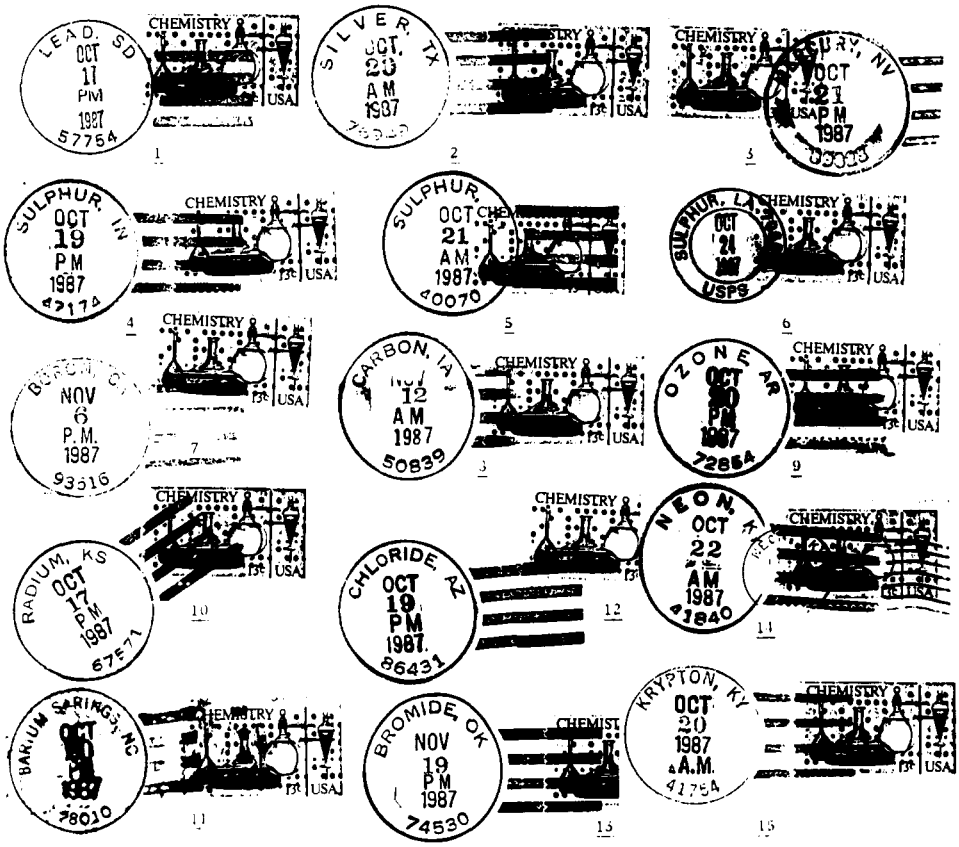


**Figure 4.**

*chemists who supplied chemophilatelic material over the years. Thanks to Dr. David Darom for his help in photographing the stamps. I thank in advance readers who will share their chemophilatelic knowledge with me.*

**Supplementary Material Available:** A list of countries, years of issue, and Scott catalog numbers of the 90 stamps (2 pages) will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper or microfiche (105 × 148 mm, 24× reduction, negatives) may be obtained from Microforms Office, American Chemical Society, 1155 16th St., N.W., Washington, DC 20036. Full bibliographic citation (journal, title of article, author's name, inclusive pagination, volume number, and issue number) and prepayment, check or money order for $10.00 for photocopy ($12.00 foreign) or $10.00 for microfiche ($11.00 foreign), are required. Canadian residents should add 7% GST.

# Reactions of Halodiazirines by $S_N2'$ and Electron Transfer Initiated Processes†

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Diazirines **1** are an intriguing class of heterocyclic compounds.[1] Like their acyclic and better known isomeric diazo compounds **2**, diazirines can be induced to lose molecular nitrogen under thermal or photochemical conditions to generate carbene intermediates. Diazo compounds **2** are available from a variety of

Xavier Creary was born on September 27, 1946, in Montclair, NJ. He received his B.S. from Seton Hall University in 1968 and his Ph.D. from Ohio State University in 1973. After a year as a postdoctoral research associate in the laboratory of Professor Joseph Bunnett at the University of California at Santa Cruz, he joined the faculty at the University of Notre Dame in 1974, where he is currently Professor of Chemistry. His current research interests are in the areas of synthetic and mechanistic organic chemistry, with special interests in the chemistry of carbocations, free radicals, carbenes, electron transfer initiated reactions, acid catalysis, and the chemistry of diazo compounds and diazirines.

† Dedicated, with appreciation, to Professor Joseph F. Bunnett on the occasion of his retirement and on the 25th anniversary of his founding of this journal.

(1) For reviews, see: (a) Liu, M. T. H. *Chem. Soc. Rev.* **1982**, *11*, 127. (b) Heine, H. W. In *The Chemistry of Heterocyclic Compounds—Small Ring Heterocycles—Part 2*; Wiley: New York, Vol. 42, 1983; pp 588–616. (c) *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC Press, Inc.: Boca Raton, FL, 1987; Vols. I and II.

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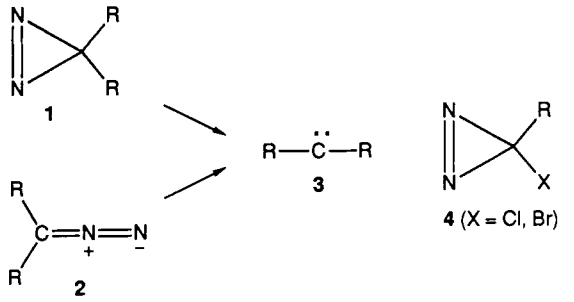
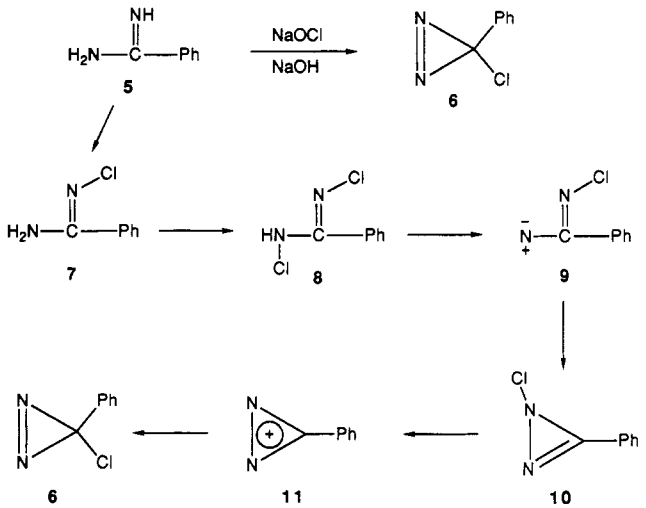
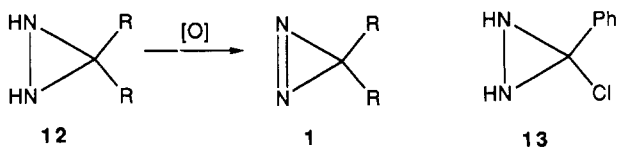



procedures, and some have been available for over 100 years.[2] However, diazirines are a much newer class of compounds, having been prepared for the first time in 1960.[3,4] Since the cyclic diazirine structure was often attributed to diazo compounds,[5] the discovery of the diazirines eliminated this cyclic structure as a possibility for diazo compounds. The related halodiazirines **4** were first prepared by Graham in 1965 using a very simple procedure involving hypohalite oxidation of amidines under alkaline conditions.[6] The ready availability of amidines therefore makes diazirines an attractive potential carbene source. Indeed, the preparation of phenylchlorodiazirine (**6**) in 48–53% yield from commercially available benzamidine hydrochloride is now described in *Organic Syntheses*.[7] This Account will deal with the chemistry of halodiazirines **4** and, in particular, the mechanisms by which they react with nucleophiles.

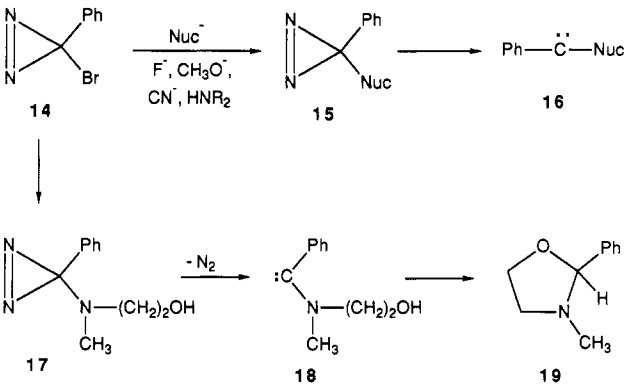



The mechanism of the hypohalite oxidation of amidines, known as the Graham oxidation, is fascinating. Graham proposed[6] that the process proceeded via N-chlorination of both nitrogens followed by base-promoted elimination of HCl. Cyclization of the nitrene intermediate **9** would give the N-chlorodiazirine **10**. Isomerization to the observed phenylchlorodiazirine (**6**) was proposed to occur by either an $S_N2'$ process or ionization of **10** to the diazirinium cation **11**. Although Graham left this isomerization mechanism up for debate, the analogy between the diazirinium cation **11** and the well-known aromatic cyclopropenium cation[8] was noted.

Diazirines **1** are often prepared by oxidation of diaziridines **12**.[9] Hence it is not unreasonable to consider intermediates such as **13** in the Graham oxidation. Indeed, this structure has been suggested as an isolable intermediate in an alternative mechanism for the formation of halodiazirines.[10] However, it was subsequently shown that the structure of the isolable intermediate was actually **7**.[11] In other instances *N,N'*-dichloroamidine analogues of **8** could also be isolated. These observations partially establish the mechanism of the Graham reaction. With these mechanistic suggestions in mind, we now turn attention to reactions of halodiazirines with nucleophiles.



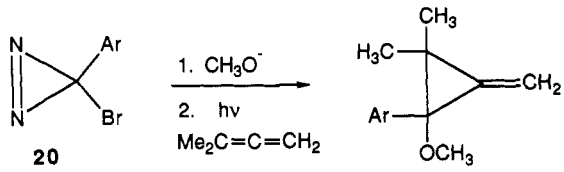

**Substitution Reactions of Halodiazirines.** The halodiazirines have proven to be a particularly useful class of diazirines. In addition to their providing a convenient source of halo carbenes,[7] Moss has found that they undergo a very important exchange reaction when reacted with certain nucleophiles. This is illustrated for diazirine **14**, where nucleophiles are fluoride,[12] cyanide,[13] methoxide,[14] and amines.[15] This reaction has




much synthetic potential since the substituted diazirines provide a convenient source of carbenes of the type **16**. An interesting example is the novel amino carbene **18**, which has been generated and trapped intramolecularly to give the heterocycle **19**.[15] Syntheti-

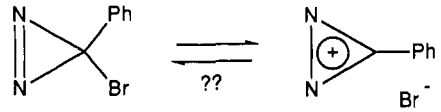
(2) For leading references, see: *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978.
(3) Paulsen, S. R. *Angew. Chem.* **1960**, *72*, 781.
(4) Schmitz, E.; Ohme, R. *Angew. Chem.* **1961**, *73*, 115.
(5) For a typical example, see: Nenitzescu, C. D.; Solomonica, E. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 496.
(6) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.
(7) Padwa, A.; Pulwer, M. T.; Blacklock, T. J. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 203.
(8) (a) Breslow, R.; Hover, H.; Chang, H. W. *J. Am. Chem. Soc.* **1962**, *84*, 3168. (b) Breslow, R.; Groves, J. T.; Ryan, G. *J. Am. Chem. Soc.* **1967**, *89*, 5048. (c) Farnum, D. G.; Metha, G.; Silberman, R. G. *J. Am. Chem. Soc.* **1967**, *89*, 5048.
(9) Schmitz, E.; Ohme, R. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 897.
(10) Berneth, H.; Hunig, S. *Chem. Ber.* **1980**, *113*, 2040.
(11) Moss, R. A.; Wlostowska, J.; Guo, W.; Fedorynski, M.; Springer, J. P.; Hirshfield, J. M. *J. Org. Chem.* **1981**, *46*, 5050.
(12) Cox, D. P.; Moss, R. A.; Terpinski, J. *J. Am. Chem. Soc.* **1983**, *105*, 6513.
(13) Moss, R. A.; Kmiecik-Lawrynowicz, G.; Cox, D. P. *Synth. Commun.* **1984**, *14*, 21.
(14) (a) Wlostowska, J.; Moss, R. A.; Guo, W.; Chang, M. *J. Chem. Soc., Chem. Commun.* **1982**, 432. (b) Moss, R. A.; Shen, S.; Hadel, L. M.; Kmiecik-Lawrynowicz, G.; Wlostowska, J.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1987**, *109*, 4341.
(15) Moss, R. A.; Cox, D. P.; Tomioka, H. *Tetrahedron Lett.* **1984**, *25*, 1023.

cally, we have used this methodology to prepare the methoxy-substituted methylenecyclopropanes **21**, which have been studied in order to probe substituent effects on free radicals.[16] The halodiazirines and diazirines derived from exchange reactions have also been of fundamental importance in developing the concept of ambiphilic carbenes.[17]




**20** Ar = Ph, p-$CF_3C_6H_4$, m-$CF_3C_6H_4$ **21**

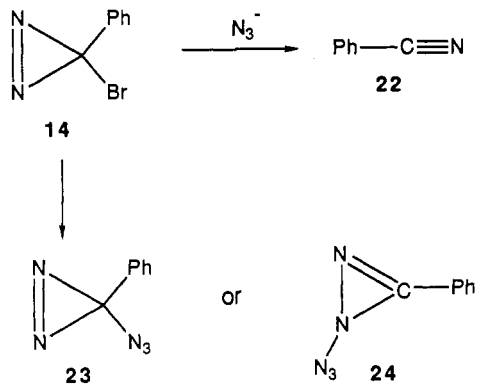
It has been suggested that the diazirinium cation **11** (as a tight ion pair), formed by ionization of **14**, is involved in the reaction of this halodiazirine with nucleophiles.[17] An equilibrium constant for this ionization




**14** **11**

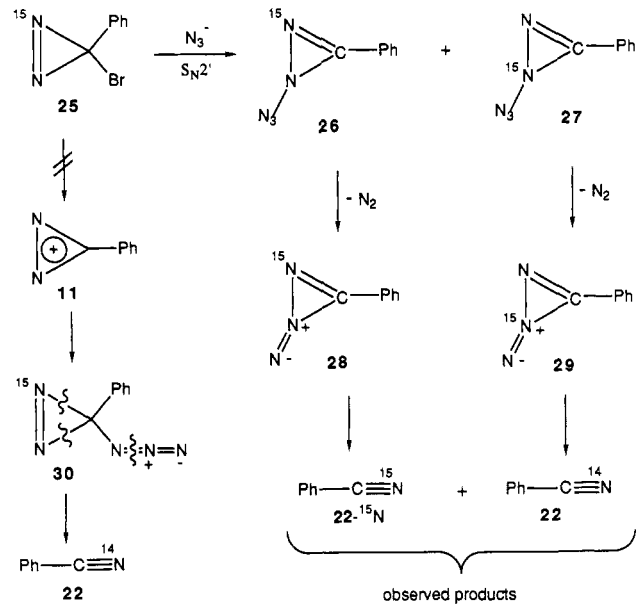
in acetonitrile has also been reported,[18] and this cationic intermediate has also been proposed as the catalytic agent in the phenylbromodiazirine-catalyzed isomerization of diethyl maleate to diethyl fumarate.[19] In light of these findings we attempted solvolytic substitution reactions of **14** in an attempt to produce acetoxy and trifluoroethoxy analogues of **15**.[20] To our initial surprise, no reaction was observed. We therefore questioned the intermediacy of the diazirinium cation **11** in reactions of phenylbromodiazirine.

The reaction of azide ion with **14** gives benzonitrile in high yield as well as molecular nitrogen.[21] No intermediate azidodiazirines are observed when the reaction is monitored by NMR spectroscopy. A mechanism involving the diazirinium cation **11** which captures azide ion to give the *C*-azidodiazirine **23** as transient intermediate was originally suggested. However, since



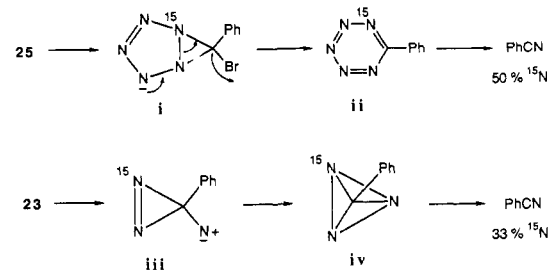

**23** **24**

we could not easily generate the cation **11** under solvolytic conditions, the $S_N2'$ mechanistic alternative has been considered by our laboratory.[22] In this process, nucleophilic attack occurs at nitrogen with concurrent loss of bromide ion from carbon. This mechanism has also been considered independently by Professor Dailey.[23] In the $S_N2'$ mechanism, the intermediate *N*-azidodiazirine **24** could potentialy lose two molecules of nitrogen to give benzonitrile directly. Once it is recognized that benzonitrile may not necessarily arise from the *C*-azidodiazirine **23**, it becomes a simple matter to distinguish the two mechanisms by a labeling experiment.

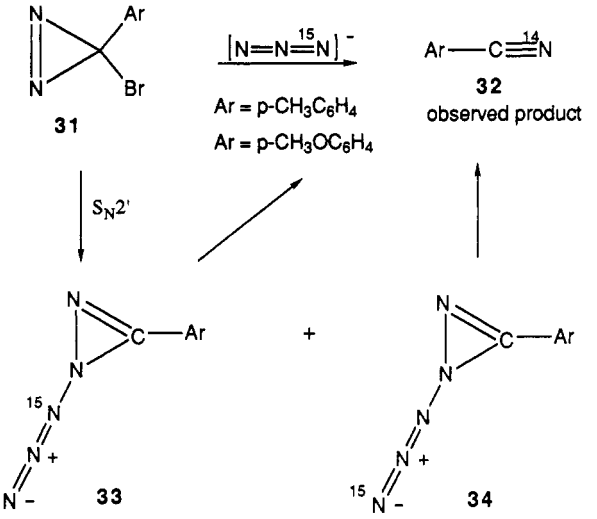



Reaction of the $^{15}N$-labeled bromodiazirine **25** with azide ion gave the statistical mixture of labeled and unlabeled benzonitrile **22**-$^{15}N$ and **22** that would be predicted by the $S_N2'$ mechanism. This is inconsistent with the mechanism involving the diazirinium cation **11** and the *C*-azidodiazirine **23**, which predicts no label incorporation in the product.[24] A complementary labeling study on **31** using terminally $^{15}N$ labeled azide ion (which is commercially available with 99% $^{15}N$ in one of the terminal nitrogens) gave a nitrile product with no $^{15}N$-label incorporation. Even in the case where the aryl group was the potent cation-stabilizing *p*-anisyl

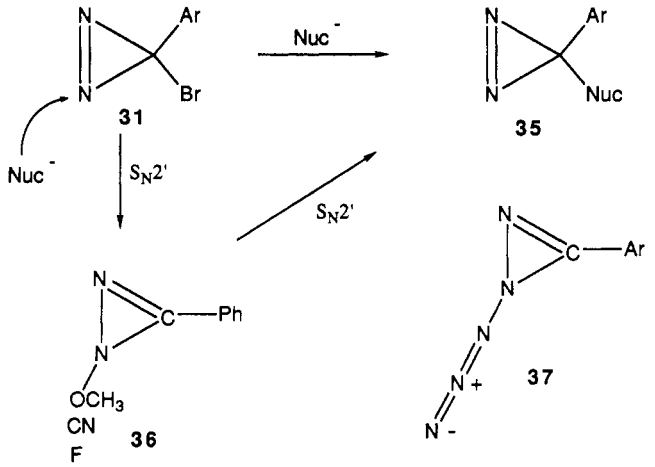
(16) Creary, X.; Sky, A. F. *Tetrahedron Lett.* **1988**, *29*, 6839.
(17) For an excellent discussion of carbene philicity, see: Moss, R. A. *Acc. Chem. Res.* **1989**, *22*, 15.
(18) Liu, M. T. H.; Paike, N. *Tetrahedron Lett.* **1987**, 3763.
(19) Liu, M. T. H.; Doyle, M. P.; Loh, K.-L.; Anand, S. M. *J. Org. Chem.* **1987**, *52*, 323.
(20) Creary, X.; Sky, A. F. *J. Org. Chem.* **1988**, *53*, 4637.
(21) Moss, R. A.; Terpinski, J.; Cox, D. P.; Denney, D. Z.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1985**, *107*, 2743.
(22) Creary, X.; Sky, A. F. *J. Am. Chem. Soc.* **1990**, *112*, 386.
(23) Bainbridge, K. E.; Dailey, W. P. *Tetrahedron Lett.* **1989**, *30*, 4901.
(24) It should be kept in mind that one never *proves* a mechanism by a labeling study since there may be other mechanisms not yet conceived that are also consistent with labeling results. The best that one can do is to eliminate certain mechanisms. For example, a mechanism (conceived by Professor M. V. George) involving cycloaddition of azide to **25** to give i, followed by formation of ii and subsequent elimination of $2N_2$, would also be consistent with our labeling study. A mechanism involving formation of the triazatetrahedrane iv (conceived by Professor A. M. Trozzolo), while fascinating, does not predict precisely the observed label incorporation.



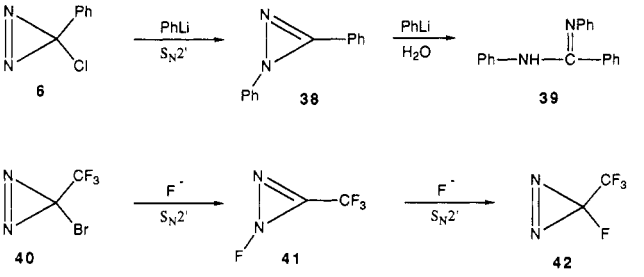
group, the labeling study was still consistent with the $S_N2'$ mechanism.




We believe that other nucleophiles also react with halodiazirines by an initial $S_N2'$ attack at nitrogen. This is followed by a second $S_N2'$ attack at carbon to give the observed products **35**. In the case of azide ion, the intermediate **37** does not live long enough to undergo the second $S_N2'$ attack, but this intermediate simply extrudes a stable small molecule, i.e., molecular nitrogen. The difference between azide ion and nucleophiles such as methoxide and cyanide lies in the fact that these latter nucleophiles lead to N-substituted derivatives **36** which cannot extrude a stable small molecule. Hence further $S_N2'$ reaction can occur.




This suggestion that nucleophiles can react with halodiazirines via an $S_N2'$ mechanism is not unique. Graham considered this possibility in his original paper dealing with the synthesis of halodiazirines.[5] The reaction of phenyllithium and methyllithium with phenylchlorodiazirine was suggested to lead to products derived from initial attack of the organometallic at nitrogen.[25] In the case of phenyllithium, the initial substitution product **38** reacts further with PhLi to give **39** (which is a product of N–N cleavage) in high yield. (Trifluoromethyl)bromodiazirine (**40**) reacts readily with fluoride ion to give the perfluorinated diazirine **42**.[26] On the basis of the ease of substitution and the known cation-destabilizing properties of the $CF_3$ group,[27] the reaction mechanism was proposed to involve consecutive $S_N2'$ processes.

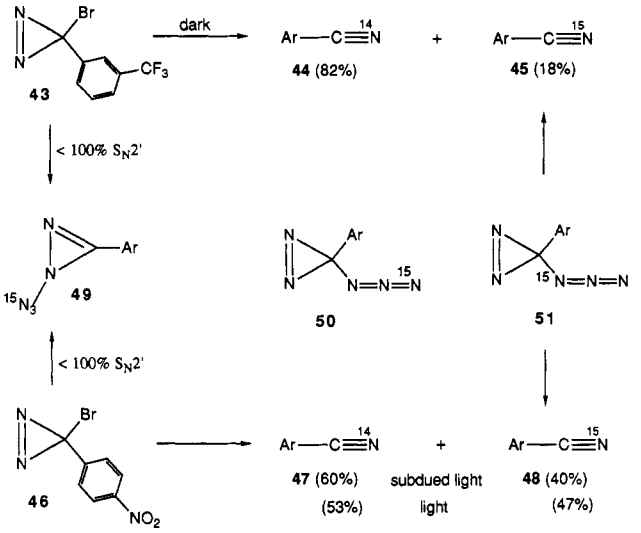



**On the Question of the Diazirinium Cation.** Where does the diazirinium cation fit in the overall chemistry of halodiazirines? Computational studies suggest that they are high-energy intermediates.[28] Additionally, we can obtain no experimental evidence for their involvement in substitution reactions of halodiazirines. The question remains as to their involvement in the Graham oxidation. Computational studies place the proposed *N*-halodiazirine intermediate **10** approximately 20 kcal/mol higher than the isomeric *C*-halodiazirine **6**.[29] This suggests that the barrier for ionization of **6** to the diazirinium cation **11** should be at least 20 kcal/mol higher than the ionization energy of the *N*-halodiazirine **10**. While heterolytic fragmentation of the N–halogen bond of **10** to give a diazirinium cation may be a viable process, ionization of the C–halogen bond of **6** should be a more difficult process. Substitution via the $S_N2'$ process appears to be a more viable process.

**Reaction of Halodiazirines by the $S_{RN}1$ Mechanism.** The study of arylbromodiazirines **31** with labeled azide ion provided good evidence for the proposed $S_N2'$ reaction with nucleophiles.[22] However, during the course of this study some puzzling data were obtained that did not completely fit our $S_N2'$ hypothesis.[30] Reaction of the *m*-$CF_3$ analogue **43** did not give completely unlabeled nitrile **44** as the $S_N2'$ mechanism would predict. In fact, the *p*-$NO_2$ derivative **46** gave a nitrile product with up to 40% $^{15}N$-label incorporation. In the case of the *m*-$CF_3$-substituted system **43**, the 18% labeled product **45** suggested that 36% of the reaction proceeded via the *C*-azidodiazirines **51** and **55**. In the case of the *p*-$NO_2$-substituted bromodiazirine **46**, 81% of the reaction appears to involve the *C*-azidodiazirines **50** and **51**. Therefore loss of nitrogen from the $S_N2'$ intermediate **53** cannot be the only source of product. We were therefore forced to consider the possibility that a diazirinium cation was involved since this would lead to **50** and **51** and would account for the label incorporation in the product. But how could *m*-$CF_3$- and *p*-$NO_2$-containing systems **43** and **46** lead to diazirinium cations while *p*-H-, *p*-$CH_3$-, and *p*-$OCH_3$-substituted systems **31** gave no evidence for such cations?

Ordinarily, reactions of azide ion with bromodiazirines were carried out under subdued lighting in order to avoid potential complications due to irradiation of the bromodiazirines. We were fortunate to observe that, in the reaction of **46** with azide ion, the rate of

(25) Padwa, A.; Eastman, D. *J. Org. Chem.* **1969**, *34*, 2728.
(26) Dailey, W. P. *Tetrahedron Lett.* **1987**, *28*, 5801.
(27) Gassman, P. G.; Tidwell, T. T. *Acc. Chem. Res.* **1983**, *16*, 279.
(28) Krogh-Jespersen, K. *Tetrahedron Lett.* **1980**, *21*, 4553.
(29) Krogh-Jespersen, K.; Young, C. M.; Moss, R. A.; Wlostowska, J. *Tetrahedron Lett.* **1982**, *23*, 2339.
(30) Creary, X.; Sky, A. F.; Phillips, G. *J. Org. Chem.* **1990**, *55*, 2005.




nitrogen evolution seemed to increase when the laboratory lights were turned on. When the reaction of **46** with $^{15}N$ terminally labeled azide ion was carried out under ordinary laboratory lighting, the amount of label incorporation increased to 47%. Figure 1 shows the effect of light on the rate of reaction of the *m*-$CF_3$-substituted bromodiazirine **43** with azide ion. The reaction is fastest when exposed to room light. In the dark, the reaction proceeds at an intermediate rate, and the reaction is slowest when light is excluded *and* a trace of galvinoxyl (a stable free radical) is added. The amount of $^{15}N$-label incorporation in the nitrile product is greatest (42%) in the reaction exposed to room light. The dark reaction led to 18% label incorporation, while the reaction with added galvinoxyl gave only 11% label incorporation. We conclude that reactions of certain arylbromodiazirines with azide ion in the light may proceed via a different mechanism than in the dark.

Having worked in the laboratory of J. F. Bunnett as a postdoctoral research associate when the $S_{RN}1$ mechanism of aromatic substitution[31] was being established, this general mechanism immediately came to mind. Indeed, the $S_{RN}1$ mechanism, in competition with the $S_N2'$ mechanism, nicely accounts for the reactivity of both **43** and **46** with azide ion. It is proposed that **43** reacts mainly (85%) by the $S_{RN}1$ chain process when exposed to room light.[32] The *p*-$NO_2$ derivative **46** gives 95% reaction by the $S_{RN}1$ mechanism under these conditions. This process involves formation of the radical anion **52** followed by loss of bromide to generate the diazirinyl radical **53**.[33] Coupling of the diazirinyl radical **53** with azide ion gives the new radical anion **54**, which would subsequently transfer an electron to the starting arylbromodiazirine. This would regenerate the radical anion **52** and propagate the chain. The *C*-azidodiazirines **55** and **56** serve as the source of nitrile product by rapid extrusion of two molecular nitrogens.

(31) 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.

(32) 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.

(33) The initiation mechanism for these reactions is unknown. However, photoinitiated electron transfer in a charge-transfer complex has been suggested in certain photoinitiated $S_{RN}1$ reactions. See: Fox, M. A.; Younathan, J.; Fryxell, G. E. *J. Org. Chem.* **1983**, *48*, 3109.

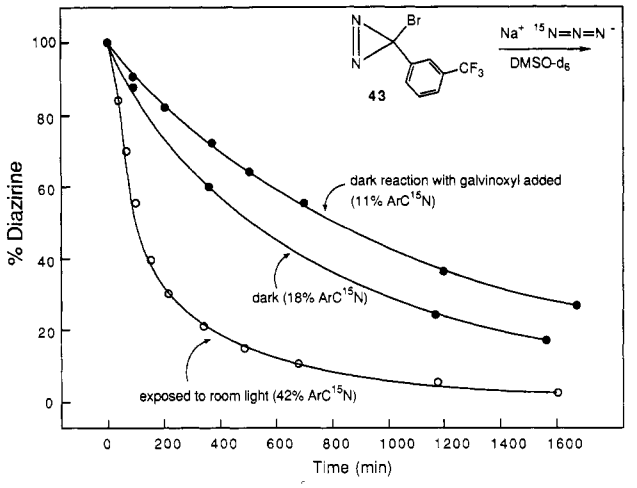



**Figure 1.** Reaction of arylbromodiazirine **43** with $^{15}N$ terminally labeled sodium azide.

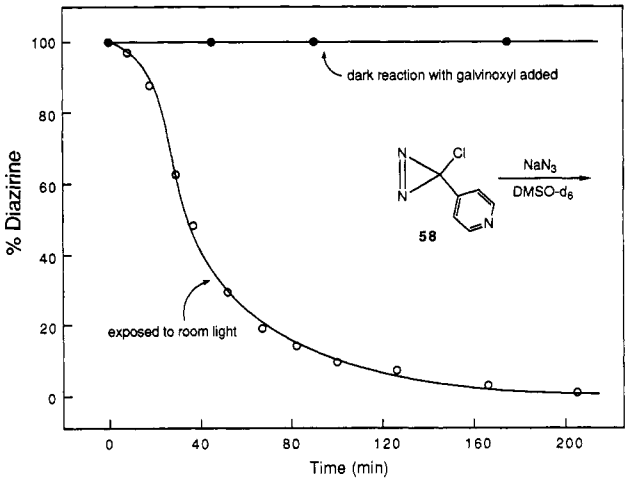
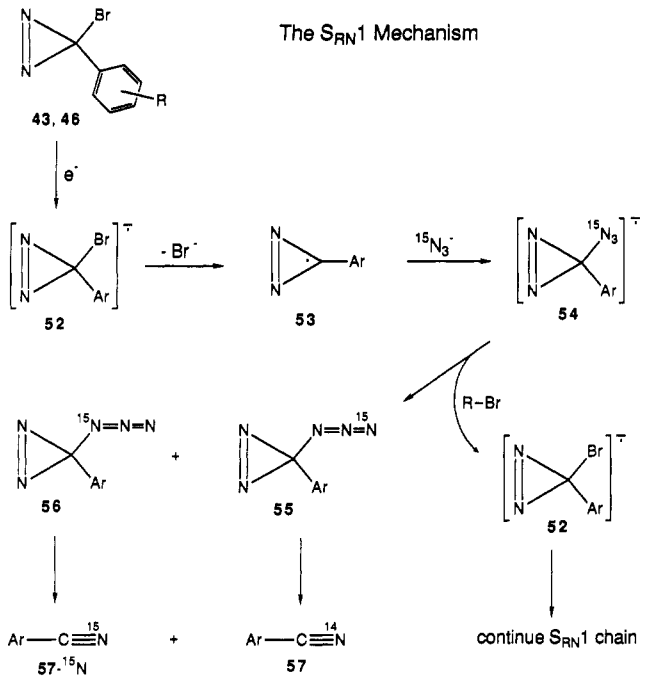



**Figure 2.** Effect of light on the reaction of 4-pyridylchlorodiazirine (**58**) with azide ion.

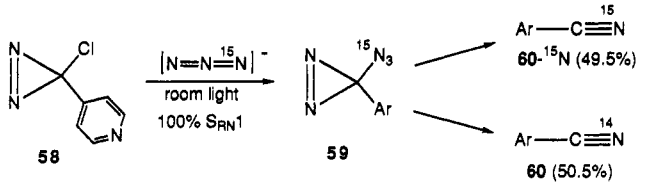
Superimposed on this radical chain substitution process is a nonchain $S_N2'$ process which generates unlabeled nitrile via the *N*-azidodiazirine **49**. For the *m*-$CF_3$-substituted bromodiazirine **43**, this competing $S_N2'$ process accounts for 15% of the reaction in the light. In the dark it accounts for 64% of the reaction, while the addition of galvinoxyl results in 78% $S_N2'$ reaction. Of interest is the fact that even in the dark with added galvinoxyl, which is known to quench other aliphatic $S_{RN}1$ processes,[34] the $S_{RN}1$ reaction of **43** can still occur to a small extent.

Arylchlorodiazirines can also be induced to react with azide ion by the $S_{RN}1$ mechanism when exposed to room light. Under these conditions, the $S_N2'$ process appears to be much slower than the $S_{RN}1$ process. This is illustrated in Figure 2 for 4-pyridylchlorodiazirine (**58**), which is one of the more reactive chlorodiazirines studied. After a short induction period, the reaction in the light proceeds smoothly to completion. By way of contrast, in the dark with galvinoxyl added, the reaction is completely quenched (presumably due to shortening of the chain length by the stable free radical, galvinoxyl).

(34) 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.




Labeling studies with $^{15}N$ terminally labeled azide ion showed that the nitrile product derived from **58** contained 49.5% $^{15}N$. This is precisely what is expected from 99% labeled azide if the reaction proceeded *exclusively* via the $S_{RN}1$ mechanism to produce the *C*-azidodiazirine **59**. Other chlorodiazirines showed similar behavior when reacted with labeled azide ion. The rate of the $S_{RN}1$ reaction appears to be substituent dependent. Qualitatively, electron-withdrawing groups on the aromatic ring increase the rate so that, for a series of arylchlorodiazirines, rates followed the order Ph < *p*-$CF_3C_6H_4$ < *p*-$NO_2C_6H_4$ < pyridyl. For phenylchlorodiazirine, which reacts sluggishly by the $S_{RN}1$ reaction, a trace of product (2%) derived from the competing $S_N2'$ reaction is apparent from $^{15}N$-labeling studies.




Further support for the $S_{RN}1$ mechanism comes from sonication experiments. It has been reported that ultrasonic treatment of the reaction of *p*-nitrobenzyl bromide with nitronate anion can induce the $S_{RN}1$ reaction.[35] Figure 3 shows a comparison of the reactivity of **58** in the dark and in the dark under ultrasonic irradiation.[36] Care was taken to insure that the temperature of the sonication bath was maintained at the temperature of the dark reaction. While the initiation by ultrasound is not as spectacular as initiation by light, it is nonetheless real and reproducible. The mechanism of initiation of the $S_{RN}1$ reaction by sonication is unknown. It cannot be a surface phenomenon since the diazirine–azide reaction in DMSO is completely homogeneous. Clearly this is an area that needs to be further studied. Finally it is interesting to note that

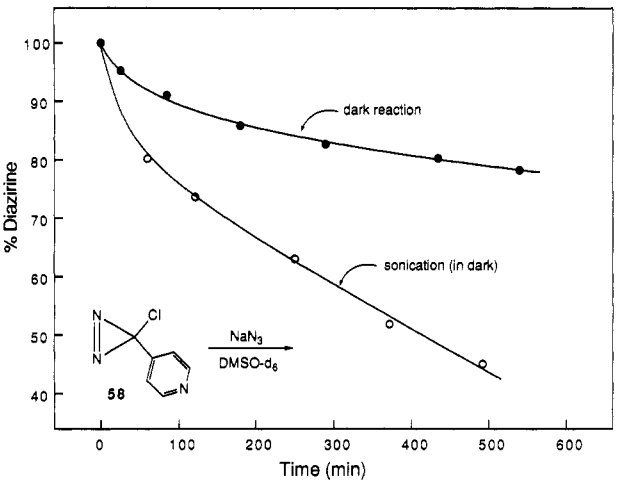
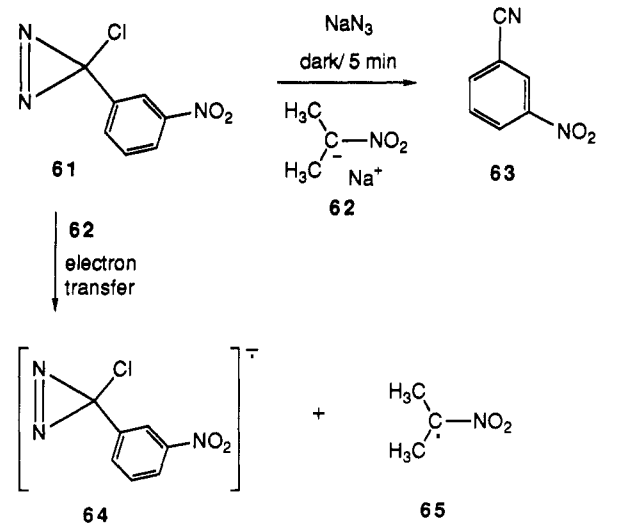



**Figure 3.** Effect of sonication on the reaction of 4-pyridylchlorodiazirine (**58**) with azide ion.

there is a significant dark reaction when galvinoxyl is omitted from the reaction. The mechanism of initiation of the dark reaction is also uncertain.

The sodium salt of 2-nitropropane, **62**, can also initiate the reaction of certain arylchlorodiazirines with azide ion.[37] Thus addition of a catalytic amount (10%) of **62** to a solution of **61** and sodium azide in DMSO *in the dark* resulted in rapid formation of a high yield of the nitrile product **63**. Under the same conditions, without addition of **62**, there was no reaction. Small amounts of sodium thiophenoxide also initiate the same transformation. The mechanism for these initiation processes presumably involves electron transfer from the nitronate salt (or from thiophenoxide) to the chlorodiazirine. This generates the radical anion **64** and sets the chain process in motion.

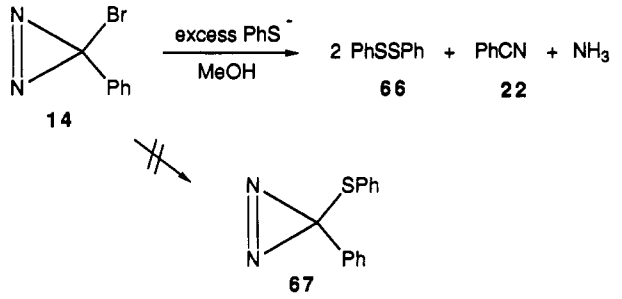



**Reaction of Halodiazirines with Thiophenoxide.** Since azide ion has been found to readily undergo $S_{RN}1$ reaction with certain halodiazirines, we wanted to determine if thiophenoxide ion could also react with arylhalodiazirines via the $S_{RN}1$ process. This nucleophile has been previously used in a variety of aliphatic and aromatic $S_{RN}1$ reactions. We have therefore reacted phenylbromodiazirine (**14**) with sodium thio-

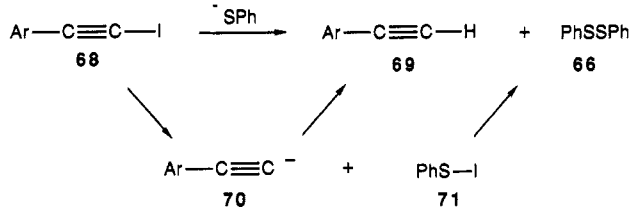
(35) Einhorn, C.; Einhorn, J.; Dickins, M. J.; Luche, J. L. *Tetrahedron Lett.* **1990**, *31*, 4129.
(36) Unpublished work from our laboratory.

(37) 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.

phenoxide in methanol at room temperature.[36] The diazirine was consumed, but no simple substitution product **67** (or any products conceivably derived from decomposition of **67** via a carbene intermediate) was observed. Additionally, no nitrogen evolution was observed over the course of the reaction. A large amount of diphenyl disulfide (**66**) was formed (2 mol of **66**/mol of **14**) along with benzonitrile (64%) and ammonia. Other arylhalodiazirines also reacted with thiophenoxide to give high yields of diphenyl disulfide. Electron-withdrawing substituents on the aryl ring slightly increased the rate of reaction.

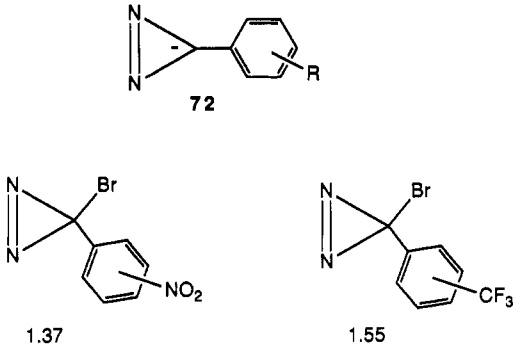



What is the mechanistic origin of the oxidized product, diphenyl disulfide, and the reduced products benzonitrile and ammonia? The formation of diphenyl disulfide is reminiscent of an attempted acetylenic $S_{RN}1$ reaction that was carried out in the Bunnett laboratory.[38] Phenyliodoacetylene (**68**) was reacted with thiophenoxide in the dark, and also in an attempted photoinitiated reaction. Under both sets of conditions, high yields of diphenyl disulfide and phenylacetylene were formed. An earlier mechanistic study in methanol[39] concluded that diphenyl disulfide is formed by nucleophilic attack by thiophenoxide at halogen and displacement of acetylide ion **70**. Subsequent reaction of



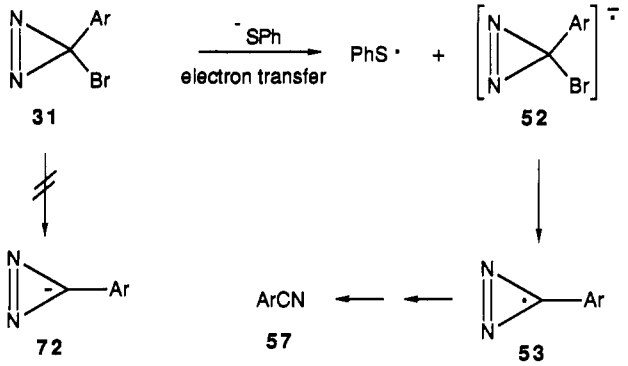

the byproduct, benzene sulfenyl iodide (**71**), with more thiophenoxide would give diphenyl disulfide. An analogous mechanism for formation of diphenyl disulfide in reaction of arylbromodiazirines with thiophenoxide is worthy of consideration. Such a mechanism would involve nucleophilic attack at halogen and displacement of a diazirinyl anion. Although a diazirinyl anion is a formal $4n$ Hückel antiaromatic intermediate, a recent study has shown that the parent unsubstituted diazirinyl anion can be generated in the gas phase.[40]

In order to probe this mechanistic possibility further, rates of reaction of the meta- and para-substituted arylbromodiazirines with thiophenoxide were compared.[36] If the anion **72** was formed in a rate-limiting process, then systems substituted with para electron-withdrawing groups would be significantly more reactive than the meta analogues since **72** should be especially stabilized by the para substituent. However, the *m*-




$NO_2$- and *m*-$CF_3$-substituted halodiazirines are actually *more reactive* than the para analogues. These para/meta ratios are inconsistent with the anion **72** being formed in a rate-limiting attack of thiophenoxide on halogen. However, these experiments do not rule out the involvement of **72** at some point after the rate-determining step.[41]

We propose that the reaction of arylhalodiazirines with thiophenoxide ion is initiated by rate-limiting electron transfer from thiophenoxide to the halodiazirine. Indeed, rates of reaction of substituted arylbromodiazirines **31** with thiophenoxide parallel $S_{RN}1$ rates with azide ion, i.e., Ph < *p*-$CF_3C_6H_4$ < *p*-$NO_2C_6H_4$. Loss of halide from an initially formed radical anion **56** would generate the diazirinyl radical **53**. This sequence has the makings of an $S_{RN}1$ chain

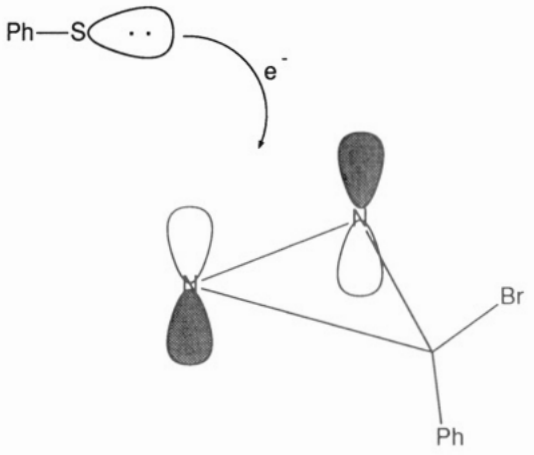



process, and indeed, this is our proposed mechanism for the thiophenoxide-initiated $S_{RN}1$ reaction of azide ion with arylchlorodiazirines. At this point, since no substitution product **67** is observed, it is believed that the mechanism diverges from the standard $S_{RN}1$ process. We could speculate further as to the origin of ultimate product, benzonitrile. However, further studies are necessary to support any speculation.

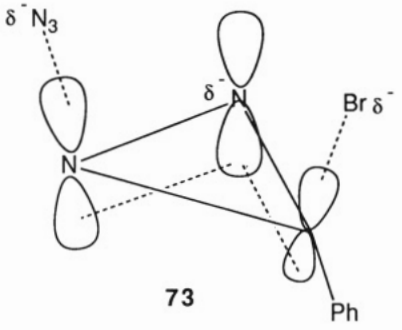
An important question concerns the differing reactivities of thiophenoxide relative to nucleophiles such as $F^-$, $CH_3O^-$, $CN^-$, and $N_3^-$ (in the dark). Why do fluoride, methoxide, cyanide, and azide ion lead to $S_N2'$ reactivity while thiophenoxide leads to electron transfer? We speculate that both the azide (as well as fluoride, methoxide, and cyanide) and the thiophenoxide reactions begin with an approach of the nucleophile to the N=N $\pi^*$ orbital from above the plane of

(38) Bunnett, J. F.; Creary, X.; Sundberg, J. E. *J. Org. Chem.* **1976**, *41*, 1707.
(39) Verploegh, M. C.; Donk, L.; Bos, H. J. T.; Drenth, W. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 765.
(40) Kroeker, R. L.; Kass, S. R. *J. Am. Chem. Soc.* **1990**, *112*, 9024.
(41) Despite potential antiaromaticity, **72** should not be considered as a "straw man". We are actively pursuing **72** as a potential intermediate (formed after the rate-determining step) in the ultimate formation of nitrile product.

the three-membered ring as in a Michael addition to a carbon–carbon double bond. In the case of thiophenoxide, an electron is transferred at long range before bonding to nitrogen has progressed significantly. This reflects the low oxidation potential of thiophenoxide in contrast to the higher oxidation potential of azide ion (or fluoride, methoxide, or cyanide). The thiophenoxy radical can diffuse away and eventually couple to give diphenyl disulfide. Less readily oxidized nucleophiles, such as azide ion, complete the addition to the nitrogen–nitrogen double bond (with simultaneous loss of bromide as in **73**) without the occurrence of electron transfer.




Electron Transfer at Long Range from Thiophenoxide to **14**




**73**

Proposed Transition State for Reaction of Azide with **14**.

**Concluding Remarks.** Arylbromodiazirines can react with azide ion, as well as with other nucleophiles, by an $S_N2'$ mechanism. Despite potential aromatic properties, $^{15}N$-labeling studies do not support the involvement of diazirinium cations. In the case of azide ion, the $S_{RN}1$ substitution mechanism may compete, especially when arylchlorodiazirines are used and the reaction is not shielded from light. The $S_{RN}1$ process can be initiated by light, addition of nitronate or thiophenoxide ions, or sonication. The initiation by sonication is fascinating and deserves further investigation. Thiophenoxide ion also reacts with arylhalodiazirines by a process initiated by electron transfer. However, $S_{RN}1$ products are not formed. The origin of the actual product, benzonitrile, is speculative, but the involvement of the potentially antiaromatic diazirinyl anion must be considered. The generality of the $S_{RN}1$ reaction needs to be further investigated since this reaction has the potential for generating previously unavailable diazirines and carbenes. It is concluded that diazirinyl radicals are viable intermediates in reactions of halodiazirines. The arylhalodiazirines therefore continue to provide a rich area for discovery of interesting intermediates and mechanisms.

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