\nu}_{max}$/cm^{-1} (KBr) 1596, 1569, 1446, 922, 761, 684; *m*/*z* (EI) 276 (M^+, 46), 241 (46), 222 (17), 205 (5), 165 (17), 138 (98), 103 (52), 89 (14), 77 (100), 63 (7), 51 (19).

2,5-Diphenyl-1,3,4-oxadiazole (PPD) [725-12-2].[32] CAUTION! (Perform within a well-ventilated fume hood.) A 25-mL round-bottom flask, equipped with a Claisen head, dropping funnel, Dimroth condenser, and drying tube was charged with hydrazine dihydrochloride (N_2H_4·2HCl) (0.393 g, 3.75 mmol), pyridine (3.5 mL), and H_2O (1.5 mL). Benzotrichloride **41** (1.463 g, 7.50 mmol) was slowly dripped into the stirred reaction flask which was then refluxed for 0.5 h. After cooling, H_2O (20 mL) was added and the mixture was suction-filtered through a Büchner funnel. The brown residue was dried in a desiccator giving 0.238 g of the crude product. The crude PPD was cleaned via chromatography (silica gel 60, 230−400 mesh) using Et_2O as eluant, giving the orange solid PPD: δ_H/ppm (360.1 MHz, $CDCl_3$) 7.44−7.63 (3 H, m), 8.10−8.17 (2 H, m); δ_C/ppm (90.6 MHz, $CDCl_3$) 124.0, 126.9, 129.1, 131.7, 164.6; *m*/*z* (EI) 222 (M^+, 100), 165 (99), 105 (86), 89 (8), 77 (73), 63 (12), 51 (17).

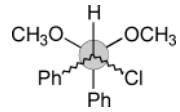


FIGURE 8. Newman projection of desyl chloride dimethyl acetal **28** showing diastereotopic methyl groups.

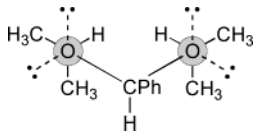


FIGURE 9. Newman projection of benzaldehyde diisopropyl acetal **21e** showing diastereotopic methyl groups.

Benzyl Benzoate (BzOBn) [120-51-4]. A 50-mL three-necked round-bottom flask, equipped with a dropping funnel, Dimroth condenser, and drying tube, was charged with benzyl alcohol (BnOH) (2.163 g, 20 mmol), pyridine (1.582 g, 20 mmol), and Et_2O (25 mL). Benzoyl chloride (BzCl) (2.811 g, 20 mmol) was slowly dripped into the stirred reaction flask, which was then refluxed for 2 h. After cooling, H_2O (10 mL) was added to dissolve the pyridinium chloride salts, and the mixture was transferred to a separatory funnel. After the aqueous layer was discarded, the ether layer was washed with H_2O (5 × 10 mL) and predried with saturated NaCl (10 mL). The ether layer was dried over anhydrous $MgSO_4$ overnight. The product mixture was suction-filtered through a sintered funnel, and the filtrate was collected and rotary-evaporated. Analysis of the product residue by GC showed it to contain BzOBn (84%), BzOH (7%), and BnOH (9%). Column chromatography (silica gel 60, 230−400 mesh), using pentane/Et_2O (19:1) as eluant, was employed after 2-D TLC confirmed that the BzOBn ester (R_f 0.40 (UV, I_2)) did not decompose to BzOH (R_f 0.04 (UV)) and BnOH (R_f 0.20 (UV)): mp 18−20 °C; n^{22}_D 1.5683; δ_H/ppm (360.1 MHz, $CDCl_3$) 5.39 (2 H, s), 7.32−7.49 (7 H, m), 7.56 (1 H, tt *J* 7.4, 1.5), 8.10 (2 H, dm *J* 8.0); δ_C/ppm (90.6 MHz, $CDCl_3$) 66.6, 128.1, 128.2, 128.3, 128.5, 129.7, 130.2, 132.9, 136.1, 166.3.

(1-Chloro-2,2-dimethoxy-2-phenylethyl)benzene (28): (Figure 8) δ_H/ppm (360.1 MHz, $CDCl_3$) 3.15 (3 H, s), 3.56 (3 H, s), 5.31 (1 H, m), 6.93 (2 H, d *J* 7), 7.06 (2 H, d *J* 7), 7.14 (2 H, t *J* 7), 7.19 (4 H, t *J* 8), 7.28 (2 H, t *J* 7); δ_C/ppm (90.6 MHz, $CDCl_3$) 48.8, 50.2, 64.3, 104.0, 126.8, 127.0, 127.9, 128.2, 129.3, 129.5, 135.0, 136.8; *m*/*z* (EI) 276 (M^+, trace), 245 (4), 210 (14), 178 (4), 167 (17), 165 (19), 151 (100), 125 (3), 105 (27), 91 (13), 77 (13), 59 (4), 51 (4).

(Dimethoxymethyl)benzene (21d) [1125-88-8]: δ_H/ppm (360.1 MHz, $CDCl_3$) 3.33 (6 H, s), 5.40 (1 H, s), 7.29−7.40 (3 H, m), 7.43−7.48 (2 H, m); δ_C/ppm (90.6 MHz, $CDCl_3$) 52.6, 103.2, 126.6, 128.1, 128.4, 138.1; *m*/*z* (EI) 152 (M^+, 2), 121 (100), 105 (18), 91 (14), 77 (30), 51 (8).

[Di(1-methylethoxy)methyl]benzene (21e) [38115-81-0]: (Figure 9) δ_H/ppm (300.1 MHz, $CDCl_3$) 1.17 (6 H, d *J* 6.2), 1.20 (6 H, d *J* 6.2), 3.90 (2 H, sept *J* 6.2), 5.60 (1 H, s), 7.26−7.66 (5 H, m); δ_C/ppm (75.5 MHz, $CDCl_3$) 22.5, 23.1, 67.8, 99.2, 126.7, 128.1, 128.2, 140.4.

***x*-(1-Chloro-1-phenylmethyl)pentanes (20i).** A mixture of three diastereomers, i.e., (*R**,*R**)-(1-chloro-2-methylpentyl)-benzene ((*R**,*R**)-**20ib**, 42%), (*R**,*S**)-(1-chloro-2-methylpentyl)benzene ((*R**,*S**)-**20ib**, 42%), and (1-chloro-2-ethylbutyl)-benzene (**20ic**, 16%) (Figure 10): δ_H/ppm (360.1 MHz, $CDCl_3$) 0.83−2.19 (11 H, m), 4.70−4.92 (1 H, m),[85] 7.26−7.42 (5 H, m); δ_C/ppm (90.6 MHz, $CDCl_3$) 10.3 (**20ic**, CH_3), 10.9 (**20ic**, CH_3), 14.0 (**20ib**, CH_3), 14.2 (**20ib**, CH_3), 15.6 (**20ib**, CH_3), 16.6 (**20ib**, CH_3), 19.8 (**20ib**, CH_2), 20.0 (**20ib**, CH_2), 21.5 (**20ic**,

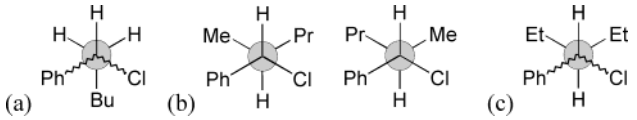


FIGURE 10. Newman projections of (a) (1-chlorohexyl)-benzene (**20ia**),[87] (b) [*S*-(*R**,*R**)]-(1-chloro-2-methylpentyl)-benzene ([*S*-(*R**,*R**)]-**20ib**) and [*S*-(*R**,*S**)]-(1-chloro-2-methylpentyl)benzene ([*S*-(*R**,*S**)]-**20ib**), and (c) (1-chloro-2-ethylbutyl)benzene (**20ic**).[88]

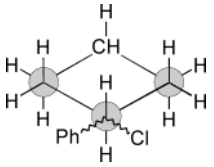


FIGURE 11. Newman projection of [chloro(cyclohexyl)methyl]-benzene (**20j**) showing diastereotopic methylidene groups.

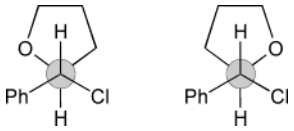


FIGURE 12. Newman projections of [*S*-(*R**,*R**)]-2-(1-chloro-1-phenylmethyl)oxolane ([*S*-(*R**,*R**)]-**20l**) and [*R*-(*R**,*S**)]-2-(1-chloro-1-phenylmethyl)oxolane ([*R*-(*R**,*S**)]-**20l**).

CH_2), 22.4 (**20ic**, CH_2), 35.5 (**20ib**, CH_2), 36.2 (**20ib**, CH_2), 41.0 (**20ib**, CH), 48.4 (**20ic**, CH), 66.9 (**20ic**, CH−Cl), 69.5 (**20ib**, CH−Cl),[86] 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.3, 128.5, 140.8, 141.1, 141.2; *m*/*z* (EI) 196 (M^+, 4), 161 (14), 160 (42), 131 (99), 117 (38), 91 (100), 71 (15).

[Chloro(cyclohexyl)methyl]benzene (20j) [28047-23-6]:[41,89] (Figure 11) R_f 0.30 (UV; pentane); δ_H/ppm (360.1 MHz, $CDCl_3$) 0.85−0.97 (1 H, qd *J* 12.4, *J* 3.7), 1.01−1.33 (4 H, m), 1.45 (1 H, dm *J* 12.4), 1.59−1.73 (2 H, m), 1.75−1.94 (2 H, m), 2.20 (1 H, dm *J* 12.4), 4.61 (1 H, d *J* 8.3), 7.25−7.37 (5 H, m);[89] δ_C/ppm (90.6 MHz, $CDCl_3$) 25.86, 25.94, 26.1, 30.3, 30.4, 45.7 (CH), 69.8 (CHCl), 127.5 (CH), 127.9 (CH), 128.3 (CH), 140.9.[89]

2-(1-Chloro-1-phenylmethyl)oxolane (20l). A 1:1 mixture of two diastereomers, i.e., (*R**,*R**)-2-(1-chloro-1-phenylmethyl)oxolane ((*R**,*R**)-**20l**) and (*R**,*S**)-2-(1-chloro-1-phenylmethyl)oxolane ((*R**,*S**)-**20l**) (Figure 12): δ_H/ppm (360.1 MHz, $CDCl_3$) 1.55−2.17 (4 H, m), 3.74−3.93 (2 H, m), 4.33 (1 H, ddd *J* 14.0, *J* 7.2, *J* 2.5), 4.80 (1 H, dd *J* 4.7, *J* 7.2), 7.27−7.43 (5 H, m); δ_C/ppm (90.6 MHz, $CDCl_3$) 25.8, 25.9, 29.3, 29.4, 65.2, 65.8, 68.8, 69.1, 82.4, 82.8, 127.8,[90] 128.3, 128.4,[90] 128.5, 138.9, 139.1; *m*/*z* (EI) 196 (M^+, 1), 161 (4), 160 (15), 125 (24), 115 (17), 104 (10), 91 (41), 77 (10), 71 (100), 63 (9), 51 (8); found M^+ 196.065(2), $C_{11}H_{13}ClO$ requires 196.0655.

(1,2,2,2-Tetrachloroethyl)benzene (20m) [4714-28-7]: δ_H/ppm (360.1 MHz, $CDCl_3$) 5.50 (1 H, s), 7.36−7.42 (3 H, m), 7.63−7.67 (2 H, m);[37c] δ_C/ppm (90.6 MHz, $CDCl_3$) 74.0 (d *J* 156), 100.6 (s), 128.0 (d *J* 165), 129.9 (d *J* 165), 130.1 (d *J* 165), 134.5 (s).

(1,2,2,2-Tetrachloroethyl-1-*d*)benzene (20m-*d*): *m*/*z* (EI) 243 (M^+, 1), 208 (4), 173 (100), 138 (42), 126 (79), 103 (72), 75 (18), 51 (21).

Preparation of 8@(α-CyD)$_2$ and (8@*β*-CyD)$_2$. Filtered solutions of 90.0% (w/w) α-CyD (4.864 g, 4.50 mmol, 72 mL H_2O) and 86.5% (w/w) *β*-CyD (2.952 g, 2.25 mmol, 219 mL H_2O) were rapidly stirred in a room-temperature water bath under the exclusion of light. Neat diazirine **8** (0.229 g, 1.50 mmol) was injected into each solution and stirred overnight. Each white suspension was separately suction-filtered through a tared sintered funnel (Porosity 4 frit), and each residue was washed with 3 mL of H_2O. Suction was continued for 2 h to facilitate air-drying. The loosely covered samples were placed in a vacuum desiccator filled with anhydrous $CaCl_2$,[91] pre-evacuated by a diaphragm pump to ca. 15 mmHg, and evacuated by a high-vacuum oil pump to ca. 0.5 mmHg and left overnight, giving 0.394 g of α-CyD IC (Figure 6).[68,92] (Found: C, 42.96; H, 6.11; N, 1.20%, corresponding to **8**@2.10α-CyD·6.3H_2O, 11% yield) and 1.463 g of *β*-CyD IC[93] (Found: C, 43.70; H, 6.00; N, 2.39%, corresponding to **8**@0.85*β*-CyD·3.1H_2O, 84% yield).[94]

Photolysis of 8@(α-CyD)$_2$ and (8@*β*-CyD)$_2$. The CyD ICs (0.200 g each) were transferred to round-bottom flasks, sealed with rubber septa, and alternately evacuated and purged with argon three times. The CyD ICs were photolyzed (Hanovia 450-W) for 8 h. A 5-mg portion of each photolyzed CyD IC was used for NMR (DMSO-d_6) and FAB MS (−*ve* FAB, diethanolamine) analyses.[70]

Photolysis of 8@(α-CyD)$_2$ in Alkaline Buffer. The α-CyD IC (0.150 g) was sealed via rubber septum in a 10-mL pear-shaped flask containing a magnetic stirbar and alkaline buffer (5 mL, pH = 9.27).[95] The white sample was photolyzed (Heraeus 700-W) in a water bath at 12 °C for 24 h. Next, the tan suspension was transferred to a tared centrifuge tube and centrifuged (2.2k rpm, T = 20 °C, 30 min), and the supernatant was decanted and set aside. The sample tube was placed in a vacuum desiccator filled with anhydrous $CaCl_2$,[91] preevacuated by a diaphragm pump to ca. 15 mmHg, and evacuated by a high-vacuum oil pump to ca. 0.02 mmHg for 2 h, giving 0.014 g of bis(1-chloro-1-phenylmethylidene)hydrazine (**18**) (including traces of α-CyD), as determined by NMR (DMSO-d_6). The supernatant was diluted to 100 mL with H_2O and continuously extracted overnight with 100 mL of refluxing anhydrous CH_2Cl_2, which was subsequently concentrated and analyzed by GC, which showed mostly benzonitrile (PhCN). Next, the extracted aqueous layer was collected and subjected to rotary evaporation (T = 50 °C), giving residual photolyzed α-CyD IC and buffer salts. Hence, analytical RP HPLC was also employed to observe and quantify the modified CyD's. Results from FAB MS analysis revealed the presence of innermolecular products: *m*/*z* (−*ve* FAB, thioglycerol) 1077.2 ([M − H]$^-$) (Figure 7a). Small amounts of HCl@$[C_6(H_2O)_5]_n$ or $[C_6(H_2O)_5]_n$·HCl were also observed: *m*/*z* (−*ve* FAB, thioglycerol) 1007.1 ([M − H]$^-$) (Figure 7a).

Photolysis of (8@*β*-CyD)$_2$ in Alkaline Buffer. The *β*-CyD IC (0.250 g) was sealed via rubber septum in a 25-mL pear-shaped flask containing a magnetic stirbar and alkaline buffer (10 mL, pH = 9.27).[95] The white sample was photolyzed (Heraeus 700-W) in a water bath at 12 °C for 24 h. Next, the tan suspension was suction-filtered through a tared sintered funnel (Porosity 4 frit) and placed in a vacuum desiccator filled with anhydrous $CaCl_2$,[91] preevacuated by a diaphragm pump to ca. 15 mmHg, and evacuated by a high-vacuum oil pump to ca. 0.02 mmHg for 2 h, giving 0.120 g of photolyzed *β*-CyD IC. A 5-mg portion was set aside for ^{1}H NMR (DMSO-d_6) and FAB MS analysis. Innermolecular products were indeed formed:

(85) δ_H/ppm = 4.72 (0.42 H, d *J* 7.8), 4.83 (0.42 H, d *J* 6.4), and 4.90 (0.16 H, d *J* 7.8).

(86) In contrast to the sole **20ib** signal at δ_c/ppm = 41.0, two peaks were resolved for (*R**,*R**)-**20ib** and (*R**,*S**)-**20ib** at δ_c/ppm = 69.47 and 69.54.

(87) Christl, M.; Braun, M. *Chem. Ber.* **1989**, *122*, 1939−1946.

(88) Baddeley, G.; Chadwick, J.; Taylor, H. T. *J. Chem. Soc.* **1954**, 2405−2409.

(89) Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron* **2001**, *57*, 1663−1670.

(90) Two carbons.

(91) A rubber band was used to fasten a paper towel covering.

(92) See the Supporting Information, Figures S2 and S6.

(93) See the Supporting Information, Figure S3.

(94) The saved filtrates were analyzed separately via UV/vis (α-CyD IC: A_{376} = 0.25, d = 1 cm; *β*-CyD IC: A_{376} = 0.18, d = 10 cm) and *both* provided a molar absorptivity (ϵ) value for diazirine **8** of ϵ_{376} = (14.2 ± 0.5) $M^{-1}cm^{-1}$. This is 1 order of magnitude below expectation.

(95) Buffer solution was prepared by dissolving 1.060 g of Na_2CO_3 and 17.552 g of $NaHCO_3$ in distilled water to afford 1 L of solution.

m/*z* (−*ve* FAB, thioglycerol) 1239.5 ([M − H]$^-$) (Figure 7b). A heavier molecule was also observed: *m*/*z* (−*ve* FAB, thioglycerol) 1345.2 ([M − H]$^-$) (Figure 7b). This corresponds to an innermolecular insertion product of *two* carbenes **9** with one *β*-CyD, which may be expected from dimeric (**8**@*β*-CyD)$_2$. The remaining sample, including the turbid filtrate, was dissolved in 100 mL of H_2O and continuously extracted overnight with 100 mL of refluxing anhydrous CH_2Cl_2, which was subsequently concentrated and analyzed by GC. Next, the extracted aqueous layer was collected and subjected to rotary evaporation (T = 50 °C), giving 0.358 g of residual photolyzed *β*-CyD IC and buffer salts. Hence, analytical RP HPLC was also employed to observe and quantify the modified CyDs.

Photolysis of 8@*γ*-CyD in Alkaline Buffer. A sample of the **8**@*γ*-CyD IC[96] was photolyzed in alkaline buffer,[95] as above, but using the Hanovia 450-W lamp. Analysis of a DMSO-d_6 solution of the solid product by ^{1}H NMR showed a peak at δ_H = 4.71 ppm (45%),[97] which is consistent with a benzylidene proton. Note that the mere inclusion of the benzylidene acetal (dimethoxymethyl)benzene (**21d**) within CyDs converted **21d** completely to PhCHO.[98] Therefore, the signal is due to an innermolecular product.

Preparation of PhCHO@α-CyD [85888-34-2]. A filtered solution of 90.0% (w/w) α-CyD (0.973 g, 0.90 mmol, 14.4 mL H_2O) was rapidly stirred in a room temperature water bath. Freshly distilled benzaldehyde (0.032 g, 0.30 mmol) was injected into the solution and stirred overnight. The white suspension was suction-filtered through a tared sintered funnel (Porosity 4 frit) and the residue was triturated with 3 mL of H_2O. Suction was continued for 2 h to facilitate air-drying. The loosely covered sample was placed in a vacuum desiccator filled with anhydrous $CaCl_2$,[91] preevacuated by a diaphragm pump to ca. 15 mmHg, and evacuated by a high-vacuum oil pump to ca. 0.2 mmHg for 4 h, giving 0.327 g of α-CyD IC.

(96) See the Supporting Information, Figure S4.
(97) See the Supporting Information, Figure S8.
(98) Tee, O. S.; Fedortchenko, A. A.; Soo, P. L. *J. Chem. Soc., Perkin Trans. 2* **1998**, 123−128.

Preparation of PhCHO@*β*-CyD [64691-57-2]. A filtered solution of 86.5% (w/w) *β*-CyD (0.590 g, 0.45 mmol, 44 mL H_2O) was rapidly stirred in a room temperature water bath. Freshly distilled benzaldehyde (PhCHO) (0.032 g, 0.30 mmol) was injected into the solution and stirred for 3 days. The turbid solution was transferred to two tared centrifuge tubes, centrifuged (2.2k rpm, T = 18 °C, 25 min), and the supernatants were decanted. Each precipitate was triturated with 0.5 mL of H_2O and recentrifuged. After decanting the washings, the samples were placed in a vacuum desiccator filled with anhydrous $CaCl_2$,[91] preevacuated by a diaphragm pump to ca. 15 mmHg, and evacuated by a high-vacuum oil pump to ca. 0.2 mmHg for 4 h, giving 0.124 g of *β*-CyD IC: mp 257−268 °C dec.[99]

Acknowledgment. Dedicated to Prof. M. Makosza on the occasion of his 70th birthday. This work was supported in part by the Petroleum Research Fund (Project No. 28670-AC4), administered by the American Chemical Society; the Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (Project P12533-CHE); and the Department of Chemistry, State University of New York at Binghamton (Graduate Fellowship for the Summer of 1997 in support of research). The cyclodextrins used in this study were generously provided by Cerestar USA, Inc., and Wacker Chemie, Germany.

Supporting Information Available: NMR, ICD, and FAB MS spectra of CyD ICs. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026521H

(99) See the Supporting Information, Figure S10.