unusual diastereoselectivity of the oxidative cyclization and catalytic hydrogenation clearly reveals the steric congestion associated with this novel system. Important future goals include correlating the importance of such unusual conformational effects with biological activity and defining the scope and mechanism of the novel oxidative cyclization.[18]

Acknowledgment. We thank the General Medical Sciences Institute of the National Institutes of Health for their continuing generous support of our programs. P.D.G. and M.G.S. thank the NIH for postdoctoral fellowships. We are especially grateful to Mr. Chris Myers for the X-ray structural determination. We thank Dr. Pichael Wiriyachitra of the Faculty of Pharmacy, Chiang Mai University, for an authentic sample of (-)-rocaglamide. Mass spectra were gratefully provided by the Mass Spectrometry Facility, University of California—San Francisco, supported by the NIH Division of Research Resources.

Supplementary Material Available: Characterization data for **1**, **3**, **4**, **9**, **11**, **12a,b**, **13**, **14**, **15c**, and **16a,b** (3 pages). Ordering information is given on any current masthead page.

(18) The initial exploratory work of M.G.S. was performed at the Department of Chemistry, University of Wisconsin—Madison.

Diazirinyl Anion: A Cyclic 4π-Electron System

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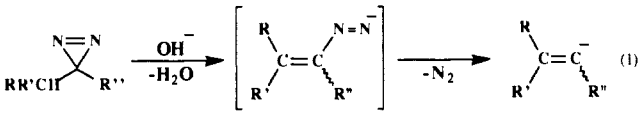
3*H*-Diazirines (**1**)[1] are cyclic isomers of diazo compounds and are characterized by a three-membered ring with a nitrogen–nitrogen double bond. This ring system was originally proposed in the literature about 100 years ago in order to explain the structure of diazomethane and ethyl diazoacetate.[2] However, it was not until 1960/1961 that Paulsen, and then Schmitz and Ohme, prepared the first authentic derivatives of **1**.[3] They were found, somewhat surprisingly, to be remarkably stable thermally and chemically.[4] Hundreds of diazirines have subsequently been prepared, and they have become the subject of increasing attention.[5]

We have recently reported that diazirines are practical reagents for the gas-phase preparation of vinyl anions (eq 1).[6] The mechanism for this reaction presumably involves an elimination pathway leading to a diazenyl anion intermediate (**2**), which rapidly evolves nitrogen to afford the observed product ions. This



1 2 3

procedure is useful because vinyl anions are exceedingly reactive species that have proven to be difficult to generate by other means.[7]

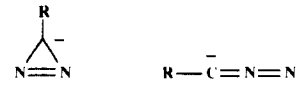
(1) Hereafter referred to simply as diazirine(s).
(2) (a) von Pechmann, H. *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 1888. (b) Curtius, T. *J. Prakt. Chem.* **1889**, *39*, 107.
(3) (a) Paulsen, S. R. *Angew. Chem.* **1960**, *72*, 781. (b) Schmitz, E.; Ohme, R. *Angew. Chem.* **1961**, *73*, 115.
(4) **CAUTION**: While many diazirines are thermally more stable than their corresponding diazo isomers, they must still be treated with great caution. Explosive decompositions have been reported.
(5) For example, see: *Chemistry of Diazirines*; Liu, M. T., Ed.; CRC Press: Boca Raton, FL, 1987; Vols. 1 and 2 and references therein.
(6) Anderson, K. K.; Kass, S. R. *Tetrahedron Lett.* **1989**, *30*, 3045.
(7) An alternative method involves collision-induced dissociation. For details, see: (a) Froelicher, S. W.; Freiser, B. S.; Squires, R. R. *J. Am. Chem. Soc.* **1986**, *108*, 2853. (b) Graul, S. T.; Squires, R. R. *J. Am. Chem. Soc.* **1988**, *110*, 607. (c) Graul, S. T.; Squires, R. R. *J. Am. Chem. Soc.* **1989**, *111*, 892 and references therein.

Table I. Summary of Results of Proton Transfer from Reference Acids and Bases to **6** and **6a**

ref compd	ΔH_{acid}[a]	ΔG_{acid}	proton transfer[b] ref acid	proton transfer[b] conjugate base
NH_3	403.7	396.0	-	+
$MeNH_2$	403.2	395.8	-	+
$EtNH_2$	399.4	391.7	+	-
Me_2NH	396.3	389.1	+	-
H_2O	390.8	384.1	+	-
MeOH	381.2	375.0	+	-

[a] Acidities are in kcal mol^{-1} and come from ref 9. [b] A "+" indicates the occurrence and a "-" denotes the absence of proton transfer.

When monosubstituted diazirines (R″ = H) are reacted, not only is the expected 1-alkenyl anion (**3**) produced, but a small amount ($\leq \sim 10\%$) of a deprotonated ion (P - 1) is also formed. Two reasonable alternatives for the structure of this product are a diazirinyl anion (**4**) or a diazo anion (**5**). The former species are



4 5

cyclic 4π-electron systems, antiaromatic at least in the Hückel sense,[8] and theoretically interesting, but have not been reported previously. In contrast, the latter ions, which could arise from the cleavage of a carbon–nitrogen bond in **4**, are well-known both in solution and in the gas phase and undoubtedly are favored thermodynamically. The identity of the P - 1 ions, however, was not ascertained because they were not formed in sufficient quantities to characterize them. In this communication, we now report that *tert*-butyldiazirine and the parent compound, neither of which can undergo an elimination reaction due to the absence of a β-hydrogen, both lead to the exclusive formation of a P - 1 ion. The reactivity of the resulting species is quite similar, and the structure, reactivity, and proton affinity of the parent system are described herein.

Diazirine (**6**) is not very acidic in the gas phase. It reacts with NH_2^- and $MeNH^-$, in our flowing afterglow apparatus, to afford a P - 1 ion (*m/z* 41), but is inert to weaker bases such as OH^-, Me_2N^-, and even $EtNH^-$ (see Table I). This data reflects either the thermodynamic acidity of **6** or the presence of a kinetic barrier to deprotonation. By examining the reverse process and noting that the P - 1 ion is a strong base (it deprotonates MeOH, H_2O, Me_2NH, and $EtNH_2$), the latter possibility can be ruled out. Consequently, we assign ΔH_{acid} (**6**) = 401 ± 3 kcal mol^{-1} and ΔG_{acid} (**6**) = 394 ± 3 kcal mol^{-1}. Diazomethane (**7**) is almost 30 kcal mol^{-1} more acidic than diazirine (ΔH_{acid} (**7**) = 373 ± 3 kcal mol^{-1} and ΔG_{acid} (**7**) = 365 ± 3 kcal mol^{-1}),[10] and thus the structure of the *m/z* 41 ion cannot be that of the diazomethyl anion (**7a**). On the basis of these results, the reactivity of the P - 1 ion, consideration of all the other isomers,[11] and molecular

(8) Cyclization to the diazirinyl anion leads to a destabilization of 0.48β if one uses the parameters for nitrogen ($\alpha_N = \alpha_C + 0.38\beta_{CC}$; $\beta_{CN} = 0.70\beta_{CC}$; $\beta_{NN} = 1.27\beta_{CC}$) given by Hess et al.: Hess, B. A.; Schaad, L. J.; Holyoke, C. W., Jr. *Tetrahedron* **1975**, *31*, 295.
(9) Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. 1.
(10) DePuy, C. H.; Van Doren, J. M.; Gronert, S.; Kass, S. R.; Motell, E. L.; Ellison, G. B.; Bierbaum, V. M. *J. Org. Chem.* **1989**, *54*, 1846.
(11) Cyanamide (NH_2CN) is quite acidic (ΔH_{acid} = 350 ± 3 kcal mol^{-1}), and given the difference between ΔH_{acid} (CH_3CN) and ΔH_{acid} (CH_3NC) (-1.8 kcal mol^{-1}),[12] it seems reasonable to anticipate that isocyanamide (NH_2NC) will also be more acidic than **6**. A reasonable model for the upper limit of the acidity of 2*H*-diazirine ($\overline{CH{=}NNH}$) is 3,3-dimethylcyclopropene (ΔH_{acid} = 381 ± 3 kcal mol^{-1}). Thus, all three compounds appear to be more acidic than **6**, and an unlikely hydrogen rearrangement from carbon to nitrogen need not be proposed. In addition, the observed reactivity of the P - 1 ion would be difficult to rationalize in terms of the conjugate bases of these three compounds.
(12) Filley, J.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1987**, *109*, 5992.
(13) Kroeker, R. L.; Bachrach, S. M.; Kass, S. R. Manuscript submitted for publication.

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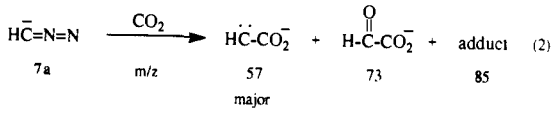
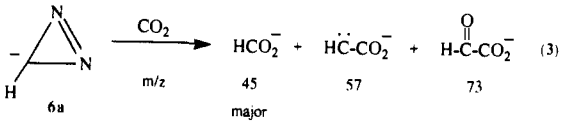
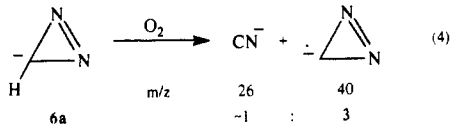
orbital calculations,[13] we conclude that the product is indeed the diazirinyl anion (**6a**).

Consistent with this assignment is the observation that **6a** exchanges one hydrogen for deuterium upon reaction with ND_3. Likewise one might expect the diazirinyl anion to react similarly to the diazomethyl anion, and this is the case with CO_2 (eqs 2 and 3).[10] Both ions lead to the formation of a carbene (m/z 57)

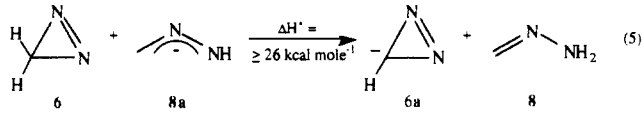




and a glyoxylate ion (m/z 73), but the latter also leads to the formation of a small amount of an adduct (15%)[10] while the former gives rise to a formal hydride ion transfer product (~80%). Given the greater basicity of the diazirinyl anion, one might also expect it to be more reactive than **7a**. Indeed, the diazomethyl anion is inert to O_2, whereas **6a** undergoes a rapid reaction affording two product ions (eq 4). The structure of the m/z 40 ion (P − 2, $CN_2^{\bullet-}$) is intriguing. Three possibilities, cyclic, C–N–N, and N–C–N, exist, and an independent preparation of the two acyclic ions via the reaction of $O^{\bullet-}$ with cyanamide and diazomethane has enabled us to conclude that the reaction product is cyclic. This assignment is based on the different reactivities of the P − 2 ions and indicates that the C–H bond in **6a** is quite weak (≤49 kcal mol^{-1}).[14]



Having established the structure of the diazirinyl anion, we are in a position to address the question of its stability. In this regard, it is of interest to compare **6a** to its acyclic analogue (**8a**, eq 5). The reaction enthalpy is the difference in acidity between **6** and **8**. The latter quantity has not been measured, but the proton affinity of 3-methyl-1-azaallyl anion, 375 ± 3 kcal mol^{-1},[15] can be taken as an upper limit. The acyclic ion is clearly the more stable isomer. This is consistent with the notion of antiaromaticity, but can also be accounted for by the charge repulsion in a constrained allylic system.[16]



Recently Zhou and Parr[17] described the use of relative and absolute hardness in determining the stability and reactivity of cyclic conjugated systems. Their model predicts that the diazirinyl anion should be nonaromatic.[18] This is consistent with more detailed ab initio molecular orbital calculations[13] and suggests that **6a** will be a viable species in solution. Investigations to test this hypothesis are currently underway and will be reported in due course.

Acknowledgment. Kraig Anderson carried out the initial experiments that led to this work, and Professors Steven Bachrach and Joel Liebman read this manuscript and made helpful suggestions. Financial support from the National Science Foundation (CHE-8907198); the donors of the Petroleum Research Fund, administered by the American Chemical Society; a research award from the American Society for Mass Spectrometry; and a McKnight Professorship administered by the University of Minnesota are gratefully acknowledged.

(14) We thank one of the referees for pointing this out to us. The bond dissociation energy of O_2-H (49 kcal mol^{-1}) is taken from ref 9.

(15) Dahlke, G. D.; Kass, S. R., unpublished results.

(16) Streitwieser et al. have shown that as the central bond angle of an allylic anion is reduced, the energy rapidly increases. Boerth, D. W.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 750.

(17) Zhou, Z.; Parr, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 7371.

(18) Absolute hardness (η) is given by $\eta = (\epsilon_{LUMO} - \epsilon_{HOMO})/2$, where the dividing line between aromatic ($\eta > -0.25\beta$) and antiaromatic ($\eta < -0.15\beta$) compounds is about -0.2β. For the diazirinyl anion, $\eta = -0.21\beta$ (HOMO α -0.46β; LUMO α -0.89β).

Design of Organic Structures in the Solid State: Hydrogen-Bonded Molecular "Tapes"[1]

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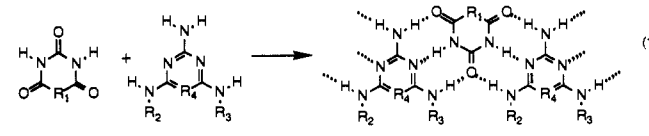
We have begun a program whose objective is to develop methods to predict the packing of organic molecules in crystalline and noncrystalline solids, starting from the atomic structures of these molecules.[2] The ability to relate molecular and crystalline structure for organic solids will clarify the interactions that underlie molecular recognition and self-assembly, simplify the preparation of optically or electronically active organic solids, and help to rationalize the macroscopic properties of organic materials in terms of microscopic, molecular structures.

One problem that has frustrated efforts to relate molecular and crystalline structures is the very large number of orientations the molecules can, in principle, adopt: calculating relative energies of all possible packing structures is currently impractical. To limit the scope of the problem, we wish to constrain the possible orientations of the molecules in the solid state. We are developing systems in which strong, directional hydrogen bonds provide the required constraint.

Using the network proposed for melamine/cyanuric acid as a model,[3,4] we are examining the structures of 1:1 cocrystals of derivatives of melamine (M) and barbituric acid (B), functionalized in patterns that break up the sheet structure but permit the formation of hydrogen bonds that yield "tapes" (eq 1). Tapes are likely to pack with their axes parallel. This enforced parallelism will, we believe, significantly simplify the computational analysis of these solid-state structures.



Here we summarize evidence that this strategy is successful in generating a family of closely related solid-state structures and that these structures can be classified according to a hierarchy of elementary structural features (Figure 1). The two components, M and B, form tapes with an alternating sequence, ···M·B·M·B···; the tapes pack into sheets with their long axes parallel; the sheets stack and form three-dimensional solids. Table I summarizes crystallographic data for the structures we have examined; complete data will follow in a full paper. We believe that this system has sufficient simplicity to be the object of a systematic study of the influence of molecular structure on crystal structure.

(1) Supported by the National Science Foundation, Grant CHE-88-12709 to G.M.W. and Grant DMR-89-20490 to the Harvard University Materials Research Laboratory.

(2) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: New York, 1989. Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120. Hagler, A. T.; Dauber, P. *Acc. Chem. Res.* **1980**, *13*, 105.

(3) Seto, C.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *112*, 6409.

(4) We have not yet been able to obtain diffraction-quality single crystals from cocrystallizations of derivatives of melamine and cyanuric acid.

0002-7863/90/1512-9025$02.50/0