$S_{RN}1$ Reactions of Arylhalodiazirines with Azide Ion

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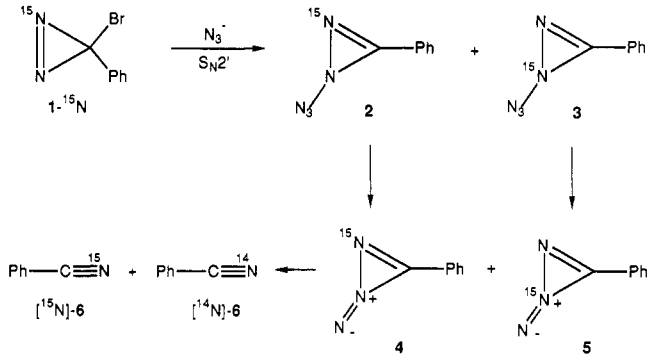
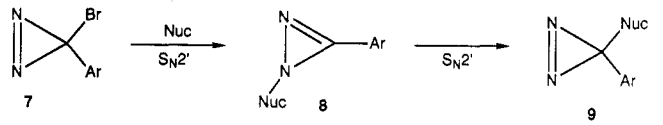
(*m*-(Trifluoromethyl)phenyl)bromodiazirine, **10**, reacts with ^{15}N terminally labeled sodium azide in dimethyl sulfoxide to give *m*-(trifluoromethyl)benzonitrile which, in all cases, contains ^{15}N incorporation. The largest amount of label incorporation (42%), and the fastest rate, is observed when the reaction is carried out in room light. The smallest amount of label incorporation (11%), and the slowest reaction, is observed when the reaction is carried out in the dark and a trace of the free radical, galvinoxyl, is added. The reaction in the light is proposed to occur mainly via the $S_{RN}1$ chain process. The intermediate *C*-azidodiazirine substitution product is not observed, but presumably rapidly loses 2 mol of nitrogen to give the nitrile product. (*p*-Nitrophenyl)bromodiazirine, **20**, can also react with azide ion via an analogous $S_{RN}1$ process, and the reaction is more facile than that of **10**. Label incorporation from ^{15}N-labeled sodium azide is substantial (47.3%) and is in agreement with the proposed $S_{RN}1$ process. A variety of arylchlorodiazirines, substituted with electron-deficient aromatic groups, also react with azide ion in room light, to give nitriles via *C*-azidodiazirines, which lose molecular nitrogen. Evidence for the proposed $S_{RN}1$ process includes initiation of the reaction by exposure to room light, initiation by the addition of the sodium salt of 2-nitropropane or sodium thiophenoxide, and inhibition of the reaction by the addition of galvinoxyl. In the case of these arylchlorodiazirines, reaction with ^{15}N terminally labeled sodium azide led to ^{15}N label incorporation approaching the maximum amount possible for a reaction proceeding exclusively via *C*-azidodiazirines. These studies show the propensity for arylhalodiazirines to undergo reaction initiated by electron-transfer processes.

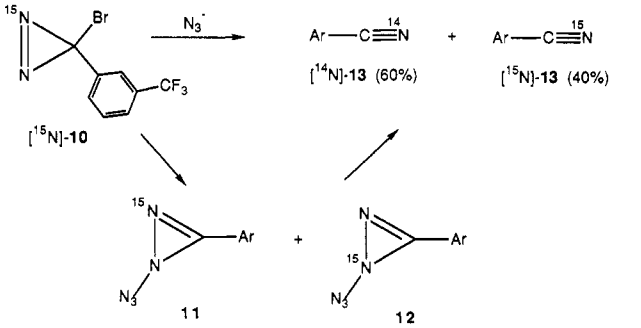
Halodiazirines undergo facile reactions with nucleophiles to give substitution products.[1] As well as being of synthetic utility, this reaction is fascinating in terms of mechanism. As a prototype for the reaction of nucleophiles with halodiazirines, the reaction of arylbromodiazirines with azide ion has been studied.[2] This reaction generates a nitrile, along with molecular nitrogen. We have also studied this reaction,[3] and on the basis of ^{15}N labeling studies we have suggested that the reaction of **1** proceeds via an S_N2' process, giving the *N*-azidodiazirines **2** and **3**.



This intermediate rapidly loses 2 mol of molecular nitrogen to give the nitrile product. Our labeling study,[3] and a related study by Dailey,[4] argue strongly against the previously proposed mechanism[2] involving a diazirinium cation intermediate. Studies on the reaction of the arylbromodiazirines **7** with ^{15}N terminally labeled sodium azide all agree with the S_N2' mechanistic suggestion. We further suggested that other nucleophiles could also react with arylbromodiazirines **7** via an S_N2' mechanism, bypassing the previously proposed diazirinium cation. A second S_N2' displacement on an N-substituted diazirine would give the observed C-substituted product.[5]



As part of this study, we also reported on the reaction of the ^{15}N-labeled arylbromodiazirine [^{15}N]-**10** with azide ion.[3] This reaction gave 40% of ^{15}N-labeled nitrile and 60% unlabeled nitrile. While this study indicates that most of [^{15}N]-**10** reacts by way of the *N*-azidodiazirines **11** and **12**, the product ratio deviates from the 50:50 ratio that



would be expected if an *N*-azidodiazirine was the only intermediate. In order to clarify this discrepancy, we have now carried out a series of studies on the reaction of unlabeled diazirine **10** and related arylhalodiazirines with ^{15}N terminally labeled sodium azide. We now present evidence that certain arylhalodiazirines can react with azide ion by an $S_{RN}1$ type process.

Results and Discussion

The (*m*-(Trifluoromethyl)phenyl)bromodiazirine System. The unlabeled diazirine **10** was reacted with ^{15}N terminally labeled sodium azide in dimethyl-d_6 sulfoxide, and the reaction was monitored by NMR spectroscopy. Three identical samples were prepared, and Figure 1

(1) (a) Cox, D. P.; Moss, R. A.; Terpinski, J. *J. Am. Chem. Soc.* **1983**, *105*, 6513. (b) Włostowska, J.; Moss, R. A.; Guo, W.; Chang, M. *J. Chem. Soc., Chem. Commun.* **1982**, 432. (c) Moss, R. A.; Shen, S.; Hadel, L. M.; Kmiecik-Ławrynowicz, G.; Włostowska, J.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1987**, *109*, 4341. (d) Moss, R. A.; Kmiecik-Ławrynowicz, G.; Cox, D. P. *Synth. Commun.* **1984**, *14*, 21.

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

(3) Creary, X.; Sky, A. F. *J. Am. Chem. Soc.* **1990**, *112*, 368.

(4) Bainbridge, K. E.; Dailey, W. P. *Tetrahedron Lett.* **1989**, *30*, 4901.

(5) Such a mechanism has been suggested in the substitution reaction of fluoride ion with 3-chloro-3-(trifluoromethyl)diazirine. See Dailey, W. P. *Tetrahedron Lett.* **1987**, *28*, 5801.

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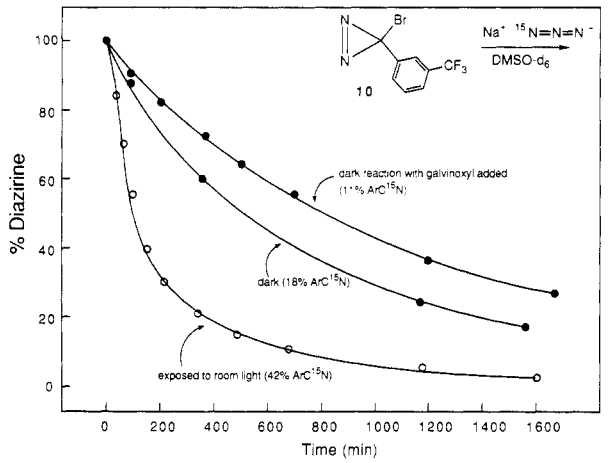
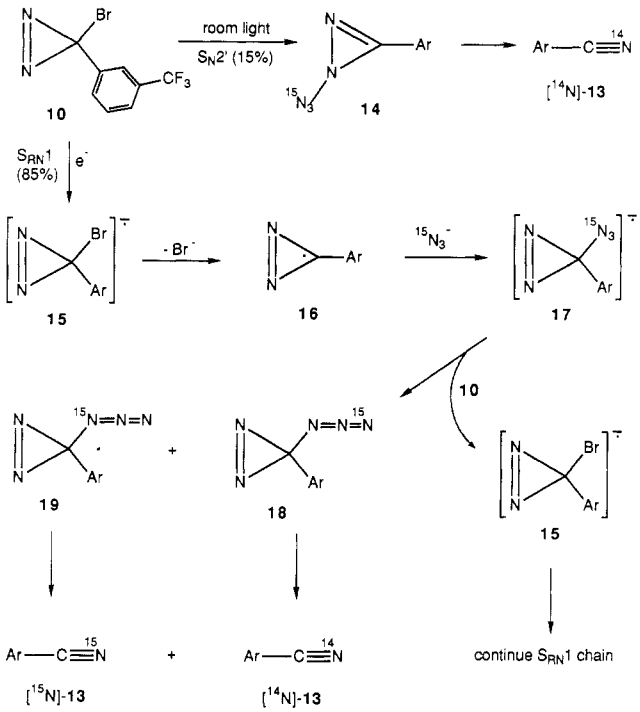


Figure 1. Reaction of arylbromodiazirine **10** with ^{15}N terminally labeled sodium azide.

summarizes kinetic results under different conditions. When the reaction was exposed to ordinary fluorescent room light, the disappearance of the arylbromodiazirine was the most rapid. When the reaction was carefully shielded from room light, the diazirine disappears less rapidly. The disappearance of diazirine was slowest when the reaction was carefully shielded from room light *and* a trace of galvinoxyl (a stable free radical) was added.

The sole product from all of the reactions represented in Figure 1 was *m*-(trifluoromethyl)benzonitrile. On completion of these three reactions, the nitrile product was isolated and analyzed by mass spectrometry. The nitrile formed in the reaction exposed to room light had 42% ^{15}N incorporation. The dark reaction led to only 18% ^{15}N incorporation while the dark reaction with added galvinoxyl gave the smallest amount of ^{15}N incorporation (11%).

These rate and labeling results indicate that **10** reacts with azide ion by competing mechanisms. It is proposed that the reaction of **10**, when exposed to room light, occurs mainly (85%)[6] by an $S_{RN}1$ chain type of process.[7] Such a process would involve formation of the radical anion **15** followed by loss of bromide to generate the diazirinyl radical **16**.[8] Coupling with azide ion would produce the radical anion **17**, which would subsequently transfer an electron to the starting arylbromodiazirine **10** to regenerate the radical anion **15** and propagate the chain. It is further suggested that the *C*-azidodiazirine substitution products **18** and **19** (which cannot be observed by NMR during the course of the reaction) serve as the source of the nitrile product. Rapid loss of two molecular nitrogens from **18** and **19**, as originally proposed by Moss et al.,[2] would produce the observed nitriles [^{15}N]-**13** and [^{14}N]-**13**. The 42% ^{15}N label incorporation in the product indicates that 85% of **10** reacts via this $S_{RN}1$ process which generates



labile *C*-azidodiazirines. Superimposed on this radical chain substitution process is the nonchain S_N2' process (15%), which generates unlabeled nitrile via the *N*-azidodiazirine **14**.

When the reaction of **10** is carried out in the dark, the extent of ^{15}N incorporation in the nitrile product drops substantially to 18%. This implies that the major substitution process occurring in the dark is the S_N2' process, but that the $S_{RN}1$ chain process still accounts for 37% of the product. When the free-radical scavenger, galvinoxyl, is added to the mixture, the amount of the $S_{RN}1$ chain process decreases even further, but still occurs to a small extent (22%). These results are consistent with the fact that the $S_{RN}1$ reaction of azide ion with certain aliphatic substrates is initiated by exposure to light.[9,10] It is also known that the $S_{RN}1$ process is inhibited by the presence of the stable free radical, galvinoxyl, which presumably shortens the chain length in the $S_{RN}1$ process.[11] This dual mechanism proposal also explains our previously observed 60:40 ratio of unlabeled:labeled nitrile when the labeled diazirine [^{15}N]-**10** was reacted with unlabeled azide ion.

The (*p*-Nitrophenyl)bromodiazirine System. The *p*-nitro-substituted diazirine **20** can be prepared, albeit in low yield (11%) by the Graham procedure.[12] The reaction of this diazirine with sodium azide also produced the corresponding nitrile. The rate of this reaction next was examined in order to evaluate the *p*-nitro substituent effect. It was expected that this substrate would be less reactive than the unsubstituted analogue since electron-withdrawing groups have been shown to retard the reaction of azide with arylbromodiazirines.[2] Under identical conditions, in diffuse room light, the disappearance of **20** and the unsubstituted analogue **1** were monitored by NMR spectroscopy. Initially, the *p*-NO_2 system **20** reacted more slowly than the unsubstituted **1**. However the rate of

(6) The ^{15}N terminally labeled sodium azide contained 99% ^{15}N in one of the terminal nitrogens. The maximum ^{15}N label incorporation in the nitrile product is therefore 49.5%.

(7) For review of the $S_{RN}1$ mechanism in aliphatic systems, see: Kornblum, N. In *The Chemistry of Functional Groups, Supplement F: The Chemistry of Amino, Nitroso, and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; p 361. For a discussion of the $S_{RN}1$ reaction in aromatic systems, see: Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413. See also: Rossi, R. A.; De Rossi, R. H. In *Aromatic Substitution by the $S_{RN}1$ Mechanism*; ACS Monograph 178, American Chemical Society, Washington, DC, 1983.

(8) Analogous diazirinyl radicals have been generated and observed by EPR spectroscopy. These radicals lead to benzonitrile presumably by dimerization and subsequent extrusion of nitrogen. Labeling studies in this paper rule out an analogous diazirinyl radical coupling process as a route to benzonitriles. See: Ingold, K. U.; Maeda, Y. *J. Am. Chem. Soc.* **1979**, *101*, 837.

(9) Russell, G. A.; Danen, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 5663.

(10) Wade, P. A.; Morrison, H. A.; Kornblum, N. *J. Org. Chem.* **1987**, *52*, 3102 and references therein.

(11) Kornblum, N.; Cheng, L.; Davies, T. M.; Earl, G. W.; Holy, N. L.; Kerber, R. C.; Kestner, M. M.; Manthey, J. W.; Musser, M. T.; Pinnick, H. W.; Snow, D. H.; Stuchal, F. W.; Swiger, R. T. *J. Org. Chem.* **1987**, *52*, 196.

(12) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.

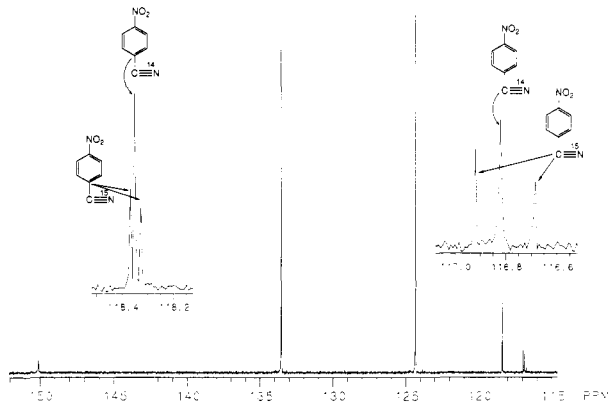
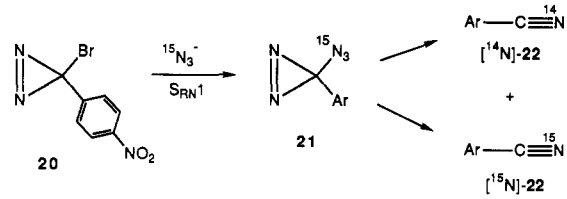


Figure 2. ^{13}C NMR spectrum of the products of reaction of **20** with ^{15}N terminally labeled sodium azide.

reaction of **20** increased after an induction period and was completed before the unsubstituted analogue. In a second series of experiments a mixture of **20** and sodium azide in dimethyl-d_6 sulfoxide was placed about 6 in. from an ordinary laboratory fluorescent light for 5 min. The reaction proceeded at a much faster rate than a control sample which was shielded from room light. Nitrogen evolution was so rapid from the irradiated sample that it was difficult to obtain more quantitative NMR rate data. This rate behavior indicates that **20** and **1** are reacting by different mechanisms.

The *p*-NO_2-substituted diazirine **20** was next reacted with ^{15}N terminally labeled sodium azide in DMSO-d_6 under room light. Figure 2 shows the ^{13}C NMR spectrum of the nitrile product. Clearly ^{15}N has been incorporated into the product. The nitrile carbon of the *p*-$NO_2C_6H_4C^{14}N$ appears at δ 116.819, while the nitrile carbon of *p*-$NO_2C_6H_4C^{15}N$ appears as a doublet (J = 17.8 Hz) at δ 116.802. The ipso carbon of *p*-$NO_2C_6H_4C^{15}N$ at δ 118.343 is also coupled to the ^{15}N (J = 3.2 Hz) and also experiences a small isotope effect shift relative to *p*-$NO_2C_6H_4C^{14}N$ (δ 118.348). The mass spectrum shows that the product contains 47.3% ^{15}N-labeled nitrile [^{15}N]-**22** and 52.7% unlabeled nitrile [^{14}N]-**22**.



It is proposed that **20** reacts with azide mainly by an $S_{RN}1$ chain mechanism analogous to that suggested for reaction of the *m*-CF_3-substituted derivative **10**. As before, the *C*-azidodiazirine substitution product **21** could not be detected by NMR spectroscopy and presumably rapidly loses molecular nitrogen. The labeling result would imply that only about 4% of the reaction occurs by the competing S_N2' mechanism.

The behavior of the *p*-NO_2-substituted diazirine **20** is consistent with what is known about the $S_{RN}1$ reaction and the effect of the *p*-NO_2 substituent. Kornblum has shown that *p*-NO_2 substitution promotes aliphatic $S_{RN}1$ substitution reactions.[11] Consequently *p*-nitrocumyl halides give facile $S_{RN}1$ substitution with certain nucleophiles (including azide ion) while the unsubstituted cumyl halides do not give facile aliphatic $S_{RN}1$ substitution processes. The ability of the *p*-NO_2 substituent to enhance aliphatic $S_{RN}1$ substitution reactions of cumyl systems has been discussed[11] and is attributed to the ability of the nitro

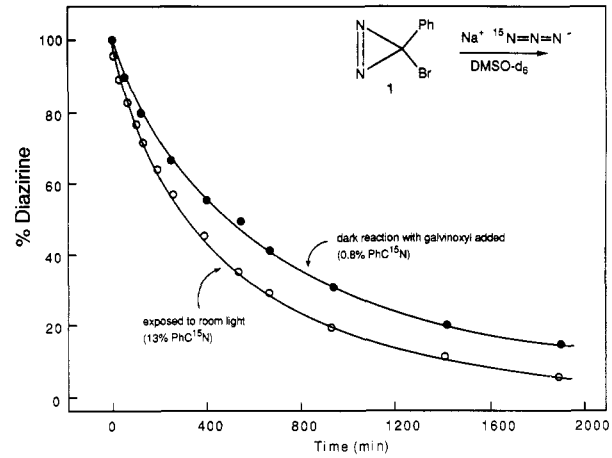


Figure 3. Reaction of phenylbromodiazirine **1** with ^{15}N terminally labeled sodium azide.

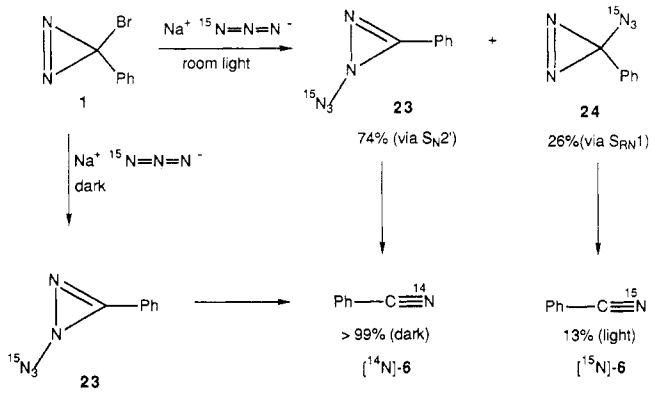
group to delocalize the unpaired electron in the intermediates involved in the $S_{RN}1$ process. The diazirine **20** is also a *p*-NO_2-substituted benzylic bromide and, as such, we suggest that it is also susceptible to the $S_{RN}1$ process.

This proposed $S_{RN}1$ mechanism for **20** is completely consistent with the induction period observed when the reaction is carried out in diffuse room light, as well as the fact that the reaction is initiated by exposure to fluorescent light. The labeling study also fits nicely into the proposed mechanism. The ^{15}N-labeled *C*-azidodiazirine should decompose to give equal amounts of labeled and unlabeled nitrile. It is assumed that the observed deviation from this ideal ratio represents the fact that the S_N2' substitution process, giving an *N*-azidodiazirine, can compete to varying degrees with the $S_{RN}1$ formation of the *C*-azidodiazirine.

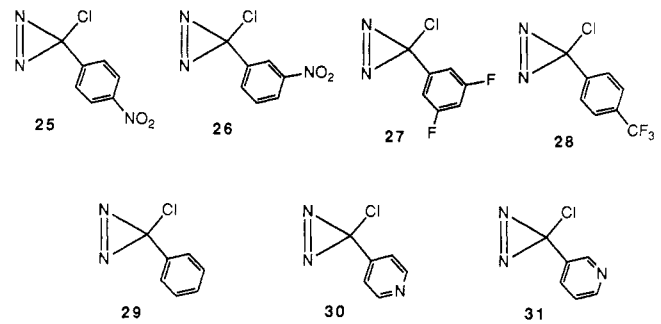
The Phenylbromodiazirine System. Encouraged by these results using the *m*-CF_3- and *p*-NO_2-substituted arylbromodiazirines **10** and **20**, the unsubstituted phenylbromodiazirine, **1**, was next examined. Two identical samples of **1** in DMSO-d_6 containing ^{15}N-labeled sodium azide were prepared. One sample was allowed to react in room light, and the other was carefully shielded from room light after the addition of a trace of galvinoxyl. NMR monitoring showed that the sample that was exposed to room light reacted somewhat faster than the dark reaction. This reactivity difference is shown in Figure 3. On completion of the reaction, the benzonitrile isolated from the dark reaction with added galvinoxyl showed 0.8% PhC^{15}N along with 99.2% unlabeled benzonitrile.[13] However the reaction carried out in room light showed 13% ^{15}N incorporation in the benzonitrile product. These results suggest that even the unsubstituted phenylbromodiazirine, **1**, can react with azide ion to a significant extent (26%) by the $S_{RN}1$ mechanism when exposed to room light. However the dominant process remains the S_N2' substitution process even when the reaction is carried out in room light. The *m*-CF_3 and *p*-NO_2 substituents apparently facilitate the $S_{RN}1$ substitution reaction of arylbromodiazirines with azide ion.

Arylchlorodiazirine Systems. Encouraged by the fact that certain arylbromodiazirines can react via the $S_{RN}1$ process, attention was next focused on the reaction of arylchlorodiazirines **25–31** with azide ion. In the dark, with added galvinoxyl, these substrates were all relatively unreactive. However, on exposure to room light, these dia-

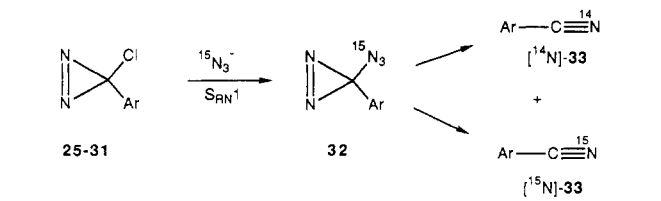
(13) Previously we reported[3] that **1** reacted with ^{15}N terminally labeled sodium azide in the dark to give benzonitrile containing no ^{15}N label incorporation. Our present finding of 0.8% ^{15}N incorporation is attributed to a more accurate mass spectroscopic determination.



zirines all reacted with azide ion to give the corresponding nitriles. Figures 4 and 5 show that a short induction period is involved in reaction of the *p*-NO_2-substituted system **25** and the 4-pyridyl substrate **30**. The 3-NO_2 and the 3-pyridyl-substituted systems **26** and **31** show analogous behavior. Figure 6 illustrates the large rate difference between reaction of **28** in the dark with added galvinoxyl, as compared to the reaction under room light. The chlorodiazirines **27** and **29** show reactivity profiles similar to Figure 6. The observed qualitative reactivity order of these substituted arylchlorodiazirines, as measured by the time necessary for half of the diazirine to react with azide ion, is 4-pyridyl > 3,5-di-F ~ 3-pyridyl > 3-NO_2 ~ 4-NO_2 > *p*-CF_3 > *p*-H.[14] Electron-deficient aromatic groups therefore appear to promote the reaction of arylchlorodiazirines with azide ion when exposed to room light.



The diazirines **25–31** were all reacted with ^{15}N terminally labeled sodium azide in room light. The nitrile products all contained substantial ^{15}N incorporation as revealed by ^{13}C NMR spectroscopy. Table I shows mass spectral results of these labeling studies.[15] The amount of ^{15}N incorporation in all cases, approached the 49.5% value[6] that would be expected if all of these reactions proceeded completely via the *C*-azidodiazirines **32** derived from 99% enriched sodium azide. These arylchlorodiazirines, when reacted with azide ion in the light, therefore appear to bypass the slower S_N2' process which would lead to *N*-azidodiazirines.[16]



(14) Although **27** and **31** are initially more reactive than the nitro-substituted chlorodiazirines **25** and **26**, the reactions of azide ion with **25** and **26** are complete before reactions of **27** and **31**. Rates of reaction of **27** and **31** slow considerably as these diazirines are consumed.

(15) The maximum experimental error in these determinations by mass spectrometry is about ±0.2%.

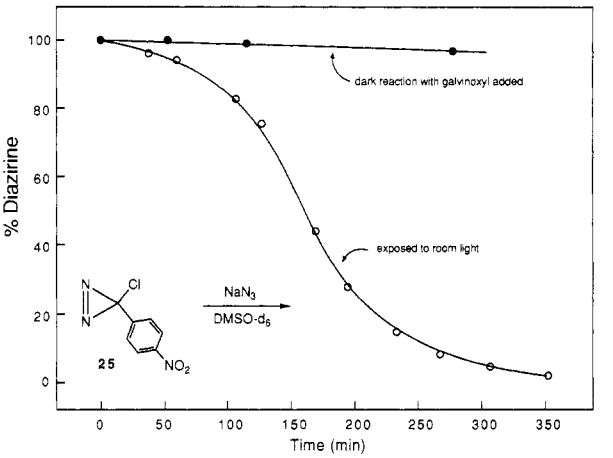


Figure 4. Reaction of arylchlorodiazirine **25** with sodium azide.

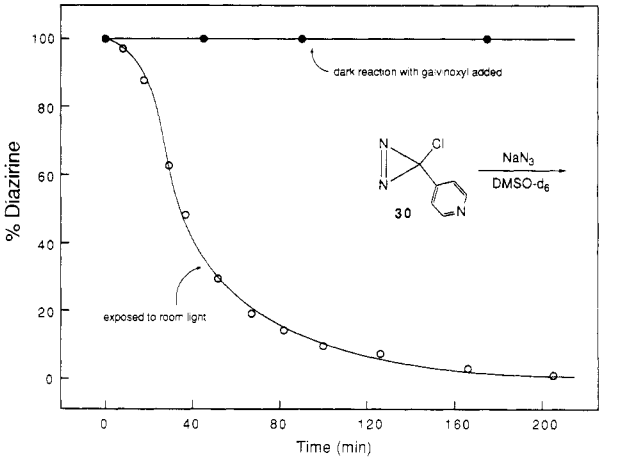


Figure 5. Reaction of arylchlorodiazirine **30** with sodium azide.

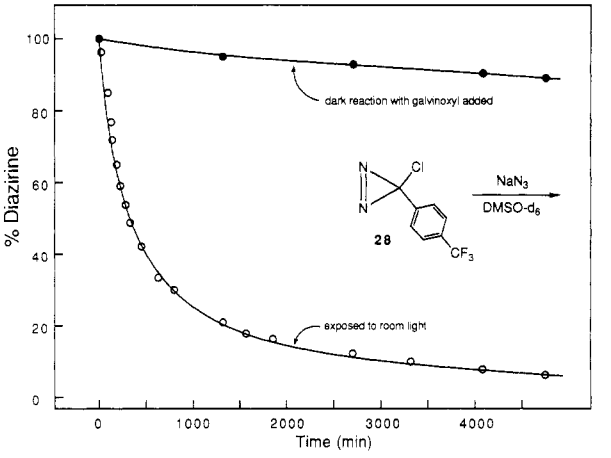


Figure 6. Reaction of arylchlorodiazirine **28** with sodium azide.

Table I. Reaction of Arylchlorodiazirines with ^{15}N Terminally Labeled Sodium Azide in Room Light

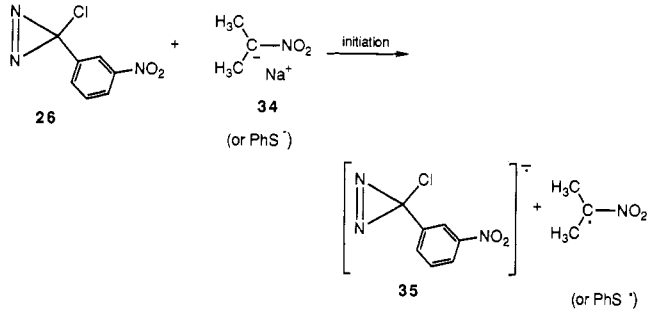
substrate	% Ar-C^{15}N	substrate	% Ar-C^{15}N
25 (*p*-NO_2)	49.4	**29** (*p*-H)	48.5
26 (*m*-NO_2)	49.5	**30** (4-pyridyl)	49.5
27 (3,5-di-F)	49.5	**31** (3-pyridyl)	49.6
28 (*p*-CF_3)	49.1		

The $S_{RN}1$ reaction again nicely accounts for these ^{15}N-labeling results as well as the initiation of the reaction by

(16) In the case of the slower reacting substrates **28** and **29**, small amounts of these substrates may be reacting by the S_N2' process. This would account for the slightly less than 49.5% ^{15}N label incorporation in the nitrile products derived from these substrates.

light. The qualitative rate observations are also consistent with an $S_{RN}1$ process, where the chlorodiazirines substituted with electron-deficient aromatic groups presumably accept an electron more readily than unsubstituted phenylchlorodiazirine. The presence of electron-withdrawing groups on the aromatic ring should facilitate the initiation process and the electron-transfer propagation step in the $S_{RN}1$ sequence. While the reactions of **25–31** with azide ion are all initiated by light, a simple photochemical decomposition of the diazirines, followed by reaction of the resultant carbene with azide ion, cannot account for the observed product.[17] Solutions of the diazirines in DMSO-d_6 can be recovered essentially unchanged when exposed to room light *in the absence of sodium azide* for the period of time necessary to complete the reactions when azide is present. It should be emphasized that these $S_{RN}1$ reactions with azide ion are not strongly irradiated, but are simply allowed to proceed on a laboratory bench in ordinary room light.

In further support for the suggested $S_{RN}1$ mechanism, it has been found that the sodium salt of 2-nitropropane, **34**, can also initiate the reaction of arylchlorodiazirines with azide ion.[18] Thus, addition of a catalytic amount (10%) of **34** to a solution of **26** and sodium azide in DMSO (which was carefully shielded from light) resulted in complete disappearance of **26** and formation of the nitrile product. It is presumed that initiation of the reaction of **26** by the nitronate salt results from electron transfer from **34** to the chlorodiazirine. The resultant radical anion **35** loses chloride ion, generating the diazirinyl radical, and propagates the $S_{RN}1$ chain. Sodium thiophenoxide is also an effective initiator. Small amounts of thiophenoxide also stimulate reaction **26** with azide ion to form the corresponding nitrile. The mechanism of thiophenoxide initiation is presumed to be an electron-transfer process similar to initiation by nitronate anion.[19]



Conclusions. Arylhalodiazirines can react with sodium azide in DMSO by competing S_N2' and $S_{RN}1$ mechanisms. When certain arylbromodiazirines are reacted with azide ion in the dark, the S_N2' process dominates. When reactions are carried out in room light, it is proposed that bromide ion can be displaced with azide ion by a competing $S_{RN}1$ process. The intermediate *C*-azidodiazirines are not observed, but presumably lose molecular nitrogen to generate a nitrile. Arylchlorodiazirines can also react with azide ion via the $S_{RN}1$ process. Evidence for the $S_{RN}1$ process includes initiation of the reaction by exposure to room light, initiation by the addition of nitronate or thiophenoxide anions, inhibition of the reaction by the addition of galvinoxyl, and ^{15}N labeling experiments which are consistent with the proposed *C*-azidodiazirine intermediate. Electron-withdrawing groups on the aromatic ring promote the $S_{RN}1$ process, but even unsubstituted phenylchlorodiazirine can react slowly by the $S_{RN}1$ process when exposed to room light. In the case of the reaction of arylchlorodiazirines with azide ion in room light, the $S_{RN}1$ process predominates since the S_N2' process is slowed to a much greater extent as a result of the poorer chloride leaving group. The $S_{RN}1$ process does not appear to affected to the same extent by changing the leaving group from bromide to chloride. Electron transfer initiated reactions therefore appear to be viable processes for arylhalodiazirines.

Experimental Section

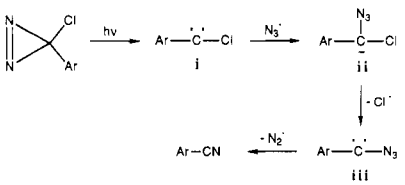
NMR spectra were recorded on a Chemagnetics A-200 spectrometer or on a General Electric GN 300 spectrometer. Mass spectra were recorded on a Finnigan MAT 8430 high-resolution spectrometer equipped with a gas chromatograph. Samples were analyzed either by using the gas chromatography–mass spectrometry method (GC–MS) or by using a 500-mL gas expansion bulb for sample introduction.

Preparation of (*m*-(Trifluoromethyl)phenyl)bromodiazirine, 10. The preparation of the ^{15}N-labeled analogue, **10**-^{15}N, using literature methods, has been described.[2,12] The preparation of **10** was completely analogous.

Preparation of (*p*-Nitrophenyl)bromodiazirine, 20. *p*-Nitrobenzonitrile (10.15 g) was stirred with 90 mL of methanol, and 7.4 mL of 1.0 M sodium methoxide in methanol was added. The mixture was warmed in an oil bath until the nitrile dissolved, and the solution was allowed to stand at room temperature for 55 h; 3.69 g of NH_4Cl was then added, and the mixture was heated in an oil bath at 43 °C for 36 h. The solution was cooled and filtered, and the solvent was removed using a rotary evaporator. The solid was slurried with acetone to dissolve the unreacted *p*-nitrobenzonitrile and collected on a Buchner Funnel. The salt was washed with an additional portion of acetone and dried under vacuum. The yield of *p*-nitrobenzamidine hydrochloride was 5.14 g (37%).

p-Nitrobenzamidine hydrochloride (2.396 g, 0.0256 mol) was dissolved in 25 mL of dimethyl sulfoxide (DMSO), and 35 mL of hexanes was added followed by 3.56 g of NaBr. A solution of NaOBr was prepared by addition of 11.8 g of bromine to a solution of 7.02 g of NaOH in 75 mL of water at 20 °C. When all of the bromine had reacted, 4.31 g of NaBr was added, and the flask was swirled to dissolve all of the NaBr. The benzamidine hydrochloride–DMSO solution was cooled in an ice bath, and the NaOBr solution was added in portions over a 5-min period. The mixture was stirred at 0 °C for 3 h, and the layers were separated. The lower aqueous phase was extracted twice with CH_2Cl_2 and then combined with the hexane extract. The combined organic extracts were then washed twice with water and saturated NaCl solution and dried over $MgSO_4$. The solvent was removed using a rotary evaporator, and the crude residue was dissolved in a minimum amount of CH_2Cl_2 and chromatographed on 15 g of silica gel. The column was eluted with 2% ether in hexanes. Fraction 1 (0.353 g) contained the bromodiazirine **20** contaminated with a small amount of *p*-nitrobenzonitrile. A second fraction consisted of *p*-nitrobenzonitrile (0.340 g). The first fraction was rechromatographed on 10 g of silica gel and eluted using 5% ether in hexanes. Solvent removal using a rotary evaporator gave 0.323 g (11%) of diazirine **20** as an off-white solid: mp 33–35 °C; ^1H

(17) A hypothetical photochemically induced nonchain carbene process, as shown below, would require enough light to completely decompose the diazirine.



(18) The lithium salt of 2-nitropropane has been used as an initiator of $S_{RN}1$ processes. See: Kornblum, N.; Swiger, R. T.; Earl, G. W.; Pinnick, H. W.; Stuchal, F. W. *J. Am. Chem. Soc.* **1970**, *92*, 5513.

(19) A reviewer has suggested that an anion such as ii, formed as shown in ref 17, could be responsible for the photoinitiated reactions. We have no evidence against or in support of this hypothesis.

NMR ($CDCl_3$) δ 8.247 and 7.326 (AA'BB' quartet); ^{13}C NMR ($CDCl_3$) δ 148.402, 143.096, 127.781, 123.655, 35.771.

Preparation of Arylchlorodiazirines 25–31. The arylchlorodiazirines **25**,[20] **26**,[21] **27**, **28**, **29**,[22] **30**,[23] and **31** were all prepared using previously developed procedures based on the original preparation of Graham. These arylchlorodiazirines were all purified by silica gel chromatography. Arylchlorodiazirines **27–31** were also distilled under vacuum (0.03 mm) at less than room temperature. Phenylchlorodiazirine, **29**, is reported to be more shock sensitive than nitroglycerine.[24] Although we have experienced no problems, *the distillations and handling of these diazirines were carried out with extreme care and using safety shields.* They were routinely stored at −80 °C.

Diazirine **27** was prepared in 38% yield from the arylamidine hydrochloride salt: ^1H NMR ($CDCl_3$) δ 6.852 (t of t, J = 8.6, 2.3 Hz, 1 H), 6.645 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 162.980 (d of d, J = 250, 13 Hz), 139.614 (t, J = 10 Hz), 109.639 (d of d, non-first-order), 105.018 (t, J = 25 Hz), 45.814 (t, J = 3.5 Hz).

Diazirine **28** was prepared in 25% yield from the arylamidine hydrochloride salt: ^1H NMR ($CDCl_3$) δ 7.67 and 7.25 (AA'BB' quartet); ^{13}C NMR ($CDCl_3$) δ 139.510, 131.628 (quartet, J = 33 Hz), 126.513, 125.615 (quartet, J = 3.5 Hz), 123.700 (quartet, J = 273 Hz), 46.242.

Diazirine **31** was prepared in 43% yield from the arylamidine hydrochloride salt: ^1H NMR ($CDCl_3$) δ 8.655 (d of d, J = 4.8, 1.6 Hz, 1 H), 8.383 (d of d, J = 2.5, 0.9 Hz, 1 H), 7.46 (d of d of d, J = 8.0, 2.5, 1.6 Hz, 1 H), 7.347 (d of d of d, J = 8.0, 4.8, 0.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 150.356, 147.149, 133.610, 131.726, 122.988, 45.029.

Reaction of Arylbromodiazirine 10 with ^{15}N Terminally Labeled Sodium Azide. ^{15}N terminally labeled sodium azide (43.9 mg of 99% enriched; ICON Services Inc.) was dissolved by warming in about 2.4 mL of DMSO-d_6, and 58.7 mg of freshly distilled bromodiazirine **10** was added to the solution in the dark. One part of the solution was added to an NMR tube, which was exposed to fluorescent room light. A second portion of the solution was placed in an NMR tube, and the tube was shielded from room light by wrapping the tube with aluminum foil. About 0.5 mg of galvinoxyl was added to the third sample. This sample was placed in an NMR tube, and the tube was carefully shielded from room light by wrapping with aluminum foil. The samples were periodically monitored by 200-MHz NMR spectroscopy. Room lights were turned off before analyzing the foil-wrapped samples. The amount of *m*-(trifluoromethyl)benzonitrile was determined from the area of the 3 H multiplet at δ 8.20–7.75 and the amount of unreacted **10** was determined from the area of the 2 H multiplet at δ 7.40–7.10. Figure 1 shows a summary of the progress of these reactions.

On completion of the reactions described above (as determined by NMR), the contents of the individual NMR tubes were taken up into water and extracted with ether. The ether extracts were washed with water and dried over $MgSO_4$. The individual samples were analyzed by GC–MS. The sample that was exposed to room light showed 58% *m*-$CF_3C_6H_4C^{14}N$ and 42% *m*-$CF_3C_6H_4C^{15}N$, as determined from the m/e 171:172 ratio. The sample that was protected from light showed 82% *m*-$CF_3C_6H_4C^{14}N$ and 18% *m*-$CF_3C_6H_4C^{15}N$. The sample that was protected from light and also contained the trace of galvinoxyl showed 89% *m*-$CF_3C_6H_4C^{14}N$ and 11% *m*-$CF_3C_6H_4C^{15}N$. An authentic sample of unlabeled *m*-(trifluoromethyl)benzonitrile was also analyzed by GC–MS to experimentally determine the m/e 170:171:172 ratio used for calculation of the ^{14}N to ^{15}N ratio in the reaction products.

Reaction of *p*-(Nitrophenyl)bromodiazirine, 20, and Phenylbromodiazirine, 1, with Sodium Azide. Rate Studies. A stock solution of sodium azide in DMSO-d_6 (0.49 M) was prepared. Samples of diazirines **1** and **20** (0.154 mmol) were weighed out, and 1.0 mL of the sodium azide solution was added to each sample. The individual solutions were transferred to NMR tubes, and the tubes were placed in a constant temperature bath at 20.0 °C. The tubes were not shielded from room light, although the light intensity in the bath was relatively low. The tubes were periodically withdrawn from the bath and rapidly analyzed by NMR spectroscopy. After 1 h, 84% of **1** remained and 93% of **20** remained. After 2 h, 73% of **1** remained and 89% of **20** remained. After 5 h, 55% of **1** remained and 61% of **20** remained. After 10 h, 36% of **1** remained and 4% of **20** remained. After 15 h, 22% of **1** remained and none of **20** could be detected by NMR analysis.

Reaction of (*p*-Nitrophenyl)bromodiazirine, 20, with ^{15}N Terminally Labeled Sodium Azide. ^{15}N terminally labeled sodium azide (77.8 mg of 99% enriched) was dissolved by warming in about 2.5 mL of DMSO-d_6, and 88 mg of bromodiazirine **20** was added to the solution. The mixture was swirled to dissolve the diazirine. The solution was transferred to two NMR tubes, and the tubes were left standing in normal laboratory room light. Nitrogen evolution began after a few minutes. The tubes were periodically monitored by NMR and after 6 h, the diazirine **20** was completely reacted. A standard aqueous workup, with ether extraction, gave 41.1 mg (76%) of *p*-nitrobenzonitrile. The ^{13}C NMR spectrum of the product is shown in Figure 2. The ratio of unlabeled *p*-nitrobenzonitrile, **22**-^{14}N, to labeled *p*-nitrobenzonitrile, **22**-^{15}N, was 52.7:47.3 as determined from the m/e 148:149 ratio in a GC–MS analysis.

Reaction of Phenylbromodiazirine, 1, with ^{15}N Terminally Labeled Sodium Azide. ^{15}N terminally labeled sodium azide (40 mg of 99% enriched) was dissolved by warming in 1.8 mL of DMSO-d_6, and 43 mg of phenylbromodiazirine **1**[2,12] was added to the solution. The mixture was swirled to dissolve the diazirine, and half of the solution was transferred to an NMR tube. This tube was allowed to react in laboratory room light. About 0.5 mg of galvinoxyl was added to the remaining solution, and this was placed in an NMR tube wrapped with aluminum foil to exclude light. The samples were periodically monitored by 200-MHz NMR spectroscopy. Figure 3 shows a summary of the progress of these reactions.

After 6 days at room temperature, the contents of the individual NMR tubes were taken up into water and extracted with ether. The ether extracts were washed with water and dried over $MgSO_4$. The individual samples were analyzed by GC–MS. The sample that was exposed to room light showed 87.0% $PhC^{14}N$ and 13.0% $PhC^{15}N$, as determined from the m/e 103:104 ratio. The sample that contained the trace of galvinoxyl and was protected from light showed 99.2% $PhC^{14}N$ and 0.8% $PhC^{15}N$. An authentic sample of unlabeled benzonitrile was also analyzed by GC–MS to experimentally determine the m/e 102:103:104 ratio used for calculation of the ^{14}N to ^{15}N ratio in the benzonitrile product.

Reaction of Arylchlorodiazirines 25–31 with Sodium Azide. General Procedure for Rate Studies. Approximately 40 mg of sodium azide (0.62 mmol) was dissolved in 1.8 mL of DMSO-d_6 by warming the mixture slightly. The appropriate arylchlorodiazirine (0.25 mmol) was then added to the solution in the dark. About half of the solution was transferred to one NMR tube, and the tube was placed on a laboratory bench under ordinary laboratory fluorescent light. About 0.5 mg of galvinoxyl was added to the remaining sample, and this solution was then added to a second NMR tube, which was carefully wrapped with aluminum foil to exclude all light. The tubes were periodically monitored by 200-MHz NMR spectroscopy. Room lights were extinguished before analysis of the sample containing the added galvinoxyl. The amount of unreacted arylchlorodiazirines were determined from appropriate integrals corresponding to diazirine and nitrile product. Figures 4–6 are representative plots showing kinetic behavior.

Reaction of Arylchlorodiazirines 25–31 with ^{15}N Terminally Labeled Sodium Azide. General Procedure. Approximately 50 mg (0.76 mmol) of ^{15}N terminally labeled sodium azide (99% enriched) was dissolved in 1.8 mL of DMSO-d_6 by warming the mixture slightly. The appropriate arylchclorodiazirine (0.35 mmol) was then added, and the solution was transferred to two NMR tubes. The tubes were placed on a laboratory bench under ordinary laboratory fluorescent light and periodically monitored by 200-MHz NMR spectroscopy. When the reactions were complete, as determined by NMR, the contents of the tubes were taken up into water and extracted with ether. The ether extracts were

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washed with water and saturated NaCl solution and dried over $MgSO_4$. The ether solvent was removed using a rotary evaporator. The nitrile products were analyzed by ^{13}C NMR spectroscopy to confirm the presence of ^{15}N in the nitrile products and by mass spectrometry to quantitatively determine the extent of ^{15}N incorporation. The error in the mass spectrometric analysis was estimated to be ±0.1% when samples were introduced using a gas expansion bulb inlet system or ±0.2% when samples were analyzed by GC–MS method. Nitrile products derived from reaction of ^{15}N terminally labeled sodium azide with **27**, **30**, and **31** were analyzed by the former method, while nitrile products derived from **25**, **26**, **28**, and **29** were analyzed by the later method. Product ratios were calculated from the m/(m + 1) ratio. A spectrum of an authentic sample of the appropriate nitrile was also recorded to experimentally determine the intensity of the m − 1 and the m + 1 peaks which were used in the calculation of ^{14}N to ^{15}N ratios.

In the case of the reaction of phenylchlorodiazirine, **28**, with labeled sodium azide, approximately 25% unreacted **28** still remained after 40-h exposure to room light. At the end of this period, an aqueous workup was carried out and the benzonitrile product was separated from the unreacted **28** by silica gel chromatography.

Reaction of (*m*-Nitrophenyl)chlorodiazirine, 26, with Sodium Azide. Initiation Using the Sodium Salt of 2-Nitropropane. The sodium salt of 2-nitropropane was prepared by addition of 1.05 g of 2-nitropropane to 20 mL of 0.5 M $NaOCH_3$ in methanol. The methanol was removed using a rotary evaporator, and the solid was washed with two portions of ether. The ether was decanted and the solid was dried under vacuum to give 1.04 g (94%) of the nitronate salt **34**. This salt was relatively insoluble in DMSO-d_6.

To a stirred solution of 43.8 mg of NaN_3 in 1.8 mL of DMSO-d_6 (in the dark under N_2) was added 40.1 mg of (*m*-nitrophenyl)-chlorodiazirine, **26**. The solid nitronate salt **34** (2.2 mg) was immediately added to the stirred solution. Nitrogen evolution began immediately and continued over about 5 min. After 15 min a sample was withdrawn and analyzed by ^1H NMR spectroscopy which showed no unreacted diazirine **26**. A standard aqueous workup followed using ether extraction. The ether extract was washed with a portion of water and saturated NaCl solution and dried over $MgSO_4$. Solvent removal using a rotary evaporator left 26.3 mg (88%) of *m*-nitrobenzonitrile, which was spectroscopically identical with an authentic sample.

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Registry No. **1**, 4222-25-7; **10**, 125330-15-6; **20**, 115127-49-6; **25**, 39184-67-3; **26**, 53442-61-8; **27**, 125330-16-7; **28**, 115127-52-1; **29**, 4460-46-2; **30**, 74671-01-5; **31**, 125330-17-8; **34**, 24163-39-1; *p*-nitrobenzonitrile, 619-72-7; *p*-nitrobenzamidine hydrochloride, 15723-90-7; sodium azide, 26628-22-8; galvinoxyl, 2370-18-5; sodium thiophenoxide, 930-69-8.

Pyrolysis of *sec*-Butyl Acetate. Is the Stereospecific Syn Elimination a Homogeneous or Heterogeneous Reaction?

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A kinetic isotope effect of ca. 2 was obtained for the pyrolysis of either 1,1,1-trideuterio-2-butyl acetate or *erythro*-2-butyl-3-d_1 acetate over glass beads. Under the same reaction conditions, except for the use of a high surface area silica rather than glass beads, the isotope effect was lower. With the high area silica, 2-butanol dehydration produced no isotope effect, and, in contrast to acetate pyrolysis, the silica catalyzed H–D exchange during the formation of the butene products. Butene and D_2O did not undergo exchange under the alcohol dehydration conditions. It is concluded that surface catalysis during acetate pyrolysis over low surface area glass beads does not make an important contribution but may with high surface area silica.

Introduction

The pyrolysis of esters is a well-established convenient method for the preparation of alkenes. The products are those predicted for β-elimination, and usually the products undergo minimal secondary reactions.[1] With other synthetic methods, such as catalytic dehydration of alcohols, secondary reactions may be a significant problem.[2] This reaction is also of interest from a mechanistic viewpoint, and many studies have been devoted to various aspects of the elimination pathway, for example.[1,3–6]

Maccol[7] considered this reaction to be especially attractive for study because in the gas phase it is possible to investigate the behavior of a single molecule, uninfluenced by the presence of the remainder of the system. The effect of substitution in a parent molecule upon the rate of a given reaction can thus be studied without the complications arising from the cooperative effects of the solvent, as may occur in reactions in solutions. Obviously, for this assertion to be valid surface effects of the reaction vessel must be minimal, or absent. Wertz and Allinger[8] indicated that surface effects may be a significant factor. They stated that the isomer ratios observed in the alkene products are generally inconsistent with a one-step gas-phase reaction that occurs by a cyclic transition state, but they are consistent with a surface-catalyzed reaction. These latter authors believed that, while true gas-phase reactions appear to have been observed in kinetic experiments, the experimental conditions employed in most cases where isomer ratios have been reported for the products, which are the conditions commonly used for preparative work, resulted from a surface-catalyzed reaction.

Observations which are consistent with a gas-phase mechanism for ester pyrolysis are[1,8] (1) the loss of a cis

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