C-Azidodiazirines in the $S_{RN}1$ Reaction of Azide Ion with Arylchlorodiazirines. Further Insights into Reaction Mechanism

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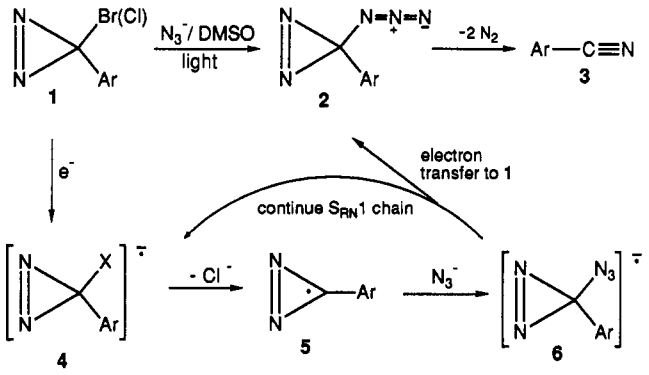
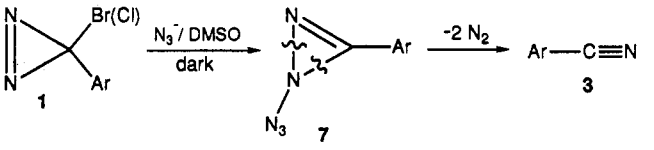
Mixtures of arylchlorodiazirines and sodium azide in DMSO form visible charge transfer complexes. Irradiation of these solutions with fluorescent room light leads to $S_{RN}1$ displacement of chloride and the transient formation of *C*-azidodiazirines. Relative reactivity studies (using competition experiments) show that nitro-substituted arylchlorodiazirines are substantially more reactive than other arylchlorodiazirines. This is attributed to facile electron transfer in the propagation cycle, involving the nitro-substituted aromatic ring. *C*-Azidodiazirines can be isolated in solution and spectroscopically characterized when the $S_{RN}1$ reaction is initiated by addition of catalytic amounts of the sodium salt of 2-nitropropane. These azidodiazirines readily decompose at room temperature by first order processes to give molecular nitrogen and benzonitriles. Solvent and substituent effects on decomposition rates are minimal. Computational studies on potential intermediate carbenes in the decomposition of azidodiazirines have been carried out at the HF/6-31G* level. Singlet α-azidocarbenes RCN_3, where R = NH_2, OH, F, vinyl, phenyl, and CH_3, are energy minima at this computational level. Isodesmic calculations show that the azido group is comparable to OH in its carbene stabilizing ability. Subsequent loss of N_2 from α-azidocarbenes, leading to nitriles, is a highly exothermic process (126 kcal when R = vinyl and 128 kcal when R = phenyl).

In 1990 we presented evidence that certain arylhalodiazirines **1** could react with azide ion via the $S_{RN}1$ mechanism.[1] The ultimate products of these reactions were the benzonitriles **3**, which were suggested to be derived from decomposition of the initial $S_{RN}1$ product, the *C*-azidodiazirine **2**. Evidence for the $S_{RN}1$ mechanism included initiation of the reaction by light, sonication, or traces of single-electron reductants such as thiophenoxide ion or nitronate ion. The reaction can also be quenched by galvinoxyl, a stable free radical. Finally, labeling studies using ^{15}N-labeled sodium azide showed that the nitrogen in the benzonitrile product was derived from the azide ion.



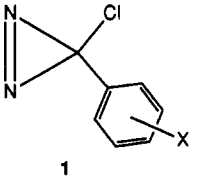
The $S_{RN}1$ Mechanism

This $S_{RN}1$ reaction competes with the S_N2' mechanism, in which azide ion reacts at nitrogen of the diazirine to form an *N*-azidodiazirine **7**.[2] Decomposition of **7** also leads to benzonitriles. When this S_N2' mechanism operates, labeling studies show that the nitrogen atom of the benzonitrile is derived from one of the diazirine ring nitrogens.[2] The features that favor each of these competing mechanisms have been discussed.[1,3]



The S_N2' Mechanism

The $S_{RN}1$ substitution mechanism of halodiazirines continues to hold our interest. What is the initiation step in this light-promoted chain reaction? Can the proposed *C*-azidodiazirines **2** be detected? What is the mechanism of decomposition of this intermediate? Presented here are our further mechanistic studies on the arylchlorodiazirines **1a–m**, which provide insights into the $S_{RN}1$ mechanism, electron transfer processes in general, and the chemistry of *C*-azidodiazirines **2**.



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1a X = H
1b X = 3-NO_2
1c X = 4-NO_2
1d X = 3-NO_2-4-CH_3
1e X = 3,5-di-NO_2
1f X = 3,5-di-F
1g X = 4-CF_3
1h X = 3-N (3-pyridyl)
1i X = 4-N (4-pyridyl)
1j X = 4-CH_3
1k X = 4-OCH_3
1l X = 4-Cl
1m X = 3-CF_3

Results and Discussion

Comments on the Initiation Step. Sodium azide in dimethyl sulfoxide gives a colorless solution which is transparent down to 285 nm. Arylchlorodiazirines in DMSO also give virtually colorless solutions. However when arylchlorodiazirines are added to a solution of sodium azide in DMSO, a light yellow color develops. Figure 1 shows a spectrum of (3-nitrophenyl)chlorodiazirine (**1b**) in DMSO and also of **1b** in 0.4 M NaN_3 in DMSO. The tail into the visible region of the spectrum is attributed to formation of a charge-transfer complex. There is no product formation under these conditions as can be shown

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(1) Creary, X.; Sky, A. F.; Phillips, G. *J. Org. Chem.* **1990**, 55, 2005.
(2) Creary, X.; Sky, A. F. *J. Am. Chem. Soc.* **1990**, 112, 368.
(3) Creary, X. *Acc. Chem. Res.* **1992**, 25, 32.

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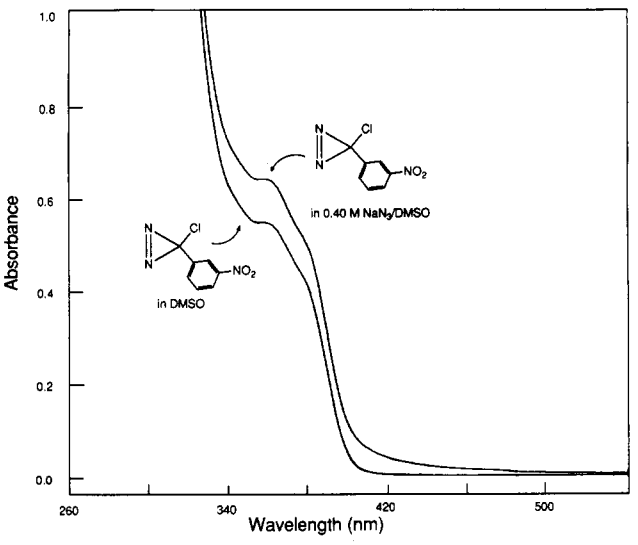
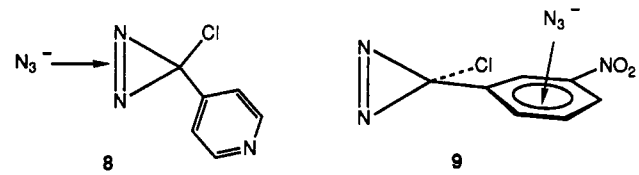


Figure 1. UV spectra of **1b** in DMSO.

by NMR spectroscopy in DMSO-d_6. Similar behavior is observed for other arylchlorodiazirines, which all form light yellow solutions when added to sodium azide in DMSO. For example, 4-pyridylchlorodiazirine (**1i**) also develops this characteristic faint yellow color in the presence of azide ion. 4-Cyanopyridine and pyridine both remain colorless in the presence of azide ion. We speculate that azide ion is associated with the N=N linkage in the case of 4-pyridylchlorodiazirine as in **8**. In the case of nitroaromatic systems, the azide ion could also be associated with the nitroaromatic ring as in **9**. In support of this suggestion, a control experiment shows that nitrobenzene (in contrast to pyridine) forms a visible charge-transfer complex with sodium azide in DMSO. We suggest that photoinduced



8 **9**

electron transfer in such charge transfer complexes is the process that initiates the $S_{RN}1$ reaction of azide ion with arylhalodiazirines when these mixtures are exposed to room light. Along these lines, Kornblum, Morrison, and Wade have also observed the formation of charge-transfer complexes between azide ion and *p*-nitrocumyl chloride in HMPA.[4] Photoinitiated $S_{RN}1$ reactions of these *p*-nitrocumyl derivatives were proposed to involve these charge-transfer complexes. Photoinitiated $S_{RN}1$ reaction of acetone enolate ion and potassium diethyl phosphite with iodobenzene have also been suggested to proceed via excitation of charge-transfer complexes.[5]

Relative Rate Studies. In our initial study of the $S_{RN}1$ reaction of azide ion with arylhalodiazirines,[1] we observed, based on the time required for half of the arylchlorodiazirine to react, that electron-withdrawing groups on the aromatic ring generally increased reactivity. Since this reaction proceeds via a radical chain mechanism, chain lengths, rates of initiation, and termination rates control

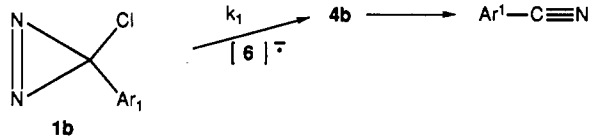
(4) Wade, P. A.; Morrison, H. A.; Kornblum, N. *J. Org. Chem.* **1987**, 52, 3102.
(5) Fox. M. A.; Younathan, J.; Fryxell, G. E. *J. Org. Chem.* **1983**, 48, 3109.

Table I. Relative Rates of Photoinitiated $S_{RN}1$ Reaction of Arylchlorodiazirines with Sodium Azide in DMSO-d_6

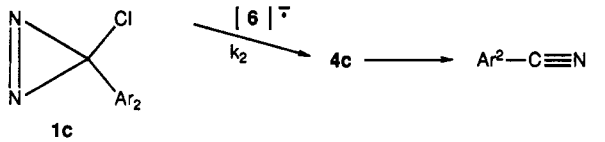
arylchlorodiazirine	rel rate[a]	rel rate[b]
1e (3,5-$(NO_2)_2$)	large	
1c (4-NO_2)	1.0	
1b (3-NO_2)	0.64	
1d (3-NO_2-4-CH_3)	0.05	
1i (4-pyridyl)	small (0.002)[c]	
1i (4-pyridyl)		1.0
1m (3-CF_3)		0.83
1f (3,5-F_2)		0.82
1g (4-CF_3)		0.75
1h (3-pyridyl)		0.63
1l (4-Cl)		0.53
1a (p-H)		0.30
1j (4-CH_3)		0.26
1l (4-OCH_3)		0.21

[a] Determined by competition with **1c**. [b] Determined by competition with **1i**. [c] Indirectly determined by competition with **1d**.

overall reactivity. In order to better understand the electron-transfer step in the propagation cycle, i.e., the relative reactivities of the arylchlorodiazirines, the competition method has been used to determine relative rates of reaction of a series of arylchlorodiazirines. Mixtures of two arylchlorodiazirines were reacted with azide ion and the reaction was monitored at various times prior to completion. Relative reactivities (Table I) were calculated from the amounts of each arylchlorodiazirine reacted. These relative reactivities represent relative rates of electron transfer in the propagation step.



1b

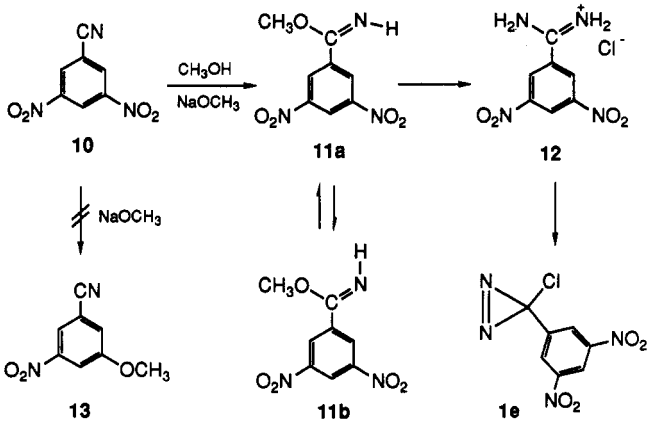


1c

The relative reactivities of arylchlorodiazirines with azide ion under photoinitiation fall into two general categories. The nitroaromatic systems are all considerably more reactive than the other arylchlorodiazirines under competition conditions. Among the mononitro-substituted systems, the 4-NO_2-substituted diazirine **1c** is the most reactive, being 1.6 times more reactive than the 3-NO_2 analog **1b**. Methyl substitution further decreases reactivity such that the 3-NO_2-4-CH_3 system **1d** is 20 times less reactive than **1c**. These nitro-substituted diazirines are all far more reactive than the other arylchlorodiazirines. Under competition conditions, essentially all of **1b** (3-NO_2) is consumed before substrates such as **1f** (3,5-di-F) and **1h** (3-pyridyl) begin to react. These large rate differences under competitive conditions contrast with our earlier determination of reactivity[1] when each diazirine individually reacts with azide ion. Our earlier study showed that individually 3-pyridyl- and 3,5-F_2-substituted diazirines **1h** and **1f** are quite reactive and are consumed at rates comparable to that of the 3-NO_2-substituted diazirine **1b**. However, under competitive conditions, **1b** is far more reactive. This lends credence to the suggestion that rates of initiation and termination steps control reactivities of the arylchlorodiazirines when they are

reacted with azide ion individually, while rates of electron transfer in the propagation cycle control relative reactivities when the diazirines react in competition.

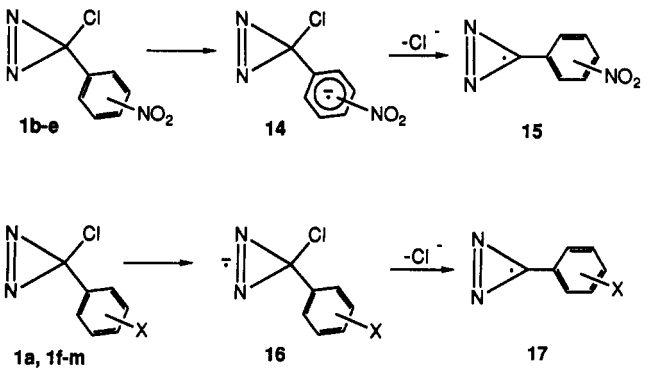
In order to determine the effect of further electron-withdrawing substituents on relative reactivity, we have prepared the 3,5-dinitro-substituted chlorodiazirine **1e** starting with the nitrile **10**. Reaction with sodium methoxide in methanol gave the imino ester **11**. This reaction is noteworthy in that it has been claimed that the substitution product **13** is produced.[6] While this reaction was considered to fall into the S_NAr category (addition–elimination mechanism), the nitro groups in **10** are not activated toward nucleophilic substitution. The isolation and complete characterization of the actual imino ester product **11** is consistent with our expectations that **13** would be difficult to form by S_NAr displacement of the nitro group from **10**. Of interest is the fact that two isomers of the imino ester **11** can be observed in DMSO-d_6, where their interconversions are slow. In $CDCl_3$, NMR spectra are complicated by interconversion of these isomers on the NMR time scale.



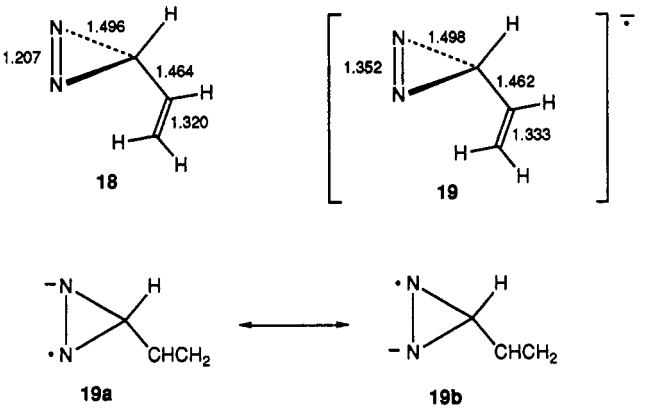
Conversion of the imino ester **11** to the chlorodiazirine **1e** using Graham's method[7] was straightforward. In competitive photoinitiated reactions with azide ion, this substrate **1e** is the most reactive of the arylchlorodiazirines studied. It is substantially more reactive than the 4-NO_2 system **1c**, being completely consumed before **1c** even begins to react.

The high reactivity of the nitro-substituted diazirines relative to the other diazirines in the $S_{RN}1$ reaction implies that the electron-transfer step in the propagation cycle is intrinsically different in the nitro-substituted diazirines. It is therefore suggested that the electron transfer involves the nitro-substituted ring in the case of the nitroaromatics (as in **14**), while the electron enters the N=N π^* system in the case of the other arylchlorodiazirines (as in **16**).[8] Electron transfer into the nitroaromatic system is intrinsically more facile than into the N=N π^* system of the diazirine. Both **14** and **16** can lead to diazirinyl radicals upon loss of chloride.

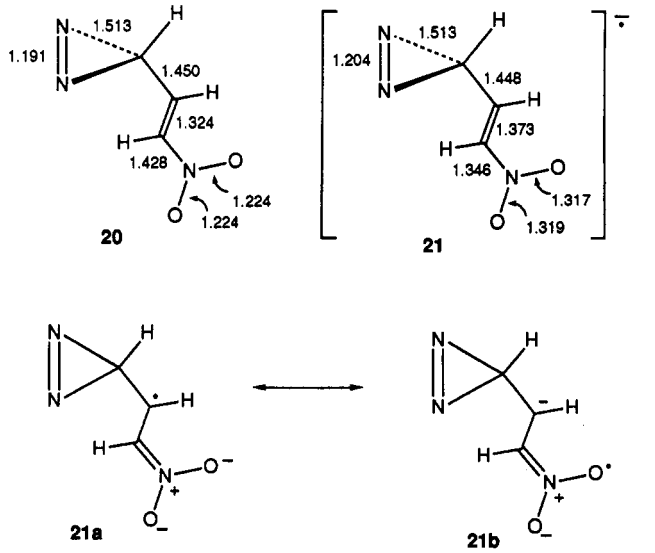
In support of this suggestion, molecular orbital calculations[9] have been carried out on the diazirines **18** and **20**, as well as the corresponding radical anions **19** and **21** at the HF/4-31G level. The radical anion **19** shows a



substantial lengthening of the N–N bond relative to that in the neutral diazirine **18**. Spin density and charge are largely localized on the nitrogen atoms. In valence bond terms, forms **19a** and **19b** are significant contributors to the structure of this radical anion. In contrast to this, the



nitrovinyl radical anion **21** shows no significant lengthening of the N–N bond relative to that in **20**. The N–O bonds of the nitro group increase in length, while the C–N bond to the nitro group decreases in length. Spin density and charge are now largely associated with the nitrovinyl group. In valence bond terms, forms such as **21a** and **21b** are



(6) Fendler, E. J.; Fendler, J. H.; Arthur, N. L.; Griffin, C. E. *J. Org. Chem.* **1972**, 37, 812.

(7) (a) Graham, W. H. *J. Am. Chem. Soc.* **1965**, 87, 4396. See also (b) Padwa, A.; Pulwer, M. T.; Blacklock, T. J. *Organic Syntheses*, Wiley: New York, 1990; Collect. Vol. VII, p 203.

(8) Radical anions of type **14** and **16** may or may not have a finite lifetime, i.e., loss of halide may be concerted with electron transfer.

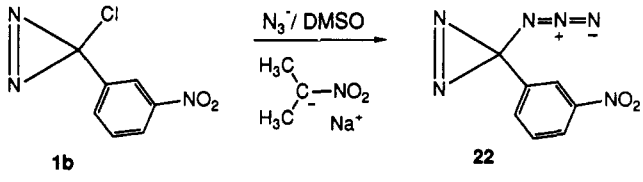
(9) *Ab initio* molecular orbital calculations were performed using the Gaussian 90 series of programs. See, Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. *Gaussian 90*, Revision I, Gaussian, Inc., Pittsburgh PA, 1990.

major contributors to the structure of this radical anion. An isodesmic reaction indicates that the nitro-substituted radical anion **21** is preferred over the radical anion **19**, i.e., the diazirine **20** is a superior electron acceptor relative to **18**. These computational studies are all consistent with the observed higher $S_{RN}1$ reactivity of the nitro-substituted arylchlorodiazirines.

$$19 + 20 \underset{\text{HF/4-31G}}{\overset{\Delta E = -36.9 \text{ kcal}}{\rightleftharpoons}} 18 + 21$$

Further support for these suggestions comes from a limited study of reduction potentials by Liu.[10] Phenylchlorodiazirine (**1a**) is reduced under electrochemical conditions more readily than (*p*-methoxyphenyl)chlorodiazirine, which contains the donor methoxy group. Relative potentials are −1.87 and −2.05 V, respectively. On the other hand, 4-(nitrophenyl)chlorodiazirine (**1c**) shows anomalous behavior, giving two waves at −1.3 and −1.4 V. The much more facile reduction of **1c** relative to **1a** under electrochemical conditions is therefore consistent with our relative reactivity data in the $S_{RN}1$ reaction. The further increase in reactivity of (3,5-dinitrophenyl)chlorodiazirine (**1e**) relative to the mononitro systems, reflects the greater ease of reduction of **1e** due to the electronegative effect of the additional nitro group.[11]

Detection of *C*-Azidodiazirines. The photoinitiated reaction of (3-nitrophenyl)chlorodiazirine (**1b**) with sodium azide in DMSO is easily monitored by ^{1}H NMR. This substrate **1b** is one of the more reactive diazirines that we have studied. During the course of a particular photoinitiated run that was proceeding at a relatively fast rate, analysis by NMR showed traces of an unidentified product (about 5%) along with the starting diazirine **1b** and the product 3-nitrobenzonitrile. This trace product (which is partially obscured by the starting chlorodiazirine **1b**) was observed only when NMR analysis was carried out quickly and it rapidly disappears. On the basis of chemical shifts, which were similar to those of the chlorodiazirine **1b**, we speculated that this trace product was due to a small buildup of a *C*-azidodiazirine, the putative initial $S_{RN}1$ product. We have therefore used the nitronate ion-initiated $S_{RN}1$ reaction[12] in an attempt to rapidly generate this intermediate under conditions where it might be observable in larger amounts and unobscured by starting chlorodiazirine **1b**. Thus a catalytic amount of the sodium salt of 2-nitropropane was added to a solution of **1b** in



1b **22**

DMSO-d_6 and the mixture was quenched with cold water after 12 s. Cooling and rapid extraction with cold $CDCl_3$ gave a yellow solution which was analyzed by ^{1}H and ^{13}C NMR at −20 °C (Figures 2 and 3). These spectra, which show no trace of the starting chlorodiazirine **1b**, are consistent with the *C*-azidodiazirine **22**. Also present is about 20% of the final decomposition product, the 3-nitrobenzonitrile. Particularly revealing is the signal at δ 42.33 in the ^{13}C NMR, which is characteristic of the diazirine ring carbon of **22**. Even at −20 °C the *C*-azidodiazirine **22** slowly converts to 3-nitrobenzonitrile, with loss of molecular nitrogen. Figure 4 shows time-dependent infrared spectra of **22** at room temperature in $HCCl_3$ when **22** is produced in a nitronate-initiated $S_{RN}1$ reaction and extracted into $HCCl_3$. The presence of the azido functional group is indicated by the absorbance at 2116 cm^{-1}. This peak readily disappears at room temperature and the less-intense cyano functional group of 3-nitrobenzonitrile appears simultaneously at 2224 cm^{-1}.

In the hope that further electron-withdrawing substituents would increase the thermal stability of *C*-azidodiazirines, the dinitro-substituted chlorodiazirine **1e** has been reacted with azide ion in a nitronate-catalyzed reaction. Unfortunately a rapid workup with $CDCl_3$ extraction gave

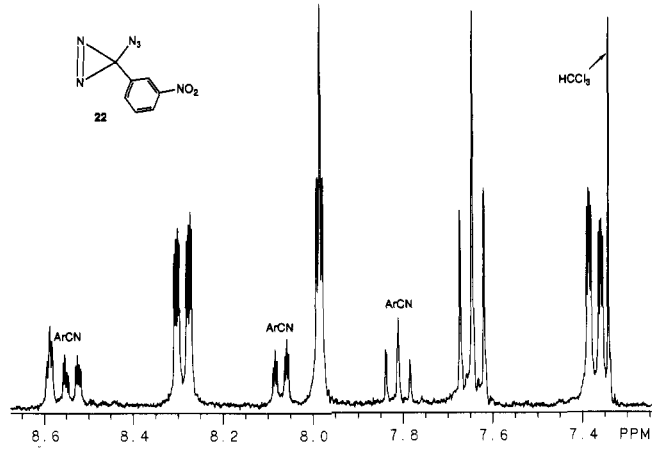


Figure 2. ^{1}H NMR of **22** in $CDCl_3$ at −20 °C.

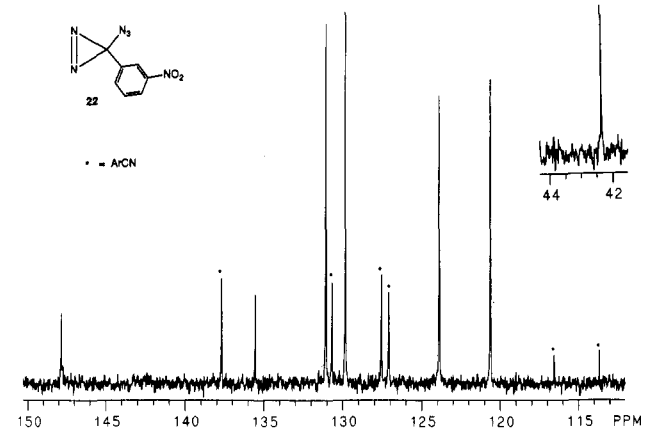


Figure 3. ^{13}C NMR of **22** in $CDCl_3$ at −20 °C.

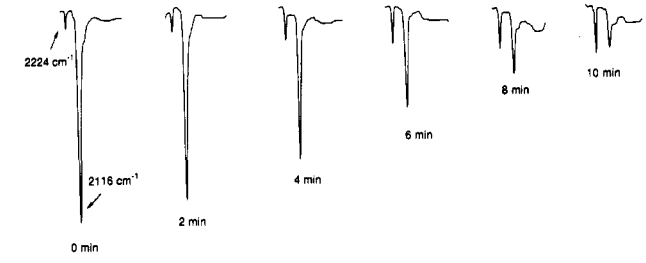


Figure 4. Time-dependent IR spectra of **22** in $CHCl_3$ at room temperature.

(10) (a) Liu, M. T. H.; Elson, C. M. *J. Chem. Soc. Chem. Commun.* **1982**, 415. (b) Elson, C. M.; Liu, M. T. H. In *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC Press, Inc.: Boca Raton, FL, 1987; Vol. II, p 111.

(11) Dinitrobenzenes are more easily reduced electrochemically than nitrobenzene. See Todres, Z. V.; Pozdeeva, A. A.; Chernova, V. A.; Zhdanov, S. I. *Tetrahedron Lett.* **1972**, 3835.

(12) For an early example of the use of the lithium salt of 2-nitropropane to initiate the $S_{RN}1$ reaction, see Kornblum, N.; Swiger, R. T.; Earl, G. W.; Pinnick, H. W.; Stuchal, F. W. *J. Am. Chem. Soc.* **1970**, 92, 5513.

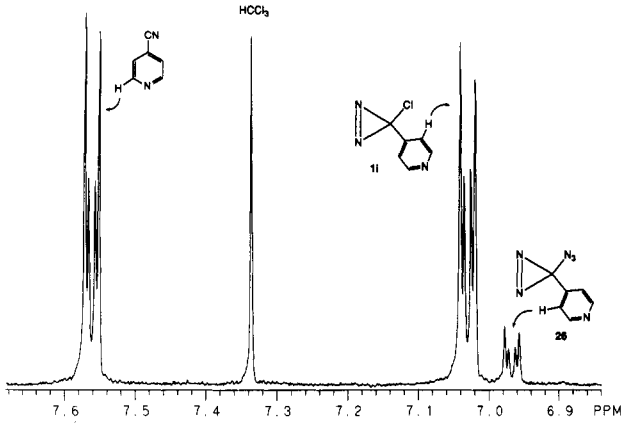
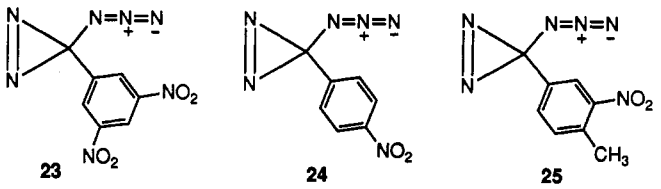


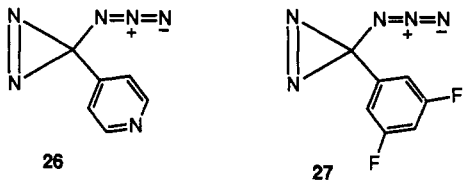
Figure 5. Initial ^1H NMR ($CDCl_3$) after photoinitiated reaction of **1i** with NaN_3 in DMDO-d_6.

a solution containing only 8% of the corresponding *C*-azidodiazirine **23**, with the decomposition product **10** being the major product. Apparently the additional nitro group in **23** does not increase its thermal stability. Kinetic data (presented subsequently) confirm this. The nitro-substituted *C*-azidodiazirines **24** and **25** have also been generated by the nitronate ion-catalyzed reaction of the corresponding chlorodiazirines with azide ion. However, both of these azidodiazirines also appear to be slightly less stable than **22** and NMR spectra show substantial decomposition to give the corresponding benzonitriles.

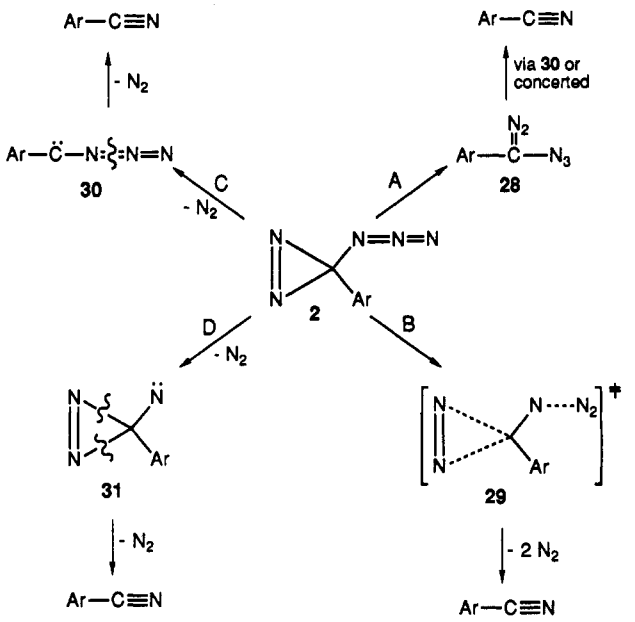


With the limited success of the nitronate ion-catalyzed $S_{RN}1$ reaction using nitro-substituted chlorodiazirines **1b–e**, attempts have been made to generate other *C*-azidodiazirines by this method. Unfortunately, substrates such as 4-pyridylchlorodiazirine and (3,5-difluorophenyl)chlorodiazirine, which react quite easily under photoinitiation, give mainly unreacted starting material in the nitronate ion-catalyzed reactions. Only traces of a transient intermediate (presumably the *C*-azidodiazirines) can be observed. The relative inefficiency of the nitronate ion-catalyzed reactions of these substrates suggests that chain lengths are shorter than for reactions involving nitro-substituted chlorodiazirines. However, the photoinitiated reaction of 4-pyridylchlorodiazirine (**1i**) (which is individually quite reactive in the $S_{RN}1$ reaction) with azide ion can be used to generate and observe the corresponding *C*-azidodiazirine **26** in small amounts. Figure 5 shows a portion of the ^1H NMR spectrum of a $CDCl_3$ extract when a solution of azide ion and **1i** in DMSO-d_6 is exposed to fluorescent room light for 6 min. Signals at δ 8.64 and 6.97 (8% of the total) readily convert to 4-cyanopyridine and are attributed to the *C*-azidodiazirine **26**. A similar photochemically initiated reaction can also be used to generate the *C*-azidodiazirine **27** in small but detectable amounts.

Decomposition of *C*-Azidodiazirines. The mechanism by which *C*-azidodiazirines decompose to give nitriles is of interest. Four reasonable possibilities (A–D) are summarized below. Mechanism A involves rate-limiting thermal isomerization of the diazirine to a diazo compound



28, followed by rapid loss of nitrogen from **28**. This mechanism has precedent in the decomposition of certain alkyl-substituted diazirines, in which diazo compounds can be detected.[13] Mechanism B involves a concerted loss of two molecules of nitrogen from **2** (via a transition state resembling **29**), with no involvement of discrete intermediates. This mechanism has previously been proposed on the basis of a theoretical study in 1985 which suggested that carbene or nitrene intermediates were not energy minima in decomposition of azidomethyldiazirine.[14] Mechanism C involves the rate-limiting loss of one nitrogen to generate the carbene **30**. Finally, mechanism D involves



rate-limiting formation of the nitrene **31**, followed by loss of a second nitrogen from this discrete intermediate **31**.

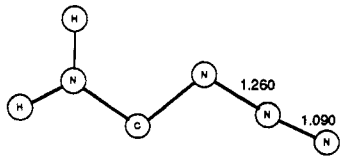
In an attempt to shed further light on the decomposition mechanism, the azidodiazirine **22** was decomposed in methanol solution. When a chloroform solution of **22** was added to methanol, 3-nitrobenzonitrile remained the exclusive product. There was no product derived from methanol capture of an intermediate. If mechanism C operates, then the carbene **30** must be an extremely short-lived intermediate which ejects another nitrogen much faster than solvent capture.

Kinetic studies have also been carried out on **22** and on other *C*-azidodiazirines. Rates of decomposition of *C*-azidodiazirines can be easily monitored spectrophotometrically, where excellent first-order kinetic behavior is observed. Table II summarizes rate data. The effect of substituents on rate is quite small. The additional nitro group in **23** slightly increases the decomposition rate

(13) (a) Liu, M. T. H.; Jennings, B. M. *J. Am. Chem. Soc.* **1976**, 98, 6416. (b) Liu, M. T. H.; Ramakrishnam, K. *J. Org. Chem.* **1977**, 42, 3450. (c) Liu, M. T. H.; Tencer, M.; Stevens, I. D. R. *J. Chem. Soc. Perkin Trans. 2* **1986**, 211. (d) Doyle M. P.; High, K. G.; Oon, S.-M.; Osborn, A. K. *Tetrahedron Lett.* **1989**, 30, 3039.

(14) Moss, R. A.; Terpinski, J.; Cox, D. P.; Denney, D. Z.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1985**, 107, 2743.

Chart I



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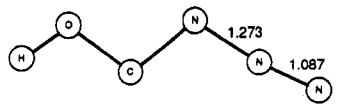

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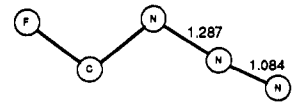

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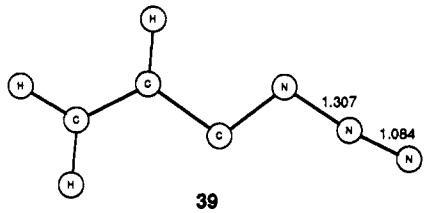

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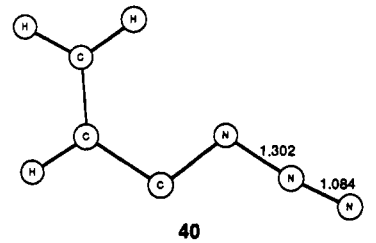

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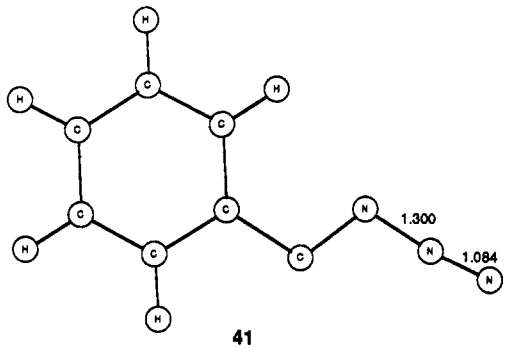

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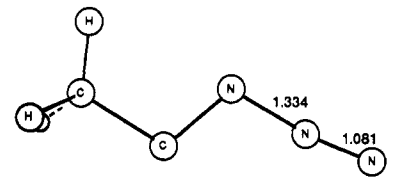

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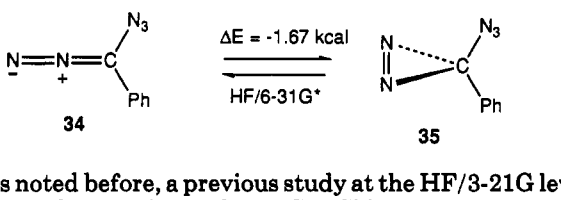
Table II. Rates of Decomposition of Arylazidodiazirines in CH_3OH at 25.0 °C

arylazidodiazirine	k, s^{-1}
22 (3-NO_2)	3.42×10^{-3}
	1.77×10^{-3} (19.6 °C)
	9.77×10^{-4} (15.0 °C)
	4.26×10^{-3} ($HCCl_3$)
	3.21×10^{-3} (hexane)
23 (3,5-(NO_2)$_2$)	8.28×10^{-3}
24 (4-NO_2)	8.52×10^{-3}
25 (3-NO_2-4-CH_3)	3.48×10^{-3}
26 (4-pyridyl)	8.02×10^{-3}
27 (3,5-F_2)	3.05×10^{-3}

relative to **22**, while the electron-donor methyl group in **25** has essentially no effect on rate. The 4-pyridyl and 3,5-difluorophenyl systems **26** and **27** also react at rates similar to that of the nitro-substituted *C*-azidodiazirines. The effect of solvent polarity on decomposition rate of **22** is also negligible, with very little rate differences being observed in hexane, chloroform, and methanol. Activation parameters for **22** in methanol are $\Delta H = 20.6$ kcal and $\Delta S = -0.8$ eu. While these solvent and substituent effects suggest that there is no large charge separation in the transition state for decomposition of *C*-azidodiazirines, they do not provide further insight into the mechanism of reaction.

Theoretical Studies. Molecular orbital calculations have been carried out on the potential intermediates that could be involved in decomposition of *C*-azidodiazirines by mechanisms A–D. These computational studies were initially focused on the relative energetics of *C*-azidodiazirines versus the isomeric diazo compounds. Previous computations on unsubstituted diazirine, CH_2N_2, show that the cyclic structure is 9.9 kcal less stable than the open analog, diazomethane, at the HF/6-31G*//3-21G level.[15] Since the experimental studies carried out in the present paper involved aryl-substituted *C*-azidodiazirines, we have carried out computational studies on the vinyl analogs **32** and **33** as well as the the phenyl-substituted systems **34** and **35**. At the HF/6-31G* level (full geometry optimization), the vinylazidodiazirine **33** is 2.8 kcal more stable than the isomeric diazo compound **32**. Single-point calculations on the phenyl-substituted systems **34** and **35** (HF/6-31G*//4-31G) gave a 1.67 kcal energy difference, with the diazirine again being lower in energy.

32 33

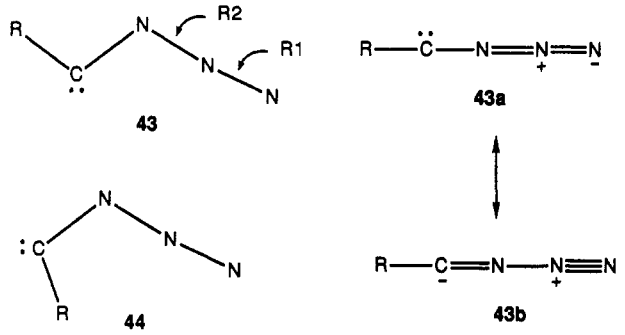


34 35

As noted before, a previous study at the HF/3-21G level suggested that the carbene CH_3CN_3 is not an energy minimum on a potential energy surface.[12] However, the azido functional group has recently been found to be quite effective as a cation-stabilizing group, despite its electronegative character.[16,17] With this in mind, higher level

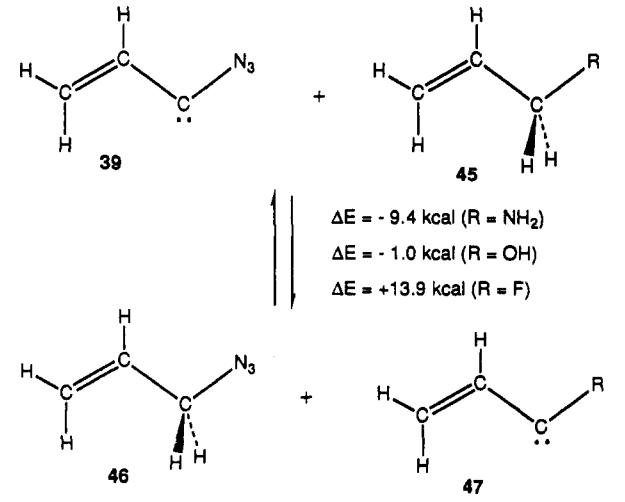
(15) Thomson, C.; Glidewell, C. *J. Comput. Chem.* **1983**, *4*, 1.
(16) Hoz, S.; Wolk, J. L. *Tetrahedron Lett.* **1990**, *31*, 4085.
(17) Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 1867.

computational studies have been carried out on a variety of α-azido carbenes at the HF/6-31G* level. At this level, the carbenes **36–42** are all energy minima (Chart I). As the donor ability of the group R decreases, the nitrogen–nitrogen bond length R2 increases and R1 decreases (approaching that of molecular N_2). In the case of R = CH_2CH, two isomeric carbenes (**39** and **40**) exist as energy minima, with **39** being lower in energy by 4.8 kcal. When the group R is hydrogen, the carbene HCN_3 is not a minimum and dissociates without barrier to N_2 and HCN. These bond changes reflect the increased demand for stabilization of the carbene **43** by the α-azido group as the ability of the group R to interact decreases. In valence bond terms, the importance of form **43b** increases as the ability of the group R to interact with the carbene vacant orbital decreases. As greater stabilization demands are placed on the α-azido group, the carbene tends to dissociate to give nitrogen and the corresponding nitrile.



Due to the nonlinear nature of the CNN angle in α-azidocarbenes, a second set of isomeric carbenes are possible. These isomeric "cisoid" carbenes **44** are higher energy in the cases of R = NH_2, OH, and F. When R = CH_2CH, Ph, and CH_3, the carbenes **44** are not energy minima, but these structures dissociate to give molecular nitrogen and the corresponding nitrile.

How does the carbene-stabilizing ability (thermodynamic) of the azido group compare with that of other groups? The answer to this question was approached computationally using an isodesmic reaction of carbene **39** with allyl fluoride, allyl alcohol, and allyl amine. At the HF/6-31G* level, the α-azido carbene **39** is comparable in stability to the analogous α-hydroxy carbene **47** (R = OH). On the basis of the pertinent isodesmic reactions,



the azido group is more effective than fluoro, but less effective than amino, in its carbene-stabilizing abilities. These results compare favorably with the recent computational study that suggested that the α-azido group is comparable to hydroxy in its carbocation-stabilizing ability.[16]

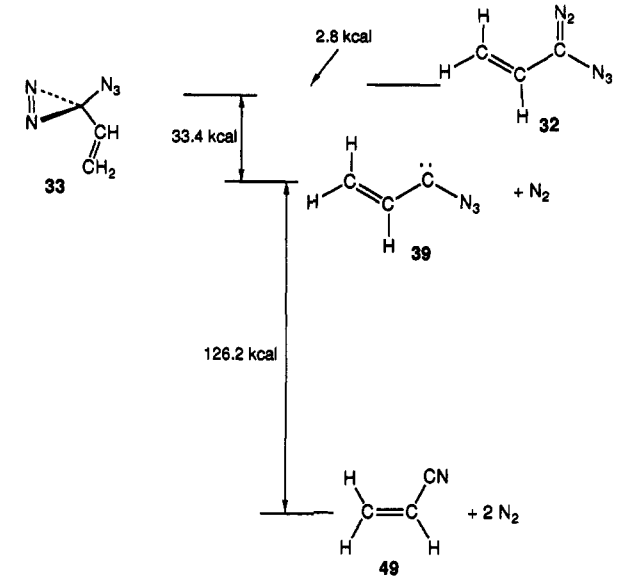


Figure 6. Calculated (HF/6-31G*) energy levels.

The potential nitrene intermediate **48** was next addressed in a computational study. At the HF/6-31G* level the nitrene **48** is not an energy minimum, but dissociates without barrier to acrylonitrile and molecular nitrogen. A single-point calculation on **48** using bond angles and lengths derived from **33** places this nitrene 43.8 kcal above the isomeric carbene **39**.

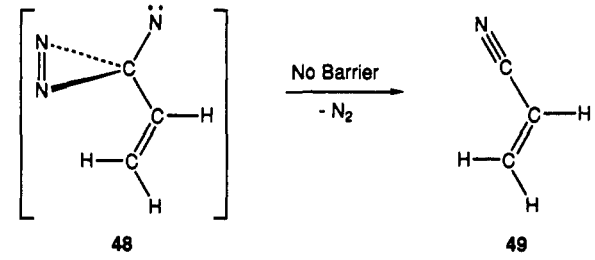


Figure 6 shows the relative energies (HF/6-31G*) of all of the potential intermediates in the decomposition of vinylazidodiazirine **33**, as well as the ultimate decomposition product, acrylonitrile (**49**). Of interest are the energy levels of the carbene **39** and molecular nitrogen, which lie 33.4 kcal *below* the *C*-azidodiazirine **33**. Formation of the carbene reactive intermediate by loss of nitrogen from **33** is not an endothermic process. This is undoubtedly a reflection of the "stability" of molecular nitrogen. What insights do these computational studies convey concerning the decomposition mechanism of *C*-azidodiazirines? Mechanism D (involving the nitrene) appears improbable since this is a very high energy structure which does not appear to lie at an energy minimum. However, mechanism A (involving the isomeric diazo compound) is indeed plausible, given the experimentally determined activation energy of 20 kcal for decomposition of the *C*-azidodiazirine **22**. Along these lines, Liu and co-workers[13c] have suggested that, depending on substituents, decomposition of diazirines may or may not proceed via isomerization to diazo compounds.

Mechanism C (involving the carbene) remains a possibility since certain α-azidocarbenes appear to be discrete intermediates at the HF/6-31G* computational level. If decomposition of *C*-azidodiazirines **22–27** is energetically similar to that shown in Figure 6, then, according to the Hammond postulate, the transition state for carbene formation will occur relatively early. Substituent effects will therefore not be very large. Furthermore, if one assumes that the carbene derived from *C*-azidodiazirines such as **22** will be about 30 kcal lower in energy than the starting diazirine, then there is a large amount of energy that must be dissipated by a potential carbene and the evolved nitrogen. Before deactivation by collision with solvent, this energy will be stored in the vibrational modes of the carbene and nitrogen. Further loss of nitrogen from a vibrationally excited carbene may well occur before collisional deactivation with solvent. Therefore the fact that methanol does not trap a carbene intermediate when **22** is decomposed does not rule out a carbene as a very transient intermediate. However, these calculations may not be the final word, since it is uncertain whether higher level computational studies will be necessary to give results that conform to reality. In any case, any carbene intermediate involved in the decomposition of **22** is too short-lived to be trapped by methanol.

Conclusions

Sodium azide forms a charge-transfer complex with arylchlorodiazirines in DMSO. Photopromoted electron transfer in this charge-transfer complex initiates the $S_{RN}1$ displacement of chloride. Nitro-substituted arylchlorodiazirines have greater reactivity under competitive conditions. This results from preferential electron transfer into the nitroaromatic system in the propagation cycle of the $S_{RN}1$ process. In certain instances, the initially formed *C*-azidodiazirines can be detected and characterized spectroscopically in the nitronate ion-catalyzed $S_{RN}1$ reaction of azide ion with arylchlorodiazirines. Decomposition of these azidodiazirines show little substituent and solvent effects. *Ab initio* molecular orbital calculations suggest that certain α-azidocarbenes are energy minima, stabilized by a conjugative interaction with the azido group. This stabilization (thermodynamic) is comparable to hydroxyl group stabilization of carbenes. Subsequent loss of N_2 from α-azidocarbenes is a highly exothermic process.

Experimental Section

General. NMR spectra were recorded on a General Electric GN 300 spectrometer. Mass spectra were recorded on a Finnigan MAT 8430 high-resolution spectrometer. Elemental analyses were carried out by MHW Laboratories, Phoenix, AZ. Chromatographic purifications were carried out using EM Science 230–400 mesh silica gel 60. All of the arylchlorodiazirines except **1d** and **1e** were available from previous studies.[1, 2]

Relative $S_{RN}1$ Reactivities of Arylchlorodiazirines with Sodium Azide by the Competition Method. General Procedure. Approximately equimolar amounts of a mixture of two diazirines were placed in a 5-mL flask and a solution of sodium azide in DMSO-d_6 (approximately 0.45 M) was added to the stirred mixture. The resultant solution was placed in an NMR tube and the tube was exposed to fluorescent room light. Amounts of benzonitrile product and unreacted diazirine were determined by periodic monitoring by ^{1}H NMR. Relative rates were calculated by standard methods.[18] The following procedures are representative.

A solution of 60 mg of sodium azide in 2.0 mL of DMSO-d_6 was added to a mixture of 34.9 mg of (3-nitrophenyl)chlorodiazirine (**1b**) and 32.0 mg of (4-nitrophenyl)chlorodiazirine (**1c**). A sample was placed in an NMR tube and the tube was exposed to room light. After 5 h, 77% of **1b** remained and 66% of **1c** remained. After 7.5 h, 24% of **1b** remained and 11% if **1c** remained. These values correspond to a reactivity ratio of 0.64:1.0.

A solution of 30 mg of sodium azide in 1.0 mL of DMSO-d_6 was added to a mixture of 12.3 mg of (*p*-methylphenyl)-chlorodiazirine (**1j**) and 12.3 mg of 4-pyridylchlorodiazirine (**1i**). A sample was placed in an NMR tube and the tube was exposed to room light. After 30 min, 73% of **1j** remained, while 29% of **1f** remained. This corresponds to a 0.26:1.0 reactivity ratio.

A solution of 46 mg of sodium azide in 1.5 mL of DMSO-d_6 was added to a mixture of 22.5 mg of (3-nitrophenyl)chlorodiazirine (**1b**) and 19.2 mg of 4-pyridylchlorodiazirine (**1h**). A sample was placed in an NMR tube and the tube was exposed to room light. After 25 min, about 70% of **1b** had reacted and none of **1h** had reacted. After 45 min, 100% of **1b** had reacted and only a trace (about 2%) of **1h** had reacted. This corresponds to a "large" **1b** to **1h** reactivity ratio.

Preparation of Imino Ester 11. A suspension of 2.000 g of 3,5-dinitrobenzonitrile (**10**) in 24 mL of methanol was stirred as 3.0 mL of 1.0 M $NaOCH_3$ in methanol was added. The mixture turned red and after a few min, the solid went into solution. After about 20 min, solid began to precipitate and stirring was continued for 18 h at room temperature. Water (70 mL) was added and the precipitate was collected on a Büchner funnel and air-dried to give 2.058 g (88%) of **11**. An analytical sample, mp 106–108 °C, was further purified by sublimation at 0.05 mm. Imino ester **11** shows fluctional behavior in $CDCl_3$ and spectra are very dependent on sample purity and factors such as extraneous acid present in the $CDCl_3$; ^{1}H NMR of **11a** and **11b** (DMSO-d_6) δ 9.96 (br s, 0.7 H), 9.00 (d, J = 2 Hz, 1.5 H), 8.92 (br, 1.5 H), 8.86 (br s, 0.3 H), 3.854 and 3.846 (two singlets, 3 H); ^{13}C NMR of **11a** and **11b** (DMSO-d_6) δ 160.76, 157.66, 148.29, 148.16, 136.51, 134.26, 127.14, 120.34, 120.29, 53.61, 53.20. Anal. Calcd for $C_8H_7N_3O_5$: C, 42.66; H, 3.13; N, 18.66. Found: C, 42.86; H, 3.62; N, 18.71.

Preparation of (3,5-Dinitrophenyl)chlorodiazirine (1e). A. 3,5-Dinitrobenzamidine Hydrochloride Preparation. A mixture of 1.159 g of the imino ester **11** in 11 mL of methanol was warmed to 55–60 °C and 290 mg of NH_4Cl was added. The mixture was stirred for 12 h at this temperature. The solution was cooled and the solvent was removed using a rotary evaporator. The residual solid was slurried with acetone and collected on a Büchner funnel. The solid was then washed with additional acetone and anhydrous ether and dried under aspirator vacuum to give 1.057 g (83%) of 3,5-dinitrobenzamidine hydrochloride (**12**); ^{1}H NMR of **12** (DMSO-d_6) δ 10.15 (br, 2 H), 9.78 (br, 2 H), 9.10 (d, J = 2.0 Hz, 2 H), 9.07 (t, J = 2.0 Hz, 1 H); ^{13}C NMR of **12** (DMSO-d_6) δ 162.59, 147.75, 130.65, 129.41, 123.00.

B. Sodium Hypochlorite Oxidation. Following the procedure of Graham,[7] a solution of 1.06 g of **12** in 20 mL of DMSO was stirred and 3.0 g of NaCl was added followed by 20 mL of ether and 20 mL of hexanes. The mixture was placed in an ice bath and, before the mixture could freeze, a solution of 5.4 g of NaCl in 45 mL of 5.25% sodium hypochlorite solution (commercial bleach) was added over a 10-min period. After stirring for 1.5 h at 0 °C, the mixture was warmed to room temperature for 20 min. The organic phase was separated and the aqueous phase was extracted with an additional portion of ether. The combined organic extracts were washed with water and saturated NaCl solution and dried over $MgSO_4$. The solvent was removed using a rotary evaporator, and the residue was chromatographed on a column prepared from 15 g of silica gel and packed with 2% ether in hexanes. The diazirine **1e** (72 mg, 7% yield) eluted with 3% ether in hexanes: ^{1}H NMR of **1e** ($CDCl_3$) δ 9.091 (t, J = 2 Hz, 1 H), 8.333 (d, J = 2 Hz, 2 H); ^{13}C NMR of **1e** ($CDCl_3$) δ

(18) For the chlorodiazirines **1b** and **1c**, at any given time, the relative reactivities are given by k_1/k_2 = ln[1/(fraction of **1b** remaining)]/ln[1/(fraction of **1c** remaining)].

148.67, 140.06, 126.10, 119.41, 44.90; HRMS (CI, isobutane) calcd for $C_7H_4ClN_4O_4$ $(M + H)^+$ 242.9921, found 242.9933.

Preparation of (3-Nitro-4-methylphenyl)chlorodiazirine (1d). A. 3-Nitro-4-methylbenzamidine Hydrochloride Preparation. A solution of 1.038 g of 3-nitro-4-methylbenzonitrile in 10 mL of methanol was stirred as 1.0 mL of 1.0 M sodium methoxide in methanol was added. The mixture was kept at room temperature for 3 days. ^1H NMR of the methanol solution showed starting nitrile and the corresponding imino ester in a 1:4.6 ratio. Solid NH_4Cl (0.367 g) was then added and the mixture was stirred at room temperature for 3 days. The methanol was then removed using a rotary evaporator and the residue was slurried with acetone and collected on a Büchner funnel. The solid was washed with more acetone and ether and dried under aspirator vacuum to give 1.127 g (82%) of 3-nitro-4-methylbenzamidine hydrochloride: ^1H NMR (DMSO-d_6) δ 9.41 (br, 4 H), 8.51 (d, J = 2 Hz, 1 H), 8.14 (d of d, J = 8.4, 2 Hz), 7.75 (d, J = 8.4 Hz); ^{13}C NMR (DMSO-d_6) δ 163.81, 148.67, 138.59, 133.47, 132.59, 126.83, 124.42, 19.62.

B. Sodium Hypochlorite Oxidation. Following the procedure of Graham,[7] a solution of 1.07 g of 3-nitro-4-methylbenzamidine hydrochloride in 20 mL of DMSO was stirred and 4.0 g of NaCl was added followed by 40 mL of hexanes. The mixture was placed in an ice bath and, before the mixture could freeze, a solution of 6.0 g of NaCl in 60 mL of 5.25% sodium hypochlorite solution (commercial bleach) was added over a 20-min period. The mixture was warmed to room temperature and stirring was continued for 3 h. The organic phase was separated and the aqueous phase was extracted with an additional portion of ether. The combined organic extracts were washed with water, saturated NaCl solution, and dried over $MgSO_4$. The solvent was removed using a rotary evaporator and the residue was chromatographed on a column prepared from 16 g of silica gel and packed with 1.5% ether in hexanes. The diazirine **1d** (550 mg, 52% yield) eluted with 2% ether in hexanes: ^1H NMR of **1d** ($CDCl_3$) δ 7.760 (d, J = 2.1 Hz, 1 H), 7.406 (d, J = 8.1 Hz, 1 H), 7.195 (d of d, J = 8.1, 2.1 Hz, 1 H), 2.626 (s, 3 H); ^{13}C NMR of **1d** ($CDCl_3$) δ 149.06, 135.10, 134.88, 133.27, 129.70, 122.47, 45.77, 20.20; HRMS (CI, isobutane) calcd for $C_8H_7ClN_3O_2$ $(M + H)^+$ 212.0226, found: 212.0253.

Preparation of Azidodiazirine 22. A solution of 55 mg of sodium azide in 1.6 mL of DMSO-d_6 was added in one portion to 41.6 mg of (3-nitrophenyl)chlorodiazirine (**1b**). The mixture was stirred at 17 °C as a slurry of 4.7 mg of the sodium salt of 2-nitropropane[19] in about 0.2 mL of DMSO-d_6 was rapidly added. After 12 s, ice–water was added and the mixture was immersed in a bath at −15 °C. About 1 mL of $CDCl_3$ was added to the stirred mixture. After a few seconds of vigorous stirring, the $CDCl_3$ extract was removed via pipet and dried over Na_2SO_4 at about −40 °C. The light yellow solution was then transferred to an NMR tube maintained at −78 °C. This entire procedure was carried out as rapidly as possible to minimize decomposition of **22**. Figures 2 and 3 show ^1H and ^{13}C NMR spectra of this solution recorded at −20 °C. ^1H NMR spectra that were recorded at 19 °C showed significantly more decomposition: ^1H NMR of **22** ($CDCl_3$) δ 8.288 (d of d of d, J = 8, 1.8, 1.0 Hz, 1 H), 7.984 (t, J = 1.8 Hz, 1 H), 7.644 (t, J = 8.0 Hz, 1 H), 7.370 (d of d of d, J = 8, 1.8, 1.0 Hz, 1 H); ^{13}C NMR of **2** ($CDCl_3$) δ 147.84, 135.53, 131.05, 129.82, 123.87, 120.61, 42.33.

The preparation of **22** used for recording of infrared spectra (Figure 4) was analogous to the above preparation. DMSO (undeuterated) was the reaction solvent and **22** was extracted into $CHCl_3$.

Detection of Azidodiazirines 23–25. The procedures used for the generation of azidodiazirines **23–25** (by the nitronate ion-catalyzed reaction of the corresponding chlorodiazirine with sodium azide in DMDO) were analogous to that used for preparation of **22**. NMR spectra were recorded as rapidly as possible after letting the $CDCl_3$ solutions warm to 19 °C. In the generation of **23** from (3,5-dinitrophenyl)chlorodiazirine, the reaction was allowed to stir for 50 s after the addition of the sodium salt of 2-nitropropane. Extraction into $CDCl_3$ gave a solution containing 92% of the decomposition product 3,5-dinitrobenzonitrile (**10**) along with 8% of **23**: ^1H NMR of **23** ($CDCl_3$) δ 8.998 (t, J = 1.8 Hz, 1 H), 8.200 (d, J = 1.8 Hz, 2 H).

In the generation of **24** from (4-nitrophenyl)chlorodiazirine, the reaction was stirred for 30 s after addition of the sodium salt of 2-nitropropane. Extraction into $CDCl_3$ gave a solution containing 79% of the decomposition product 4-nitrobenzonitrile, along with 21% of **24**: ^1H NMR of **24** ($CDCl_3$) δ 8.26 and 7.24 (AA'BB' quartet, J = 9 Hz, 4 H).

In the generation of **25** from (3-nitro-4-methylphenyl)chlorodiazirine, the reaction was stirred for 110 s after addition of the sodium salt of 2-nitropropane. Extraction into $CDCl_3$ gave a solution containing 55% of the decomposition product 3-nitro-4-methylbenzonitrile, along with 45% of **25**: ^1H NMR of **25** ($CDCl_3$) δ 7.70 (d, J = 2.1 Hz, 1 H), 7.41 (d, J = 8.1 Hz, 1 H), 7.15 (d of d, J = 8.1, 2.1 Hz, 1 H).

Detection of Azidodiazirines 26 and 27. A solution of 45 mg of sodium azide in DMSO-d_6 was added to 32 mg of 4-pyridylchlorodiazirine (**1i**) and the solution was placed in two NMR tubes. The solutions were placed about 4 ft from an ordinary laboratory fluorescent light for 6 min. The DMSO-d_6 solutions were then immediately added to a stirred mixture of 5 mL of water and 1 mL of $CDCl_3$ in an ice–salt bath. After a few seconds of vigorous stirring, the $CDCl_3$ extract was removed via pipet and dried over Na_2SO_4 at about −40 °C. The light yellow solution was then transferred to an NMR tube maintained at −78 °C. This entire workup procedure was carried out as rapidly as possible to minimize decomposition of **22**. Figure 5 shows the ^1H NMR spectrum of this solution recorded as rapidly as possible at 19 °C. This spectrum contains 8% of the azidodiazirine **26**, along with 45% of the decomposition product, 4-cyanopyridine, and 47% of unreacted 4-pyridylchlorodiazirine: ^1H NMR of **26** ($CDCl_3$) δ 8.640 (m, 2H), 6.968 (m, 2 H). The signals due to **26** readily convert to 4-cyanopyridine at this temperature.

The generation of azidodiazirine **27** from **1f** was analogous to the above procedure. The time of exposure of the solution of **1f** and NaN_3 in DMSO-d_6 to fluorescent light was 20 min. After the workup procedure described above, the ^1H NMR spectrum of the $CDCl_3$ solution showed about 75% unreacted (3,5-difluorophenyl)chlorodiazirine and 20% 3,5-difluorobenzonitrile, along with 5% of **27**. The signals due to the azidodiazirine **23** at δ 6.51 disappeared readily at room temperature.

Decomposition of Azidodiazirines. Kinetics Procedures. Rates of conversion of the azidodiazirines **22–27** to the corresponding nitriles were monitored by UV spectroscopy. A solution of the appropriate azidodiazirine in $CDCl_3$ (about 20 μL) was injected into a thermostated cuvette containing the appropriate solvent. Absorbance changes were monitored as a function of time using a Perkin-Elmer Lambda 3B spectrometer. The absorbance change for **22** was monitored at 270 nm, **23** at 320 nm, **24** at 290 nm, **25** at 272 nm, **26** at 282 nm, and **27** at 272 nm. Rate constants were calculated using standard least-squares methods, and correlation coefficients were all greater the 0.9999. Maximum standard deviations in duplicate runs were ±1%.

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **1d** and **1e** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(19) The sodium salt of 2-nitropropane was prepared by neutralization of 2-nitropropane with 1 M $NaOCH_3$ in methanol, followed by solvent removal under vacuum. For an analogous preparation of the lithium salt, see Kornblum, N.; Boyd, S. D.; Ono, N. *J. Am. Chem. Soc.* **1974**, 95, 2580.