Reaction of Arylhalodiazirines with Thiophenoxide: A Redox Process

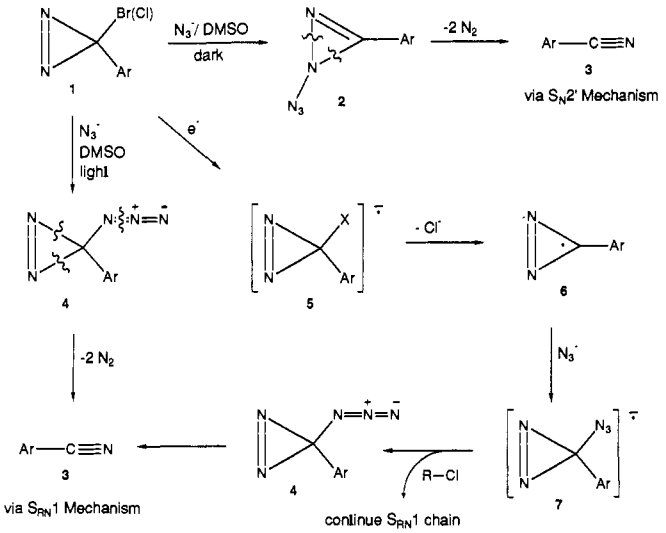
Xavier Creary,* Anthony F. Sky, Gillian Phillips, and David E. Alonso

Contribution from the Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556

Received November 24, 1992. Revised Manuscript Received May 5, 1993

Abstract: Phenylbromodiazirine reacts with thiophenoxide ion in methanol to give benzonitrile, benzamidine, ammonia, and diphenyl disulfide. The reaction is general for arylhalodiazirines, with electron-withdrawing groups on the aromatic ring exerting a small rate-enhancing effect. Three potential mechanisms are suggested for this redox process. These mechanisms include an N-sulfenylated diazirine, a diazirinyl radical, and a diazirinyl anion. Ring opening of these intermediates and subsequent transformations would lead to benzonitriles, benzamidine, and ammonia. A key intermediate in these transformations is $PhSNH_2$, **32**. This intermediate has been independently generated and found to rapidly convert to ammonia and diphenyl disulfide under the reaction conditions. Another proposed intermediate, *N*-(phenylthio)benzamidine, **38**, has also been independently generated and subjected to the reaction conditions, where benzamidine and more diphenyl disulfide result. Theoretical calculations suggest the existence of isomeric diazirinyl anions. In addition to a diazirinyl ion with charge essentially on carbon, there is also an allylic-type ion with charge on the two nitrogen atoms. Single-electron reduction of a diazirinyl radical necessarily leads to a nitrogen-centered diazirinyl anion. Conversion of this anion to the carbon-centered diazirinyl anion is a forbidden process. These theoretical studies suggest that the diazirinyl anion may be a viable intermediate in solution.

We have been interested in the chemistry of halodiazirines and in the mechanisms by which these substrates react with nucleophiles. Toward this end, we have reacted arylhalodiazirines **1** with azide ion.[1] A study using a ^{15}N-labeled diazirine (and a complimentary study using ^{15}N-labeled sodium azide) led us to the conclusion that azide ion first reacts with **1** via an S_N2' mechanism to generate *N*-azidodiazirine **2**. This intermediate rapidly loses 2 mol of nitrogen to give benzonitrile, **3**, as the only observed product. The nitrogen in the benzonitrile product is derived from one of the ring nitrogens of **1** and not from azide ion. A similar conclusion has been reached by Dailey[2] who carried out the same type of labeling study.



While this S_N2' mechanism predominates in the reaction of azide ion with **1** in the dark, we have found that, under room light, certain arylhalodiazirines **1** can undergo substitution reactions with azide ion by an $S_{RN}1$ process involving the chain process illustrated.[3] Studies using ^{15}N-labeled azide ion supported the intermediacy of *C*-azidodiazirine **4**, which presumably loses molecular nitrogen rapidly to give the corresponding nitrile **3**. Under these $S_{RN}1$ conditions, the nitrogen atom of the benzonitrile is derived from the sodium azide. With certain substrates **1**, these two mechanisms can compete.

Since azide ion has been found to readily undergo $S_{RN}1$ reaction with certain halodiazirines, we wanted to determine if thiophenoxide could also react with arylhalodiazirines via the $S_{RN}1$ process. This nucleophile has been previously used in a variety of aliphatic[4] and aromatic[5] $S_{RN}1$ reactions. Catalytic thiophenoxide ion is also an initiator in the $S_{RN}1$ reaction of halodiazirines with azide ion.[3] Reported here are the results of a study of the reaction of halodiazirines with thiophenoxide ion.

Results and Discussion

Phenylbromodiazirine, **8**, was reacted with sodium thiophenoxide in methanol at room temperature (under nitrogen). The diazirine was consumed, but no simple substitution product **12** (or any products conceivably derived from decomposition of **12** via a carbene intermediate) was observed. Additionally, *no nitrogen evolution* was observed over the course of the reaction. Examination of the organic extract on completion of the reaction revealed a large amount of diphenyl disulfide along with a moderate amount of benzonitrile (64%). The large amount of diphenyl disulfide (2 mol of PhSSPh per mole of arylbromodiazirine) does not arise from air oxidation of thiophenoxide. A control experiment carried out under the same conditions but without addition of phenylbromodiazirine, **8**, gave only a trace of diphenyl disulfide (derived from air oxidation). The moderate

(1) Creary, X.; Sky, A. F. *J. Am. Chem. Soc.* **1990**, *112*, 368.
(2) Bainbridge, K. E.; Dailey, W. P. *Tetrahedron Lett.* **1989**, *30*, 4901.
(3) Creary, X.; Sky, A. F.; Phillips, G. *J. Org. Chem.* **1990**, *55*, 2005.
(4) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.
(5) 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.

0002-7863/93/1515-7584$04.00/0

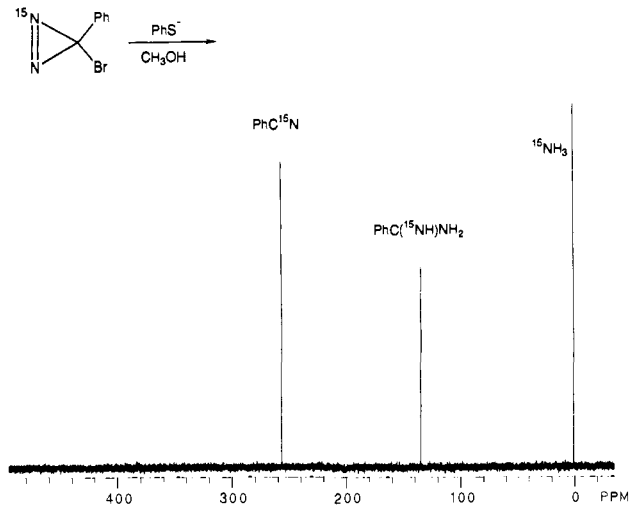
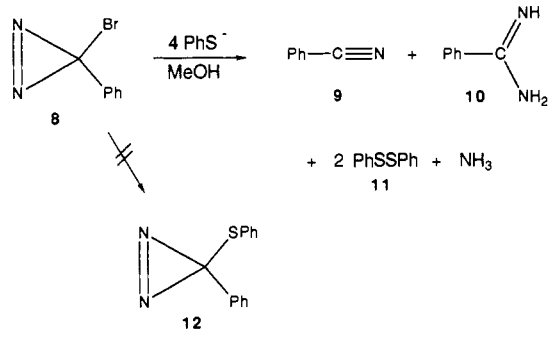


Figure 1. ^{15}N NMR spectrum of the products of the reaction of sodium thiophenoxide with ^{15}N-labeled **8**.

yield of benzonitrile was not due to losses of this material during the aqueous workup. The fates of the second nitrogen atom of **8** and the missing phenyl groups are obvious questions which were answered using ^{15}N NMR spectroscopy. Figure 1 shows a ^{15}N NMR spectrum of the products of a reaction of thiophenoxide with ^{15}N-labeled phenylbromodiazirine (before an aqueous workup). This spectrum shows that the second nitrogen of **8** ends up as ammonia and that a significant amount of benzamidine, **10**, is also produced. Both of these products, being water soluble, are lost during an aqueous workup. The reaction stoichiometry



requires 4 mol of thiophenoxide to produce two diphenyl disulfides. When an insufficient amount of thiophenoxide is added to satisfy this stoichiometry, all of the thiophenoxide is converted to diphenyl disulfide and unreacted phenylbromodiazirine is recovered. The balanced equation for this transformation also requires the formation of 3 mol of sodium methoxide as well as 1 mol of sodium bromide.

Other arylhalodiazirines also reacted with thiophenoxide to give high yields of diphenyl disulfide. In the case of electron-donor groups on the aryl ring, the substituted benzonitriles remained the major products. However, when the substituent on the aromatic ring becomes electron-withdrawing, increasing amounts of a third product, an imino ester, are formed. This is illustrated for the reaction of ^{15}N-labeled 3-pyridylchlorodiazirine with thiophenoxide ion. Figure 2 shows the ^{15}N NMR spectrum of the reaction mixture before a workup. Imino ester **16** appears as a broad signal at δ 208. The presence of this product in the reaction mixture was confirmed by ^1H NMR which also shows that, under the basic conditions of the reaction, imino ester **16** is formed by reaction of nitrile **14** with methanol.[6] It is important to note that benzamidine **15** is not derived from reaction of **14** or **16** with ammonia. Control experiments show that these are

(6) At equilibrium in methanol, the ratio of **14**:**16** was 1:3.2.

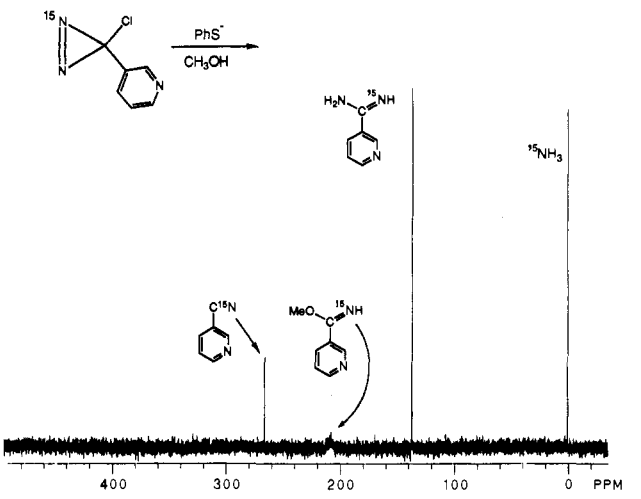


Figure 2. ^{15}N NMR spectrum of the products of the reaction of sodium thiophenoxide with ^{15}N-labeled **13**.

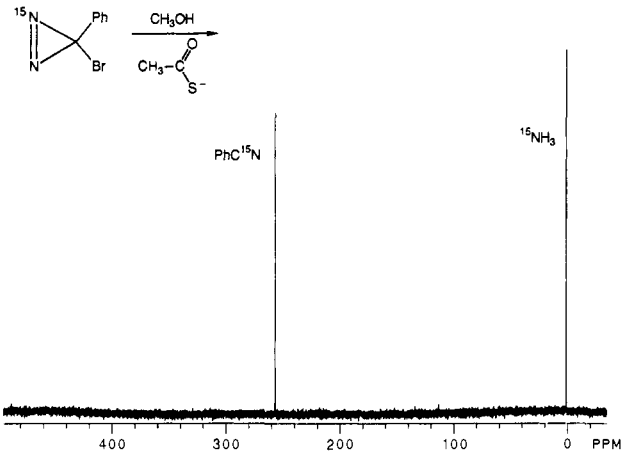
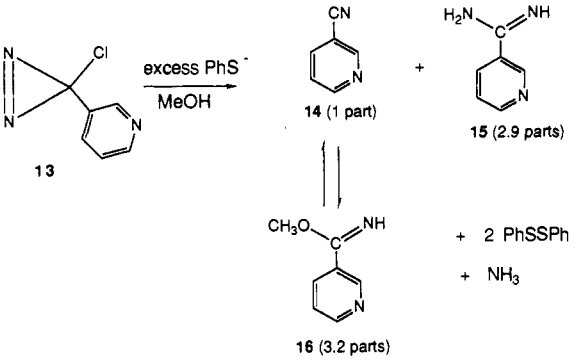


Figure 3. ^{15}N NMR spectrum of the products of the reaction of sodium thioacetate with ^{15}N-labeled **8**.

slow processes under the reaction conditions. Yet, benzamidines are formed quite rapidly under our reaction conditions.



The reaction of phenylbromodiazirine, **8**, with sodium *n*-butane thiolate follows a similar pathway, but the reaction is about 40 times faster than the thiophenoxide reaction. Reaction of **8** with sodium thioacetate follows a slightly different course, as shown in Figure 3. In this reaction, the sole aromatic-containing product is benzonitrile (with no benzamidine being formed). As before, the second nitrogen atom of **8** ends up as ammonia.

Kinetic Studies. These reactions of thiophenoxide with arylhalodiazirines can be conveniently monitored spectrophotometrically. In an attempt to gain insight into the reaction mechanism, we obtained rate data for the reaction of these halodiazirines with thiophenoxide. Figure 4 shows the effect of thiophenoxide

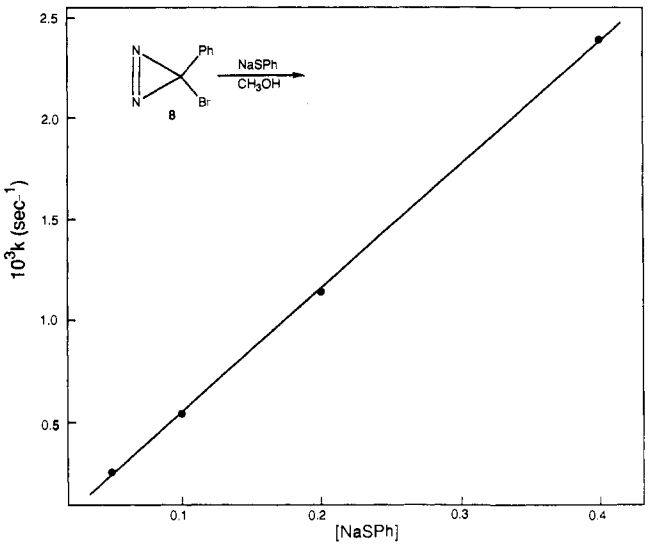
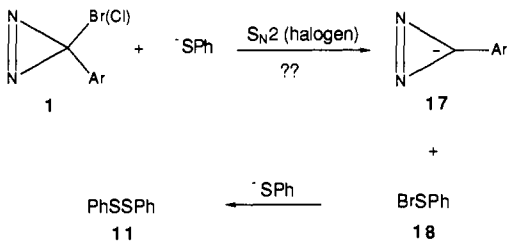


Figure 4. Plot of the rate of reaction of phenylbromodiazirine, **8**, with NaSPh in methanol at 25.0 °C vs [NaSPh].

ion concentration on the pseudo-first-order rate constant for the reaction of **8**. The linear plot shows that the reaction is first order in thiophenoxide ion concentration. The effect of aryl substituents on the rate of reaction has also been determined (Table I). Electron-withdrawing substituents increase the rate of reaction, but the substituent effect is not large. The entire rate spread is only a factor of 22 for the bromodiazirines studied and a factor of 33 for the chlorodiazirines. There is a fair correlation with Hammett σ values (r = 0.97; Figure 5). Rate data given in Table I also show that the arylbromodiazirines are approximately 14–20 times more reactive than the corresponding arylchlorodiazirines.

Mechanism of Reaction. The transformations described above are rather remarkable as well as unexpected. This high-yielding oxidation of thiophenoxide by halodiazirines, with concomitant reduction of the ring nitrogens all the way to the ammonia oxidation state, deserves some mechanistic comment. One process that immediately comes to mind involves nucleophilic attack by thiophenoxide at halogen and displacement of **17**. Subsequent reaction of the byproduct, PhSBr, with more thiophenoxide would give diphenyl disulfide. Such mechanisms for oxidation of thiophenoxide, and coupled reduction of halogenated substrates, have precedent in the reaction of haloacetylenes[7] and 2-halo-2-nitropropanes[8] with thiolates. Although **17** 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.[9] However we do not believe that this process operates in the halodiazirine–thiophenoxide reaction for the following reasons. The rate of nucleophilic attack of thiophenoxide on halogen should be quite dependent on the aryl substituent since the anion **17** should be substantially stabilized by electron-withdrawing substituents (especially para conjugating groups). This is not what is observed. As mentioned before, the rate spread is only a factor of 22 for the arylbromodiazirines and a factor of 33 for the arylchlorodiazirines. Also, there is no special rate effect resulting from anion-stabilizing para substituents (see Figure 5). Rate data for para- and meta-substituted diazirines containing NO_2, CF_3, and SO_2CH_3 substituents can be compared. In these systems, the meta-substituted halodiazirines are all actually *more reactive* than the para analogs. These para/meta ratios are completely inconsistent with the anion **17** being formed in a rate-limiting attack of thiophenoxide on halogen. If the anion **17** was being formed in a rate-limiting process, then systems substituted with para electron-withdrawing groups would be significantly more reactive since these anions should be especially stabilized by the para substituent.

The bromide/chloride rate ratio can also be used as evidence against nucleophilic attack on halogen. Haloacetylenes **19** have been reacted with thiolate,[7c] and the mechanism involves nucleophilic attack of thiolate at halogen. The bromide/chloride rate ratio is 2.6 × 10^3 and reflects the greater polarizability of the bromine atom. The bromide/chloride rate ratio is 10^5 when sulfide (S^{2-}) is the nucleophile. By way of contrast, the bromide/chloride rate ratio for reaction of arylhalodiazirines with thiophe-

Table I. Rate Constants for Reaction of Arylhalodiazirines **1** with 0.20 M NaSPh in Methanol at 25.0 °C

aryl group	k, s^{-1}
Bromodiazirines	
C_6H_5	1.14×10^{-3}
	2.39×10^{-3} (0.40 M)
	5.41×10^{-4} (0.10 M)
	2.50×10^{-4} (0.05 M)
p-$CH_3C_6H_4$	8.27×10^{-4}
p-$CH_3OC_6H_4$	9.18×10^{-4}
m-BrC_6H_4	6.17×10^{-3}
p-$CF_3C_6H_4$	7.22×10^{-3}
m-$CF_3C_6H_4$	1.12×10^{-2}
p-$NO_2C_6H_4$	1.87×10^{-2}
m-$NO_2C_6H_4$	2.55×10^{-2}
Chlorodiazirines	
C_6H_5	5.57×10^{-5}
p-$CF_3C_6H_4$	4.64×10^{-4}
3,5-$F_2C_6H_3$	8.41×10^{-4}
p-$NO_2C_6H_4$	1.28×10^{-3}
m-$NO_2C_6H_4$	1.83×10^{-3}
p-$CH_3SO_2C_6H_4$	9.07×10^{-4}
m-$CH_3SO_2C_6H_4$	1.32×10^{-3}

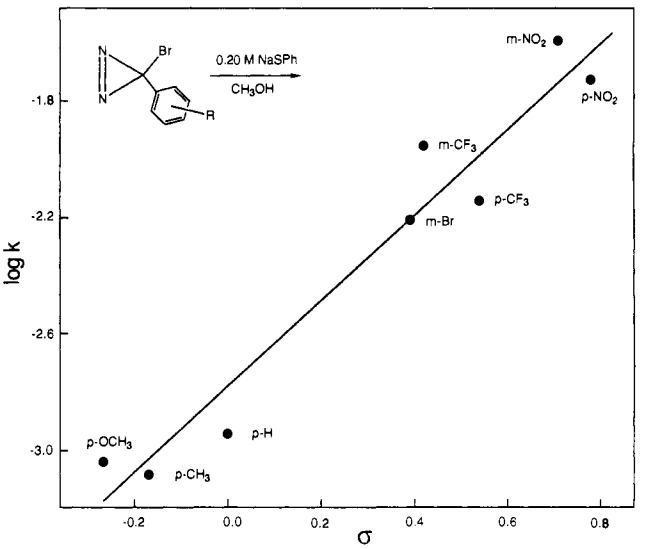
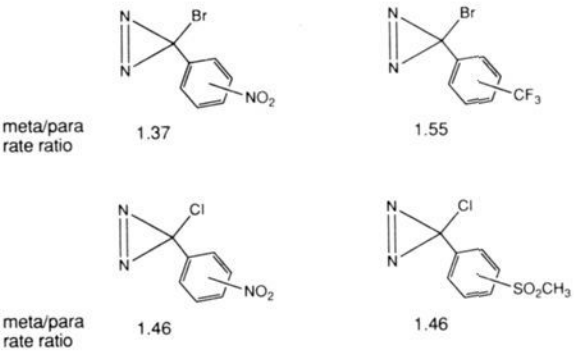


Figure 5. Plot of log K for the reaction of arylbromodiazirines **1** with 0.20 M NaSPh in methanol at 25.0 °C vs σ.

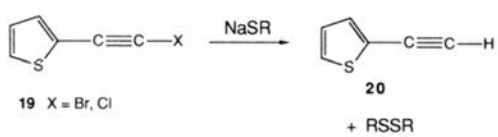
(7) (a) Truce, W. E.; Hill, H. E.; Boudakian, M. M. *J. Am. Chem. Soc.* **1956**, *78*, 2760. (b) Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1963**, *82*, 183. (c) Verploegh, M. C.; Donk, L.; Bos, H. J. T.; Drenth, W. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 765. (d) Bunnett, J. F.; Creary, X.; Sundberg, J. E. *J. Org. Chem.* **1976**, *41*, 1707.

(8) Bowman, W. R.; Richardson, G. D. *Tetrahedron Lett.* **1981**, *22*, 1551.

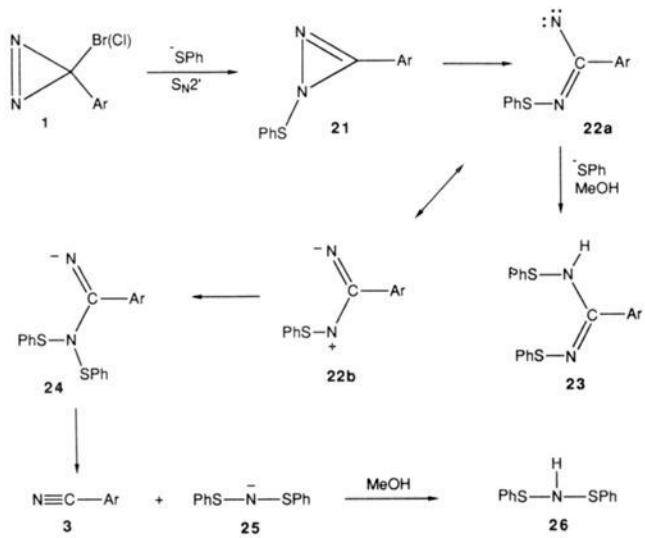
(9) Kroeker, R. L.; Kass, S. R. *J. Am. Chem. Soc.* **1990**, *112*, 9024.



noxide is ~20. These much smaller ratios suggest that the rate-limiting step of the reaction of thiophenoxide with haloacetylenes differs from that in the halodiazirine mechanism.

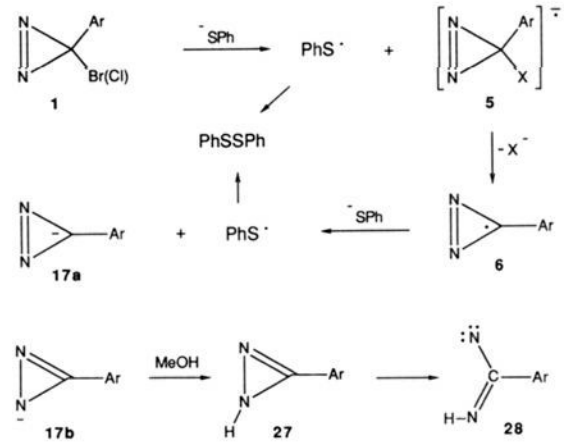


Consider the following mechanistic possibilities. A rate-limiting S_N2' attack of thiophenoxide at the ring nitrogen would give N-sulfenated diazirine **21**. Opening of this intermediate and nucleophilic attack by thiophenoxide could lead to **23** or **24**. The intermediate **24** could serve as the source of the benzonitrile by loss of the anion **25**. Subsequent reaction of **25** with thiophenoxide in methanol would lead to ammonia and diphenyl disulfide. Benzamidine could also be produced from **23** or **24**.

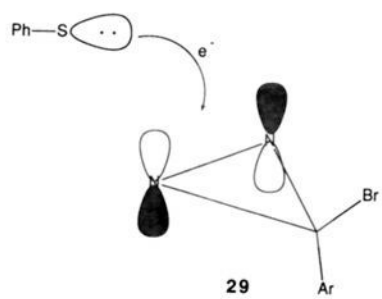


While this mechanism is an attractive possibility, two problems are apparent. If the S_N2' product **21** were indeed an intermediate in the reaction, we would expect that a second S_N2' reaction on **21** would lead to products of type **12**. Analogous substitution products are produced by consecutive S_N2' reactions when F^-, OCH_3^-, and CN^- react with halodiazirines in polar aprotic solvents. Secondly, in the S_N2' reaction of azide ion with **1** (the dark reaction), electron-donating groups on the aromatic ring increased the reaction rate.[1,10] This was attributed to aryl group stabilization of the developing carbon–nitrogen double bond in the S_N2' transition state of the azide reaction. In the reaction of thiophenoxide with arylhalodiazirines, the opposite type of substituent effect is observed, i.e., electron-withdrawing substituents increased the reaction rate. Therefore, *while the S_N2' mechanism cannot be eliminated*, the available data suggest that other mechanisms should be considered.

Consider next the possibility that reaction of arylhalodiazirines with thiophenoxide ion might be initiated by *rate-limiting electron transfer* from thiophenoxide to the halodiazirine. Loss of halide from an initially formed radical anion, **5**,[11] would generate the diazirinyl radical **6**. In order to account for the observed products, two potential fates of the diazirinyl radical **6** are considered. If **6** were to be further reduced by electron transfer from thiophenoxide, then the anion **17** would result. Coupling of thiophenoxy radicals would formally produce diphenyl disulfide. Protonation of the diazirinyl anion **17** on nitrogen would give **27**, which could open to imino nitrene **28**. Subsequent transformations of **28** would lead to the observed products.



We have previously observed[3] that a catalytic amount of thiophenoxide ion can initiate the radical chain $S_{RN}1$ reaction of certain arylhalodiazirines with azide ion. For certain substrates, this electron-transfer-initiated $S_{RN}1$ reaction with azide ion can compete with the S_N2' mechanism. In the reaction of pure thiophenoxide ion with arylhalodiazirines in methanol, electron transfer from thiophenoxide ion to the halodiazirine is therefore a reasonable alternative to the S_N2' mechanism. This suggestion would involve approach of the polarizable thiophenoxide ion to the N=N bond with electron transfer occurring into the π^* orbital, as in **29**. The effect of substituents on the aryl group should not be large since they represent only a minor perturbation of the N=N bond. Our rate data are consistent with this suggestion since electron-withdrawing groups are known to decrease the reduction potential of the diazirine. An electrochemical study on phenylchlorodiazirine and the *p*-OCH_3 and *p*-NO_2 analogs showed that the ease of reduction followed the order *p*-NO_2 > *p*-H > *p*-OCH_3.[12]

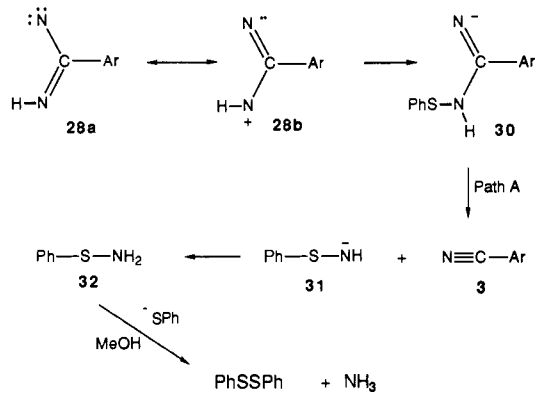


(10) For the original rate data for reaction of **1** with azide ion, see: Moss, R. A.; Terpinski, J.; Cox, D. P.; Denney, D. Z.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1985**, *107*, 2743. See ref 1 for an interpretation of this data in terms of an S_N2' mechanism.

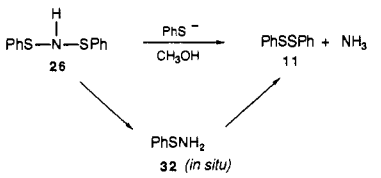
(11) Radical anions of type **5** are shown in brackets to indicate that they may or may not have a finite lifetime, i.e., loss of halide may be concerted with electron transfer.

This second mechanism suggests that the initially formed radical anion **5** rapidly loses halide[11] to generate the diazirinyl radical **6**. This sequence has the makings of an $S_{RN}1$ chain-substitution process, and indeed, this is our proposed mechanism for the thiophenoxide-initiated $S_{RN}1$ reaction of azide ion with arylchlorodiazirines.[3] However, according to this mechanism, the reaction of thiophenoxide with halodiazirines in methanol does not continue along the $S_{RN}1$ pathway, i.e., **6** does not couple with thiophenoxide to generate a new radical anion as in the $S_{RN}1$ reaction. This scheme involves *reduction* of the diazirinyl radical by thiophenoxide ion instead of coupling and is reminiscent of the reaction of 2-iodo-*m*-xylene with thiophenoxide under $S_{RN}1$ conditions.[13] Substantial amounts of *m*-xylene and diphenyl disulfide are produced. This is presumably due to a slower rate of coupling of 2,6-dimethylphenyl radicals with thiophenoxide due to the ortho methyl groups. Apparently, thiophenoxide can reduce 2,6-dimethylphenyl radicals to 2,6-dimethylphenyl anions (which are the source of *m*-xylene) in competition with $S_{RN}1$ coupling. An analogous reductive process on the diazirinyl radical by thiophenoxide ion would produce the formally antiaromatic anion **17**.[14]

In methanol, protonation of the diazirinyl anion **17** on nitrogen would give **27** and subsequent opening would give imino nitrene **28**. This opening of **27** is analogous to the opening of an oxirene to an α-keto carbene[16,17] and generates an electrophilic center. Reaction of **28** with thiophenoxide could give **30**, which would serve as a source of benzonitrile. Elimination of the anion $PhSNH^-$, **31**, from **30** would lead to benzonitrile and $PhSNH_2$ (after protonation). Reaction of **32** with thiophenoxide ion in methanol is a source of additional diphenyl disulfide and ammonia. Although $PhSNH_2$ is an unknown compound,[19] we have reacted

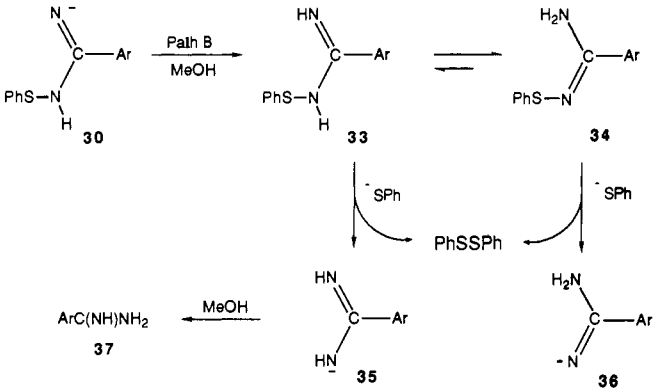


the known dithioamide **26**[20] with thiophenoxide in methanol.



Ammonia and diphenyl disulfide are rapidly formed, presumably from *in situ* generated $PhSNH_2$. This supports the suggestion that $PhSNH_2$ (or $(PhS)_2NH$, **26**) can indeed be a source of ammonia under our reaction conditions.

What is the source of benzamidine? Under the reaction conditions, benzonitrile is not converted to benzamidine. It is suggested that **30** (or **24**) can also be protonated and that **33** (or the tautomer **34**) can serve as the source of benzamidine by sulfenylation of the thiophenoxide ion.[21]

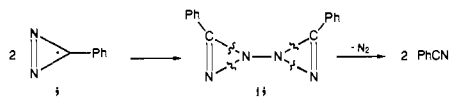


To support this suggestion, benzamidine, **10**, has been sulfenylated using (phenylsulfenyl)phthalimide. The product has the structure of **38** (and not the tautomeric structure analogous to **33**). This was determined from the ^{15}N NMR spectrum of the labeled analog, which shows a downfield singlet at δ 203.7 ($^{15}NSPh$) as well as an upfield triplet at δ 84.2, J_{N-H} = 87 Hz ($^{15}NH_2$). Reaction of **38** with thiophenoxide in methanol gives exclusively PhSSPh and benzamidine (and no benzonitrile).

(12) Under electrochemical reduction conditions, nitriles are produced from arylchlorodiazirines. See: (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.

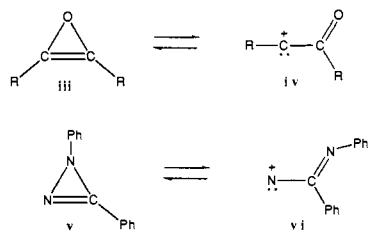
(13) Bunnett, J. F.; Creary, X. *J. Org. Chem.* **1974**, *39*, 3173.

(14) Ingold has observed benzonitrile as a product derived from the diazirinyl radical generated from another source.[15] The proposed source of benzonitrile was the coupling of diazirinyl radicals at nitrogen, as in **ii**, and subsequent loss of N_2, as shown below. While such a mechanism may account for Ingold's observations, a similar dimerization process cannot account for our observations since no nitrogen evolution is observed. Additionally, such a mechanistic sequence would give only 1 mol of diphenyl disulfide per mole of phenylbromodiazirine. Our observation of 2 mol of PhSSPh per mole of halodiazirine argues against this radical-coupling process under our conditions.



(15) Ingold, K. U.; Maeda, Y. *J. Am. Chem. Soc.* **1979**, *101*, 837.

(16) Oxirene **iii** has been suggested to be in facile equilibrium with α-keto carbene, **iv**.[17] An analogous ring-opening process has been suggested for **v**, which is a proposed intermediate in the reaction of phenyllithium with **1**.[18]



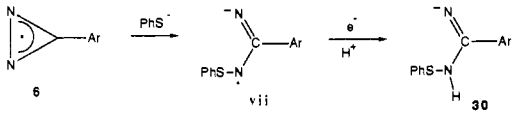
(17) For a review of oxirene chemistry, see: Lewars, E. G. *Chem. Rev.* **1983**, *83*, 519.

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

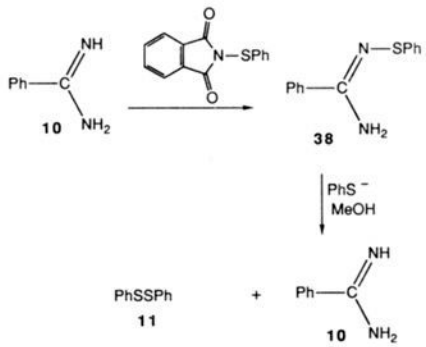
(19) Sulfenamides $ArSNH_2$, where the aryl group is substituted with electron-withdrawing groups, are known. See: Kharasch, N.; Potempa, S. J.; Wehrmeister, H. L. *Chem. Rev.* **1946**, *39*, 269. Attempts to prepare **32** from PhSCl and ammonia[20a] result in formation of **26**. Koval et al. reported arylsulfonylimination of **32**, but no method for the preparation of **32** was given. See: Koval, I. V.; Oleinik, T. G.; Kremlev, M. M. *Zh. Org. Khim.* **1981**, *17*, 1938.

(20) (a) Lecher, H. *Chem. Ber.* **1925**, 409. (b) Mukaiyama, T.; Taguchi, T. *Tetrahedron Lett.* **1970**, 3411.

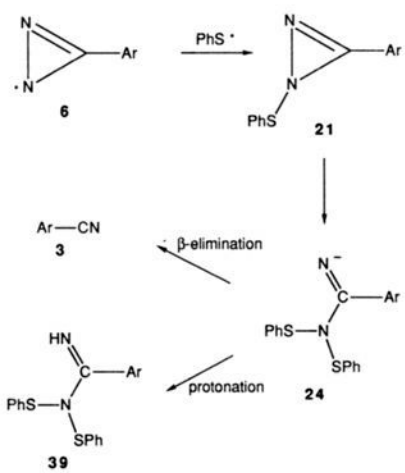
(21) A reviewer has suggested that cleavage of the diazirinyl radical **6** with thiophenoxide ion would generate the radical anion **vii**. Subsequent one-electron reduction and protonation would generate the intermediate **30**. While we would expect that any coupling of the diazirinyl radical **6** with thiophenoxide ion would occur at carbon (as does the azide ion), this possibility must be considered.



Therefore, **38** or the bis-sulfenylated analogs **23** and **39** are viable intermediates in the formation of benzamidine.



An alternative fate of the diazirinyl radical **6** could be coupling with the thiophenoxy radical at nitrogen before cage escape occurs. This would also produce the substitution product **21**. While this product is formally an S_N2' product, it would arise by a stepwise electron-transfer, radical-coupling mechanism.[22] Opening of **21** and reaction with thiophenoxide ion, as previously described, would produce the observed products. While this mechanism may also



seem reasonable, the problem again arises as to the lack of formation of products of type **12**. As previously noted, further S_N2' reaction with thiophenoxide would be expected to produce an analog of **12**. However, this negative evidence cannot be used to rule out this radical-coupling mechanism. Further studies will be necessary to decide between these mechanistic possibilities.

Theoretical Studies on the Diazirinyl Anion. A key intermediate in one of our potential mechanisms is the formally antiaromatic diazirinyl anion **17**, formed by two single-electron transfers from thiophenoxide ion. What is the viability of such an anion, which most organic chemists, at first glance, might consider to be quite unstable? As previously mentioned, the parent diazirinyl anion **42** has been previously generated in the gas phase in a flowing afterglow experiment.[9] Bachrach and Kass have also carried out *ab initio* molecular orbital calculations on this anion at the HF/6–31+G* and MP2/6–31+G* levels.[23] It was concluded that charge in **42** was highly localized on carbon and the nitrogen–nitrogen bond was essentially a double bond. Pertinent bond angles and bond lengths are shown. An additional isodesmic calculation suggested that **42** was substantially more stable than the cyclopropenyl anion, and **42** has been termed a nonaromatic

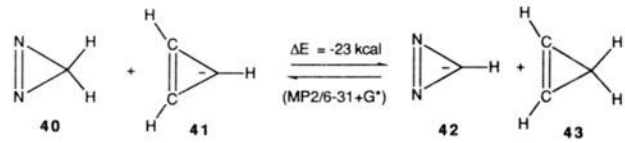
(22) For examples of this general type of substitution mechanism and leading references, see: (a) Bordwell, F. G.; Harrelson, J. A., Jr. *J. Org. Chem.* **1989**, *54*, 4893. (b) Zhang, X.-M.; Yang, D.-L.; Liu, Y.-C. *J. Org. Chem.* **1993**, *58*, 224.

(23) Kroeker, R. L.; Bachrach, S. M.; Kass, S. R. *J. Org. Chem.* **1991**, *56*, 4062.

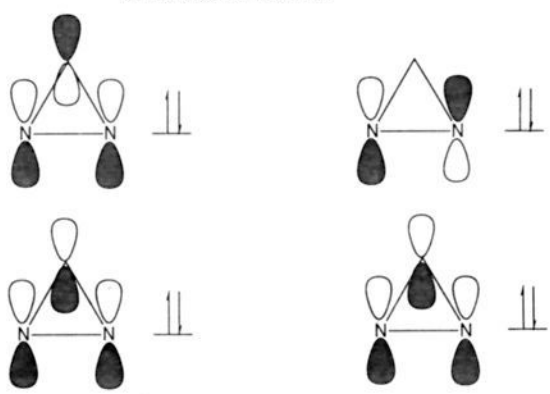
Table II. Calculated Energies (hartrees) of $(CHN_2)^-$ Ions

compd	HF/6-31+G*	MP2/6-31+G*
42	−147.179331	−147.172406
44	−147.179475	−147.169121
45	−147.223394	−147.213849

molecule. It was noted, in passing, that a second energy minimum was located, but this was not pursued.



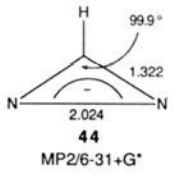
In order to gain further insights into the nature of this anion, we have repeated the calculations[24] on the diazirinyl anion and focused on the second energy minimum.[25] The second minimum **44** is completely planar and characterized by a very long nitrogen–nitrogen bond. Charge is located essentially on the two nitrogen atoms. Pertinent geometrical features are shown. The energy



of the structure of **44** (Table II) is essentially the same as that of **42** at the HF/6–31+G* level and 2 kcal higher at the MP2/6–31+G* level. Also important to note is the antibonding interaction between the two nitrogens in the highest occupied π-type orbital of **44** (in contrast to the bonding interaction in **42**). Interconversion of **42** and **44** should be a forbidden process since the highest occupied π-type orbitals of these two anions have different symmetries. Figure 6 shows the relative energies of **42** and **44** as well as that of the isomeric anion **45**. At the MP2/6–31+G* level, the N–N bond distance in **44** increases further to 2.024 Å and is indicative of only a very weak interaction between these atoms. A valence bond representation of **44** is shown in **44a** and **44b**, which emphasizes the fact that **44** is essentially an allyl-type anion. Given the large nitrogen–nitrogen distance in **44**, it might be more accurate to represent **44** as a species with no bond between the nitrogens, i.e., **44c** and **44d**.

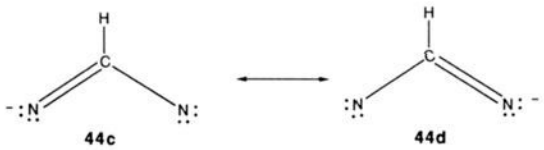
(24) *Ab initio* molecular orbital calculations were performed using the Gaussian 90 series of programs. See: Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, 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.

(25) This second minimum is obtained when one starts the computation using a relatively long N–N bond distance.



44
MP2/6-31+G*

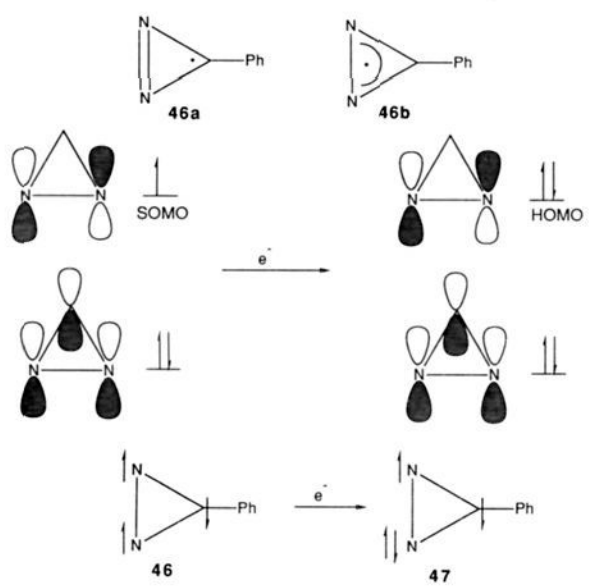
44a 44b
A Valence Bond Representation



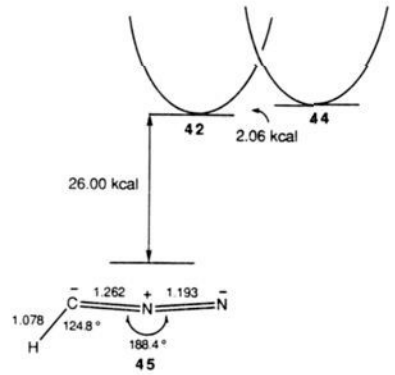
44c 44d

This computational study indicates a very weak or nonexistent nitrogen–nitrogen bond in the diazirinyl anion **44**. If this is an accurate representation of the intermediate involved in the reaction of arylhalodiazirines with thiophenoxide, then it is not surprising that ring opening occurs. In fact, if an intermediate analogous to **44** is involved, then a question arises as to the timing of protonation of **17b** vs the reaction with thiophenoxide. The order of these two steps may be reversed. In any event, our computational study suggests that a nitrogen-centered diazirinyl anion analogous to **44** must be considered in the halodiazirine–thiophenoxide reaction.

Examination of the diazirinyl radical **6** suggests a reason why a nitrogen-centered diazirinyl anion should be the pertinent intermediate formed if **6** is reduced by further electron transfer. Ingold and Maeda[15] have generated the diazirinyl radical **46**, and an ESR study indicated that spin density is localized on the two nitrogen atoms, i.e., the structure of **46b** is a better representation of this radical.[26] The pertinent SOMO of **46** is shown. Addition of an electron to this orbital in a single-electron



reduction process necessarily gives **47** (rather than the carbon-centered anion analogous to **42**). Interconversion of **47** with a carbon-centered diazirinyl anion should not occur since this is a forbidden process. A valence bond description of a single-electron reduction of **46** leads to the same conclusion, i.e, an anion, **47**, with charge localized on the two nitrogen atoms, will result. These calculations therefore point to a diazirinyl anion, **47**, that is not unusually destabilized, that will have charge localized essentially on the two nitrogen atoms, and with a very weak (or nonexistent) nitrogen–nitrogen bond.



45

Figure 6. Energy levels (MP2/6–31+G*) of isomeric $(CHN_2)^-$ anions.

Conclusions. Arylhalodiazirines react with thiophenoxide ion in methanol to give diphenyl disulfide along with benzonitriles, benzamidines, and ammonia. No simple substitution products are formed. Kinetic studies indicate that the process is *not* initiated by nucleophilic attack of thiophenoxide on the halogen of the halodiazirine. Mechanistic possibilities include formation of an N-sulfenylated diazirine intermediate or an electron-transfer-initiated process. One potential pathway involves reduction of an intermediate diazirinyl radical by thiophenoxide to the formally antiaromatic diazirinyl anion. Protonation on nitrogen, ring opening, and subsequent transformations are a potential source of benzonitriles, ammonia, and diphenyl disulfide. An alternative mechanism, involving ring opening of an N-sulfenylated diazirine, would also lead to the observed products. Theoretical calculations suggest that the diazirinyl anion, with charge essentially on the two nitrogens, may be a viable intermediate in solution. By way of contrast, our previous studies have shown that the formally aromatic diazirinyl cation *cannot* be easily generated in solution. We suggest that simple concepts concerning aromaticity and antiaromaticity may not be completely general in predicting the ease of generation of diazirinyl cations and anions.

Experimental Section

General. NMR spectra were recorded on a General Electric GN 300 spectrometer. ^{15}N NMR spectra were recorded at 30.45 MHz. Chemical shifts for ^{15}N are relative to anhydrous NH_3 (0.00 ppm) and were assigned using NH_4Cl (25.0 ppm) as a reference standard.[27] 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 reactions of halodiazirines with thiophenoxide were carried out in diffuse room light with hood lights turned off. It should be emphasized that *diazirines are potentially explosive. All manipulations with pure diazirines were carried out with extreme caution and using safety shields.*

Preparation of Arylbromodiazirines. All of the arylbromodiazirines used in Table I were prepared by oxidation of arylamidines with sodium hypobromite, using previously described procedures.[1,10,28] They were all purified by chromatography on silica gel. The preparation of ^{15}N-labeled phenylbromodiazirine, [^{15}N]-**8**, has also been described.[1]

Preparation of Arylchlorodiazirines. All of the arylchlorodiazirines used in Table I were prepared by oxidation of arylamidines with sodium hypochlorite, using previously described procedures.[3,10,28–32] They were all purified by chromatography on silica gel. 3-Pyridyl-[3] and 4-pyridyl-

(26) For a recent calculation on the unsubstituted diazirinyl radical, which also suggests that spin density will be localized on the two nitrogens, see: Byun, Y.-G.; Saebo, S.; Pittman, C. U., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 3689.

(27) Lichter, R. L. In *The Multinuclear Approach to NMR Spectroscopy*; Lambert, J. B., Riddell, F. G., Eds.; D. Reidell Publishing Co.: Dordrecht, Holland, 1983; pp 207–244.

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

(29) Liu, M. T. H.; Toriyama, K. *Can. J. Chem.* **1972**, *50*, 3009.

chlorodiazirine[32] were also prepared using previously described procedures. The preparation of ^{15}N-labeled 3-pyridylchlorodiazirine, [^{15}N]-**13**, using $^{15}NH_4Cl$ (99% ^{15}N) was completely analogous to the preparation of the unlabeled **13**. The *m*-CH_3SO_2- and *p*-CH_3SO_2-substituted chlorodiazirines were prepared as described below.

(*p*-(Methylsulfonyl)phenyl)chlorodiazirine. Using the methodology developed by Kornblum,[33] a solution of 14.6 g (130 mmol) of potassium *tert*-butoxide in 90 mL of dimethyl sulfoxide was cooled as 10.0 g (208 mmol) of CH_3SH was bubbled into the solution. The solution was stirred as 10.25 g (69 mmol) of *p*-nitrobenzonitrile was added. After 15 h, water was added and the mixture extracted with ether. The ether extract was washed with water and saturated NaCl solution and dried over $MgSO_4$. Solvent removal using a rotary evaporator gave 10.18 g (98%) of crude *p*-cyanothioanisole as an off-white solid which was directly converted to the corresponding sulfone. Recrystallization of a small portion from hexane gave a sample of *p*-cyanothioanisole, mp 62–63 °C: ^1H NMR ($CDCl_3$) δ 7.53 and 7.26 (AA'BB' q, 4 H), 2.513 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.12, 132.17, 125.52, 118.97, 107.71, 14.72. Anal. Calcd for C_8H_7NS: C, 64.40; H, 4.73. Found: C, 64.23; H, 4.73.

A solution of 6.03 g (40.4 mmol) of *p*-cyanothioanisole in 150 mL of CH_2Cl_2 was cooled to 0 °C with stirring. Solid *m*-chloroperoxybenzoic acid (18.1 g of 85% peracid, 89.2 mmol) was added in small portions. The mixture was stirred at 0 °C for 20 min and then allowed to warm up to room temperature where stirring was continued for 5 h. The mixture was transferred to a separatory funnel with ether and water. The organic extract was then washed with 10% NaOH solution followed by a solution of $Na_2S_2O_3$–NaI–NaOH in water. The organic extract was then washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was removed using a rotary evaporator to give 6.51 g (35.9 mmol, 89%) of 4-(methylsulfonyl)benzonitrile. Recrystallization of a portion from a hexane–ether solvent mixture gave white crystals, mp 140–142 °C: ^1H NMR ($CDCl_3$) δ 8.10 and 7.91 (AA'BB' q, 4 H), 3.112 (s, 3 H); ^{13}C NMR δ 144.51, 133.22, 128.21, 117.61, 117.06, 44.23. Anal. Calcd for $C_8H_7NO_2S$: C, 53.02; H, 3.89. Found: C, 53.00; H, 4.12.

To a mixture of 5.252 g (29.0 mmol) of 4-(methylsulfonyl)-benzonitrile in 60 mL of methanol was added 2.9 mL of a 1.0 M solution of sodium methoxide in methanol. The mixture was heated to 45 °C to dissolve the sulfone, and stirring was continued at 45 °C for 21 h. Ammonium chloride (1.572 g, 29.4 mmol) was added, and the solution was stirred an additional 20 h at 45 °C. The mixture was then filtered, and the solvent was removed using a rotary evaporator. The residue was washed with reagent grade acetone followed by ether. The solid arylamidine hydrochloride salt (4.741 g, 20.2 mmol; 70% yield) was collected using a Büchner funnel. This salt was oxidized with sodium hypochlorite solution using the standard procedure[10,28] to give (*p*-(methylsulfonyl)phenyl)chlorodiazirine (26% yield) as a white solid which decomposed above 80 °C: ^1H NMR ($CDCl_3$) δ 7.99 and 7.33 (AA'BB' q, 4 H), 3.105 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 141.33, 127.68, 127.05, 45.93, 44.40; IR (CCl_4) 1560 ($\nu_{N=N}$), 1325, 1150 cm^{-1} ($\nu_{S=O}$); UV (CH_3OH) 360, 372 nm.

(*m*-(Methylsulfonyl)phenyl)chlorodiazirine. 3-(Methylthio)aniline, (10.438 g, 75 mmol) was added in 18 mL of concentrated hydrochloric acid (216 mmol) to give a suspension of the hydrochloride salt. The mixture was cooled in an ice bath, and a solution of 5.313 g (62.5 mmol) of sodium nitrite in 16 mL of water was added dropwise with stirring. The temperature was maintained below 10 °C. The excess acid was neutralized with Na_2CO_3. A solution of cuprous cyanide was prepared by the addition of a solution of 8.883 g (89.7 mmol) of cuprous chloride in 36 mL of water to 11.499 g (234.6 mmol) of NaCN in 18 mL of water. The CuCN mixture was chilled in an ice–water bath to 0–5 °C, and 20 mL of toluene was added. The diazonium solution prepared above was added to the CuCN slowly over 20 min with vigorous stirring. The mixture was kept at 0–5 °C for an additional 30 min and then allowed to warm to room temperature. After 90 min at room temperature, a distillation head was attached and the mixture was steam distilled. The distillate was extracted with ether, and the organic phase was washed with 5% KOH solution and saturated NaCl solution and dried over $MgSO_4$. The solvents were removed by distillation at 15 mmHg, and the residue was distilled to give 1.899 g (12.7 mmol; 17% yield) of 3-(methylthio)benzonitrile as a light yellow liquid, bp 90 °C (15 mmHg): ^1H NMR ($CDCl_3$) δ 7.48–7.32 (m, 4 H), 2.504 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 140.96, 130.40, 129.29, 128.84, 128.25, 118.47, 113.13, 15.40.

A solution of 1.893 g (12.7 mmol) of 3-(methylthio)benzonitrile in 40 mL of CH_2Cl_2 was cooled in an ice–water bath with stirring as 10.40 g (30.1 mmol) of 50% *m*-chloroperoxybenzoic acid was added slowly. The mixture was stirred at 0 °C for 40 min and then allowed to warm to room temperature. After 5 h, the mixture was transferred to a separatory funnel with ether and water. The organic extract was then washed with 10% NaOH solution followed by a solution of $Na_2S_2O_3$–NaI–NaOH in water and then with saturated NaCl solution. The organic extract was dried over $MgSO_4$, and the solvent was removed using a rotary evaporator. The residue was slurried with pentane to give 1.850 g (10.2 mmol; 80% yield) of 3-(methylsulfonyl)benzonitrile as a white solid. The solid was recrystallized from 10 mL of hexanes and 5 mL of EtOAc to give 1.331 g of 3-(methylsulfonyl)benzonitrile, mp 101–103 °C: ^1H NMR ($CDCl_3$) δ 8.265 (td, J = 1.8, 0.55 Hz, 1 H), 8.200 (dd, J = 7.8, 1.8, 1.2 Hz, 1 H), 7.965 (dt, J = 7.8, 1.2 Hz, 1 H), 7.759 (td, J = 7.8, 0.55 Hz, 1 H), 3.114 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 142.21, 136.87, 131.43, 131.22, 130.54, 116.85, 114.15, 44.38. Anal. Calcd for $C_8H_7NO_2S$: C, 53.02; H, 3.89. Found: C, 52.88; H, 4.01.

A mixture of 1.261 g (6.96 mmol) of 3-(methylsulfonyl)benzonitrile in 20 mL of methanol and 0.7 mL of a 1.0 M solution of sodium methoxide was heated to 50 °C to dissolve the sulfone. Stirring was continued at 45 °C for 23 h. Solid NH_4Cl (0.382 g, 7.14 mmol) was added, and stirring was continued at 45 °C for 24 h. The solvent was removed using a rotary evaporator to give a gummy residue. This residue was slurried with ether and reagent grade acetone and cooled to –20 °C to facilitate crystallization. The solid which formed was then washed with acetone and ether and dried under reduced pressure to give 1.275 g (5.44 mmol; 78% yield) of the corresponding arylamidine hydrochloride as a white solid. This salt was oxidized with sodium hypochlorite solution using the standard procedure[10,28] to give (*m*-(methylsulfonyl)phenyl)chlorodiazirine (33% yield) as a white solid which decomposes at about 75 °C: ^1H NMR ($CDCl_3$) δ 7.995 (d, J = 7.8 Hz, 1 H), 7.737 (s, 1 H), 7.642 (t, J = 7.8 Hz, 1 H), 7.395 (d, J = 7.8 Hz, 1 H), 3.098 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 141.46, 137.58, 130.87, 129.83, 128.15, 125.08, 45.99, 44.44; IR (CCl_4) 1565 ($\nu_{N=N}$), 1325, 1145 cm^{-1} (ν_{SdO}); UV (CH_3OH) 363, 376 nm.

Reaction of Phenylbromodiazirine, 8, with Sodium Thiophenoxide. Thiophenol (1.73 g, 15.7 mmol) was added to 16 mL of 1.0 M sodium methoxide (16.0 mmol) in methanol under nitrogen, and the mixture was cooled in an ice bath. A solution of 0.768 g (3.90 mmol) of phenylbromodiazirine in about 2 mL of methanol was then added in one portion, and the mixture was allowed to warm to room temperature. After about 30 min, diphenyl disulfide began to crystallize. The mixture was allowed to stand at room temperature for 18 h, and then it was transferred to a separatory funnel with ether and water. The aqueous phase was extracted with an additional portion of ether, and the combined ether extracts were washed with water and saturated NaCl solution and dried over $MgSO_4$. Gas chromatographic analysis showed the presence of benzonitrile and diphenyl disulfide. The yield of benzonitrile, as determined by gas chromatography using naphthalene as an internal standard, was 64%. In a separate run, samples of these two products were isolated by chromatography on silica gel and they were identified by spectral comparison with authentic samples. The isolated yield of diphenyl disulfide in a separate run, after chromatography, was 92%.

Reaction of ^{15}N-Labeled Phenylbromodiazirine with Sodium Thiophenoxide. Thiophenol (195 mg, 1.77 mmol) was added to 1.8 mL of 1.0 M sodium methoxide (1.80 mmol) in methanol under nitrogen. The mixture was cooled to about 15 °C, and 85 mg (0.429 mmol) of ^{15}N-labeled phenylbromodiazirine[1] in 1 mL of methanol was added. A small amount of CD_3OD was added (for NMR lock), and the mixture was placed in a 10-mm NMR tube. ^{15}N NMR spectra were periodically recorded. The ^{15}N signal for [^{15}N]-**8** at δ 452.2 disappeared rapidly and was replaced by signals at δ 256.8 (benzonitrile), 134.1 (benzamidine), and 0.4 (ammonia). Figure 1 shows the spectrum that was recorded, beginning after about 2 h of reaction time. The identities of these products were verified by comparison of the ^{15}N NMR chemical shifts with those of authentic ^{15}N-labeled materials. Additionally, the presence of ammonia was also verified by mass spectrometry of the vapor above the liquid and by placing a piece of moist pH paper in the vapor above the liquid.

Reaction of 3-Pyridylchlorodiazirine, 13, with Sodium Thiophenoxide. Thiophenol (881 mg, 8.00 mmol) was added to 7.5 mL of 1.0 M sodium methoxide (7.50 mmol) in methanol under nitrogen, and 15 mL of additional methanol was added. The mixture was cooled to –50 °C, and

(30) Liu, M. T. H.; Chien, D. T. H. *J. Chem. Soc., Perkin Trans. 2* **1974**, 937.
(31) Padwa, A.; Pulwer, M. T.; Blacklock, T. J. *Organic Syntheses;* Wiley: New York, 1990; Collect. Vol. VII, p 203.
(32) Berneth, H.; Hünig, S. *Chem. Ber.* **1980**, *113*, 2040.
(33) Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A. *J. Org. Chem.* **1976**, *41*, 1560.

a solution of 294 mg (1.91 mmol) of 3-pyridylchlorodiazirine in 1.5 mL of methanol was then added in one portion and the mixture allowed to warm to room temperature. After 4 h, the mixture was quenched with water and transferred to a separatory funnel with ether. The ether extract was washed with an additional portion of water, dilute NaOH solution, and saturated NaCl solution and dried over $MgSO_4$. The solvent was removed using a rotary evaporator, leaving 822 mg (3.76 mmol; 98% yield) of crude diphenyl disulfide. The NMR spectrum of this crude material showed no **14–16** (which are water-soluble). Chromatography on 13 g of silica gel gave 786 mg (3.60 mmol; 94% yield) of pure diphenyl disulfide, which was identified by NMR spectral comparison with an authentic sample.

In a separate run, 6.5 mL of 0.5 M $NaOCH_3$ (3.25 mmol) in methanol was added to 358 mg (3.25 mmol) of thiophenol in 4 mL of methanol. 3-Pyridylchlorodiazirine (106 mg, 0.690 mmol) was then added, and the mixture was kept at room temperature for 3 h. The mixture was then cooled in ice and centrifuged to separate the precipitated NaCl and diphenyl disulfide, and the homogeneous supernatant liquid was analyzed by ^1H NMR. ^1H NMR showed **14**, **15**, and **16** in a 1.0:2.9:3.2 ratio. The identities of these products were determined by comparison of the chemical shifts with those of authentic samples.

Sodium Methoxide Catalyzed Equilibration of 3-Cyanopyridine, 14, with Imino Ester 16. 3-Cyanopyridine, **14**, (70 mg) was dissolved in 4 mL of methanol, and 1.0 mL of 1.0 M $NaOCH_3$ in methanol was added. The mixture was monitored by ^1H NMR (unlocked mode). After 10 min, 50% of **14** had been converted to imino ester **16**. NMR of **16**: (CH_3OH) δ 9.02 (br, 1 H), 8.68 (dd, J = 4.9, 1.6 Hz, 1 H), 8.29 (dt, J = 8.0, 1.9 Hz, 1 H), 7.54 (ddd, J = 8.0, 4.9, 0.7 Hz, 1 H), 3.630 (s, 3 H). After 25 h, a spectrum showing an equilibrated mixture of imino ester **16** and nitrile **14** in a 3.2:1 ratio was obtained. This ratio was the same as that observed in the reaction of **13** with sodium thiophenoxide, described above.

Reaction of ^{15}N-Labeled 3-Pyridylchlorodiazirine with Sodium Thiophenoxide. Thiophenol (280 mg, 2.54 mmol) was added to 2.5 mL of 1.0 M sodium methoxide (2.50 mmol) in methanol under nitrogen. The mixture was cooled to about 15 °C, and 83 mg (0.537 mmol) of ^{15}N-labeled 3-pyridylchlorodiazirine was added. After 6 h at room temperature, the mixture was cooled in an ice bath and then centrifuged to separate out the precipitated NaCl and diphenyl disulfide. The supernatant liquid was placed in an NMR tube along with a small amount of CD_3OD (for NMR lock). Figure 2 shows the ^{15}N NMR spectrum of the product mixture. The ^1H NMR spectrum of this mixture was also recorded and shows nitrile **14**, benzamidine **15**, and imino ester **16**, as determined by comparison of the chemical shifts with those of authentic samples.

Reaction of Phenylbromodiazirine, 8, with Sodium Thioacetate. Thioacetic acid (140 mg, 1.84 mmol) was added to 1.8 mL of 1.0 M $NaOCH_3$ (1.80 mmol) under nitrogen, and an additional 1 mL of methanol was added. A small amount of CD_3OD was added followed by 85 mg (0.429 mmol) of ^{15}N-labeled phenylbromodiazirine. A solution was placed in an NMR tube, and ^{15}N NMR spectra were recorded. Figure 3 shows the spectrum recorded, beginning 45 min after addition of the phenylbromodiazirine.

Reaction of *N*-(Phenylthio)benzenesulfenamide, 26, with Sodium Thiophenoxide. Thiophenol (150 mg, 1.36 mmol) was added to 2.0 mL of 1.0 M sodium methoxide (2.00 mmol) in methanol under nitrogen. The mixture was stirred as 150 mg (0.643 mmol) of **26** [20] was added. After 4 h, the presence of ammonia in the vapor above the reaction mixture was detected with moist pH paper. An aqueous workup followed with ether extraction. After the ether extract was dried over $MgSO_4$, solvent removal left 260 mg (1.19 mmol; 93% yield) of diphenyl disulfide which was identified by spectral comparison with an authentic sample.

Reaction of Benzamidine with *N*-(Phenylthio)phthalimide. A solution of 200 mg (1.66 mmol) of benzamidine in 2 mL of methylene chloride was cooled to 15 °C, and 425 mg (1.66 mmol) of *N*-(phenylthio)-phthalimide[34] in 5 mL of CH_2Cl_2 was added. The mixture was stirred at room temperature for 2.5 h and then cooled to about 10 °C. The precipitated phthalimide was removed by filtration through a cotton plug in a pipet, and the CH_2Cl_2 was removed using a rotary evaporator. The residue was redissolved in ether, and a solution of 250 mg of KOH in 4 mL of water was added. The mixture was vigorously stirred and the aqueous phase discarded. The ether extract was washed with saturated NaCl solution and dried over $MgSO_4$. Solvent removal using a rotary evaporator gave 377 mg (1.65 mmol; 99% yield) of *N*-(phenylthio)-benzamidine, **38**. An analytical sample, mp 87–88 °C, was recrystallized from a hexane–ether mixture: ^1H NMR ($CDCl_3$) δ 7.84–7.75 (m, 2 H), 7.60–7.53 (m, 2 H), 7.47–7.38 (m, 3 H), 7.35 (t, J = 8 Hz), 7.15 (tt, J = 8, 1.2 Hz), 5.12 (br, 2 H); ^{13}C NMR ($CDCl_3$) δ 154.48, 139.04, 135.01, 130.09, 128.73, 128.47, 126.11, 125.33, 124.43. Anal. Calcd for $C_{13}H_{12}N_2S$: C, 68.39; H, 5.30. Found: C, 67.94; H, 5.43.

Preparation of ^{15}N-Labeled *N*-(Phenylthio)benzamidine. A suspension of 9.018 g (52.5 mmol) of $PhC(OMe)NH_2^+Cl^-$ (prepared by the Pinner reaction[35] of benzonitrile with HCl and methanol in ether solvent) in 70 mL of water and 50 mL of ether was stirred as 5.70 g (67.9 mmol) of $NaHCO_3$ was added in small portions. When carbon dioxide evolution ceased, the ether phase was separated and dried over $MgSO_4$ and the solvent was removed using a rotary evaporator. The residue was distilled to give 6.913 g (51.1 mmol; 97% yield) of $PhC(NH)OCH_3$, bp 65–66 °C (1.4 mmHg). A solution of 1.008 g (7.46 mmol) of $PhC(NH)OCH_3$ in methanol was stirred as 410 mg (7.52 mmol) of $^{15}NH_4Cl$ (99% ^{15}N) was added. The mixture was heated at 46 °C for 6 h, and the methanol solvent was then removed using a rotary evaporator. The residue was slurried with ether and the ether decanted. The solid was dried under vacuum and collected to give 1.135 g (7.20 mmol; 96% yield) of ^{15}N-labeled benzamidine hydrochloride (one ^{15}N per molecule).

To 1.127 g (7.15 mmol) of ^{15}N-labeled benzamidine hydrochloride was added 7.50 mL of 1.0 M sodium methoxide (7.50 mmol) in methanol. The mixture was filtered through a cotton plug to remove the precipitated NaCl, and the solvent was removed using a rotary evaporator. The residue was extracted with refluxing ether (3 times), and the ether was decanted from the solid residue. The ether was then removed using a rotary evaporator, leaving 833 mg (6.88 mmol; 96% yield) of ^{15}N-labeled benzamidine.

Reaction of ^{15}N-labeled benzamidine with *N*-(phenylthio)phthalimide in CH_2Cl_2, using the identical procedure described above, gave ^{15}N-labeled *N*-(phenylthio)benzamidine. The aromatic region of the ^1H NMR spectrum was identical to that of the unlabeled material. The NH_2 region shows a broad signal at δ 5.12 ($^{14}NH_2$) flanked by a sharp doublet at δ 5.12, J_{N-H} = 86.6 Hz ($^{15}NH_2$): ^{15}N NMR ($CDCl_3$) δ 203.7 (s, $^{15}NSPh$), 84.2 (t, J_{N-H} = 86.6 Hz, $^{15}NH_2$).

Reaction of *N*-(Phenylthio)benzamidine, 38, with Sodium Thiophenoxide. Thiophenol (145 mg, 1.32 mmol) was added to 3.6 mL of 1.0 M sodium methoxide (3.60 mmol) in methanol under nitrogen. The mixture was stirred as 198 mg (0.867 mmol) of *N*-(phenylthio)benzamidine, **38**, in 1 mL of methanol was added. After 1 h, a small sample was withdrawn and analyzed by gas chromatography, which showed complete reaction. After 12 h at room temperature, water was added and the mixture was transferred to a separatory funnel with ether. The ether extract was washed with NaOH solution and saturated NaCl solution and dried over $MgSO_4$. Solvent removal using a rotary evaporator gave 182 mg (0.834 mmol; 96% yield) of diphenyl disulfide which was identified by NMR spectral comparison and gas chromatographic retention time comparison with an authentic sample.

In a separate run, 64 mg of **38** was added to sodium thiophenoxide prepared from 31 mg of thiophenol and sodium methoxide in methanol. The mixture was analyzed by ^1H NMR before an aqueous workup (after addition of a small amount of CD_3OD). The spectrum was recorded 20 min after addition of sulfenamide **38**, and the reaction was complete. The spectrum shows the presence of only benzamidine, **10**, and diphenyl disulfide (which were identified by comparison with the spectrum of a 1:1 mixture of authentic benzamidine and diphenyl disulfide).

Kinetic Studies. Rates of reaction of the arylhalodiazirines described in Table I were determined by UV spectroscopy. In a typical procedure, 10–30 μL of a freshly prepared solution of arylhalodiazirine in ether (about 100 mg of diazirine per milliliter of ether) was injected via syringe into 3 mL of 0.20 M sodium thiophenoxide in methanol that had been thermally equilibrated in a constant temperature compartment of a UV spectrometer. This initiated the kinetic run. For the arylbromodiazirines, absorbance changes were monitored at 385 nm. Absorbance changes for the arylchlorodiazirines were monitored at 375 nm (except those for the sulfone derivatives which were monitored at 385 nm). Infinity readings were taken after 10 half-lives. First-order rate constants were determined by standard least-square procedures. Correlation coefficients were all greater than 0.9999. Maximum standard deviations in duplicate runs were ±1.5%.

Acknowledgment is made to the National Science Foundation for financial support of this research. We also thank Prof. Daniel Pasto of our department for helpful discussions.

(34) Behforouz, M.; Kerwood, J. E. *J. Org. Chem.* **1969**, *34*, 51.

(35) Roger, R.; Nielson, D. G. *Chem. Rev.* **1961**, *61*, 179.