Reaction of Arylbromodiazirines with Azide Ion. Evidence for *N*-Azidodiazirine Intermediates

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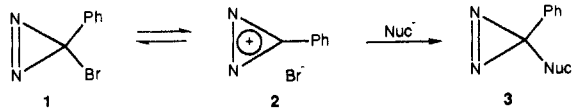
Abstract: Azide ion reacts with ^{15}N-labeled phenylbromodiazirine ([^{15}N]-**1**) to give benzonitrile that has substantial ^{15}N incorporation as determined by ^{15}N and ^{13}C NMR as well as by mass spectrometry. When unlabeled phenylbromodiazirine (**1**) is reacted with terminally ^{15}N-labeled sodium azide, the benzonitrile product contains no ^{15}N label. These results support the intermediacy of an *N*-azidodiazirine **8** formed by S_N2' attack of azide upon the nitrogen atom in the bromodiazirine. The *N*-azidodiazirine is suggested to rapidly lose nitrogen to give an analogue of a 1,1-diazene, which also loses nitrogen to give a benzonitrile product, which is consistent with the labeling results. Similar results were obtained when *m*-CF_3, *p*-CH_3, and *p*-OCH_3 analogues of **1** were reacted with azide ion. This argues against the previously proposed mechanism involving *C*-azidodiazirines having the azide moiety attached to carbon. These experiments present evidence that phenylbromodiazirine can indeed react with nucleophiles via an S_N2' pathway and bypass the previously proposed diazirinium cation. A rationale for the observed substituent effect on rate of reaction of arylbromodiazirines with azide ion is presented in terms of stabilization of the developing carbon–nitrogen double bond in the transition state leading to **8** by the aryl group. It is concluded that a mechanism involving consecutive S_N2' reactions is preferable to one involving diazirinium cations in substitution reactions of arylbromodiazirines.

Diazirines are a fascinating class of compounds that can be induced to lose molecular nitrogen with concomitant formation of carbene intermediates.[1] The halodiazirines, first prepared by Graham,[2] have been utilized by Moss in the preparation of many interesting diazirines, which can serve as precursors to previously unknown carbenes.[3] As a typical example, phenylbromodiazirine (**1**) undergoes facile substitution reactions with nucleophiles such as F^-, CH_3O^-, and CN^- in polar aprotic solvents.[4] Mechanistically, it has been suggested that these reactions proceed via reversible formation of ion pair **2**, which is subsequently captured by the nucleophile. Ion pair **2** has also been suggested to be



1 2 3

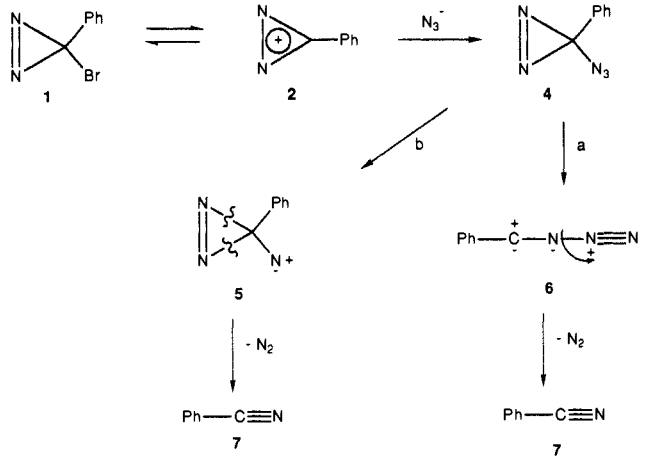
involved in the isomerization of diethyl maleate to diethyl fumarate catalyzed by phenylbromodiazirine.[5] The equilibrium constant for dissociation of the phenylbromodiazirine to **2**, as determined by conductometric measurements, has also been reported.[6]

During attempts to prepare additional substituted diazirines, we have found that cation **2** is not readily formed under solvolytic conditions.[7] Diazirine **1** is inert even in the highly ionizing solvent hexafluoroisopropyl alcohol. It also fails to react in attempted silver ion assisted solvolyses. These observations led us to question the intermediacy of ion **2** in the isomerization of diethyl maleate to diethyl fumarate. We subsequently suggested[7] that this reaction, which occurs in the nonpolar solvent CCl_4, could not involve ion **2** (which does not even form readily in highly ionizing solvents). We have found that the isomerizaton has the characteristic of a free-radical chain process. The isomerization is inhibited by the presence of oxygen and initiated by brief exposure to fluorescent light. In view of the fact that **1** does not give a precipitate of AgBr when treated with $AgNO_3$ in acetonitrile, we further suggested that the reported dissociation constant for **1** in acetonitrile cannot be correct.

In this paper we report a study of the reaction of arylbromodiazirines with azide ion. This reaction has previously been studied[8] and has been used as a model for reaction of **1** with nucleophiles. In light of our results, we suggest that ion **2** is not the intermediate under the mild conditions (room temperature or below) where substitution reactions of **1** occur. We present evidence for an alternative mechanism for the reaction of **1** with azide ion.

Results and Discussion

The major mechanistic study in which evidence is presented in favor of ion pair **2** is a study involving the reaction of **1** with azide ion.[8] The reaction of **1** with azide gave benzonitrile and was suggested to proceed via mechanism 1. It was proposed that cation **2** captured azide ion to give the azidodiazirine **4**, which could not be isolated or observed during the reaction. It was further proposed that **4** rapidly lost 2 molecules of N_2 to give the observed product nitrile in a single step. On the basis of theoretical calculations, it was suggested that potential intermediates **5** or **6** do not correspond to energy minima, and hence, conversion of **4** to benzonitrile was actually a concerted process.



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Mechanism 1

(1) 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, 1983; Vol. 42, p 588–616.
(2) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.
(3) Moss, R. A. *Acc. Chem. Res.* **1989**, *22*, 15.
(4) (a) Cox, D. P.; Moss, R. A.; Terpinski, J. *J. Am. Chem. Soc.* **1983**, *105*, 6513. (b) Włostowska, J.; Moss, R. A.; Guo, W.; Chang, M. *Chem. Commun.* **1982**, 432. (c) Moss, R. A.; Shen, S.; Hadel, L. M.; Kmiecik-Ławrynowicz, G.; Włostowska, J.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1987**, *109*, 4341. (d) Moss, R. A.; Kmiecik-Ławrynowicz, G.; Cox, D. P. *Synth. Commun.* **1984**, *14*, 21.
(5) Liu, M. T. H.; Doyle, M. P.; Loh, K.-L.; Anand, S. M. *J. Org. Chem.* **1987**, *52*, 323.
(6) Liu, M. T. H.; Paike, N. *Tetrahedron Lett.* **1987**, 3763.
(7) Creary, X.; Sky, A. F. *J. Org. Chem.* **1988**, *53*, 4637.
(8) Moss, R. A.; Terpinski, J.; Cox, D. P.; Denney, D. Z.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1985**, *107*, 2743.

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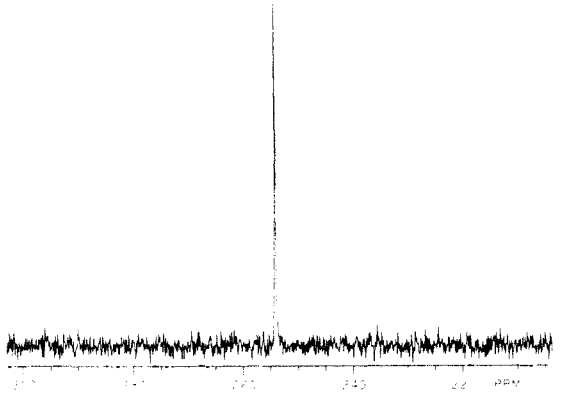
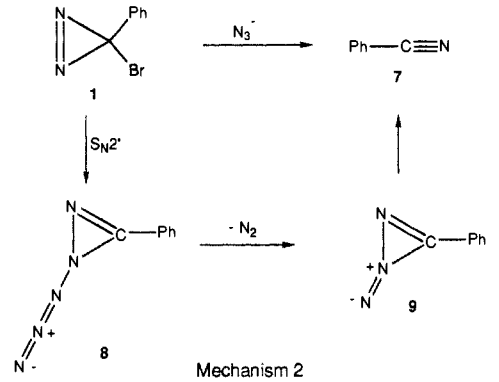


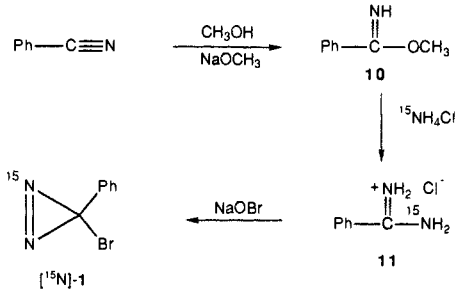
Figure 1. ^{15}N NMR spectrum of the products of reaction of [^{15}N]-**1** with $Bu_4N^+N_3^-$ in acetonitrile.

Since we considered cation **2** to be an unlikely intermediate in the reaction of **1** with azide ion, an alternative is proposed (mechanism 2). Reaction of azide at the diazirine nitrogen via an S_N2' reaction would lead to intermediate **8**. It is suggested that **8** is unstable and that benzonitrile product **7** is derived from **8** by direct loss of two molecules of N_2. Initial loss of N_2 from **8** would give **9**, which is an analogue of a diazene.[9] This intermediate should rapidly lose a second N_2 to give the observed benzonitrile product.



Mechanism 2

^{15}N-Labeling Studies. Mechanisms 1 and 2 can be readily distinguished by a labeling study. The labeled diazirine [^{15}N]-**1** was therefore prepared from benzonitrile by published procedures for the preparation of unlabeled halodiazirines.[2,8] Commercially available $^{15}NH_4Cl$ (99 atom % ^{15}N) was reacted with imino ester **10**. Oxidation of the resultant benzamidine hydrochloride **11** with NaOBr gave the desired [^{15}N]-**1**.



Diazirine [^{15}N]-**1** was reacted with tetrabutylammonium azide in acetonitrile, and the benzonitrile product was isolated. Figure 1 shows the ^{15}N NMR spectrum of the product, and Figure 2 shows the ^{13}C NMR spectrum. The ^{15}N signal at δ 254.1 shows that the label is at least partially incorporated into the product.

(9) For a review of the chemistry of 1,1-diazenes, see: (a) Lemal, D. M. In *Nitrenes*; Lwowski, W., Ed.; Interscience: New York, 1970; Chapter 10. For examples of 1,1-dialkyldiazenes that persist at low temperatures, see: (b) Dervan, P. B.; Hinsberg, W. D., III. *J. Am. Chem. Soc.* **1978**, *100*, 1608. (c) Dervan, P. B.; Hinsberg, W. D., III. *Ibid.* **1979**, *101*, 6142. (d) Schultz, P. G.; Dervan, P. B. *Ibid.* **1980**, *102*, 878.

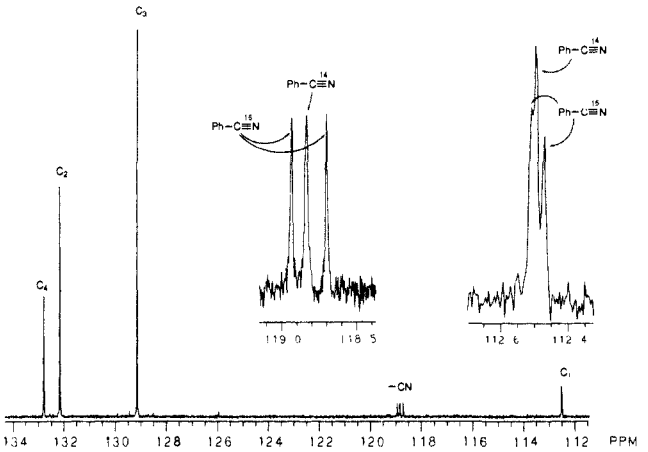


Figure 2. ^{13}C NMR spectrum of the products of reaction of [^{15}N]-**1** with $Bu_4N^+N_3^-$ in acetonitrile.

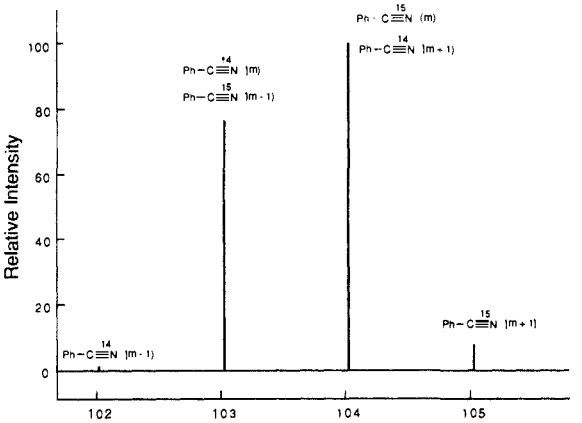


Figure 3. Mass spectrum (high-mass region) of the products of reaction of [^{15}N]-**1** with $Bu_4N^+N_3^-$.

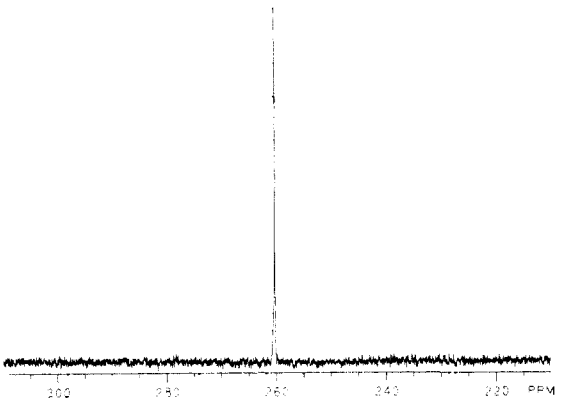


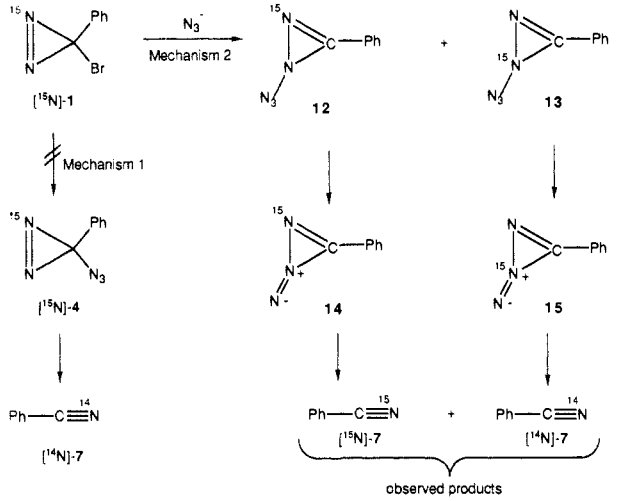
Figure 4. ^{15}N NMR spectrum of the products of reaction of [^{15}N]-**24** with $Na^+N_3^-$ in DMSO.

The ^{13}C spectrum (Figure 2) verifies that the benzonitrile product has partial incorporation of the ^{15}N label. The nitrile carbon of the $PhC^{14}N$ appears at δ 118.828, while the nitrile carbon of $PhC^{15}N$ appears as a doublet (J = 17.8 Hz) at δ 118.809. The ipso carbon of $PhC^{15}N$ at δ 112.487 is also coupled to the ^{15}N (J = 2.9 Hz) and also experiences a small isotope effect shift relative to $PhC^{14}N$ (δ 112.492).

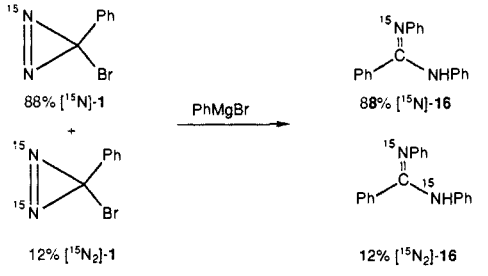
While ^{15}N and ^{13}C NMR spectra qualitatively confirm the presence of ^{15}N in the product, these methods do not allow for quantitative determination of ^{15}N content. Figure 3 shows the mass spectrum (high-mass region) of the product of reaction of [^{15}N]-**1** with azide. The peak at m/e 104 corresponds to $PhC^{15}N$ (along with the m + 1 peak due to $PhC^{14}N$). The peak at m/e 105 is the m + 1 peak due to $PhC^{15}N$. These mass spectral data correspond to 56% $PhC^{15}N$ and 44% $PhC^{14}N$. Comparable ^{15}N and ^{13}C NMR spectra as well as mass spectral results were ob-

tained when [^{15}N]-**1** was reacted with sodium azide in dimethyl sulfoxide. This implies that similar mechanisms operate in acetonitrile and dimethyl sulfoxide.

This labeling study argues against *C*-azidodiazirine intermediate **4** in mechanism 1. This mechanism predicts complete loss of the nitrogen label in the benzonitrile product, which is contrary to the observed result. On the other hand, the study is consistent with mechanism 2, involving S_N2' intermediate **8**, which predicts that a 50:50 mixture of labeled and unlabeled benzonitrile will result.[10]

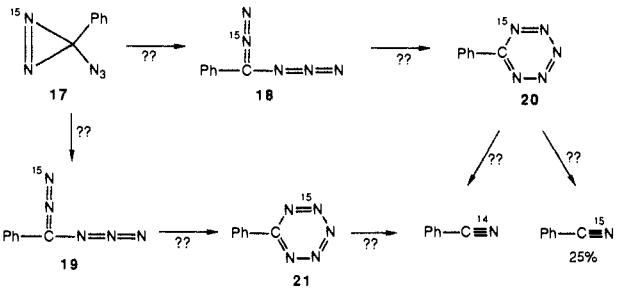


A minor problem is the fact that the observed product ratio is 56:44 in favor of the ^{15}N labeled benzonitrile product. This product ratio can be explained by determining the label content of [^{15}N]-**1**. Since this material does not withstand mass spectral analysis, [^{15}N]-**1** was reacted with phenylmagnesium bromide. The product, **16**, formed in this reaction is the same as that previously reported for the reaction of phenylchlorodiazirine with phenyllithium.[12] Mass spectral analysis shows that 12% of the

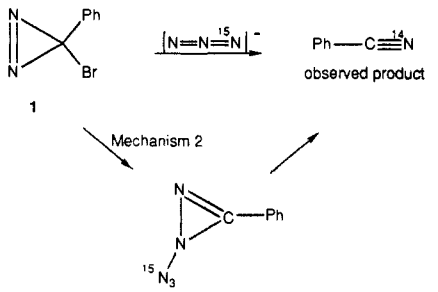


product contains two ^{15}N atoms, while 88% is monolabeled. The synthesis of [^{15}N]-**1** therefore must have led to 12% dilabeled phenylbromodiazirine along with 88% monolabeled phenylbromodiazirine. This results in 56% PhC^{15}N when the labeled diazirine is reacted with azide ion. We speculate that the origin of the dilabeled phenylbromodiazirine is a further exchange of monolabeled benzamidine hydrochloride **11** with the excess ^{15}N-H_4Cl employed in the preparation of **11**.

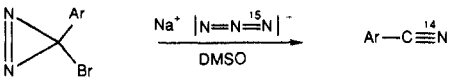
Is it possible that a labeled *C*-azidodiazirine **17** could lead to some PhC^{15}N by a mechanism involving opening to phenylazidodiazomethane, **18** and **19**, followed by closure to **20** and **21** and loss of nitrogen? Such a process should give 25% ^{15}N



incorporation in the product. In order to rule out the possibility that *any* labeled benzonitrile could arise via this process, unlabeled diazirine **1** was reacted with terminally labeled sodium azide (99% atom % ^{15}N)[13] in dimethyl sulfoxide. The benzonitrile product was *completely unlabeled* as determined by mass spectrometry. This experiment rules out the possibility that **20** could serve as a source of any of the ^{15}N-labeled benzonitrile. If **20** were involved, then reaction of unlabeled **1** with terminally labeled azide would also have led to 25% ^{15}N incorporation in the benzonitrile product. It should also be noted that previous theoretical calculations indicate that **20** does not lie at an energy minimum and, hence, is an unlikely intermediate.[8] Our complementary labeling study is completely consistent with our proposed mechanism 2.



Attention was next turned to arylbromodiazirines substituted with electron-donor substituents on the aromatic ring in an attempt to afford any diazirinium cation intermediate the maximal opportunity to demonstrate its existence. The nitrile formed from

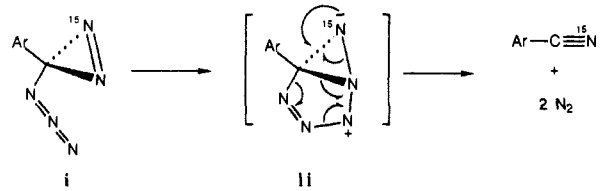


22 Ar = C_6H_4-p-CH_3

23 Ar = C_6H_4-p-OCH_3

22 was completely unlabeled, as determined by mass spectrometry. The *p*-OCH_3-substituted diazirine **23** was also reacted with labeled sodium azide. The *p*-methoxybenzonitrile product showed an m + 1 peak that was 10.12% of the parent peak. An authentic sample of unlabeled *p*-methoxybenzonitrile shows an m + 1 peak that is 9.47% of the parent peak. These results correspond to a maximum of 0.65% ^{15}N incorporation into the *p*-methoxybenzonitrile produced in the reaction of **23** with terminally labeled sodium azide. This would imply that at least 98.7% of **23** reacted

(10) A reviewer has suggested that decomposition of a *C*-azidodiazirine **i** via the intermediate/transition state **ii** would account for the observed labeling results. We will subsequently present evidence[11] that *C*-azidodiazirines **i** can be formed in $S_{RN}1$ substitution reactions of arylhalodiazirines with azide ion. Photoinitiated reactions of arylchlorodiazirines with ^{15}N terminally labeled azide ion gave approximately 50% ^{15}N label incorporation in the nitrile product. These reactions, which occur readily under photoinitiation (in contrast to dark reactions with added galvinoxyl), are presumed to proceed via *C*-azidodiazirines having a ^{15}N label in the azido group. These *C*-azidodiazirines do indeed decompose to nitriles as proposed in mechanism 1 and not as shown below.



(11) Creary, X.; Sky, A. F.; Phillips, G. Submitted for publication in *J. Org. Chem.*

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

(13) Terminally labeled Na[^{15}N=N=N] (99% ^{15}N enriched) was obtained from ICON Services, Inc. The label content of the sodium azide was qualitatively verified by reaction with benzyl bromide. The ^{13}C NMR spectrum of the benzyl azide product showed a characteristic doublet (J_{C-N} = 2.4 Hz) at δ 55.017 due to the benzylic carbon of PhCH$_2$^{15}N=N=N in addition to a singlet at δ 55.056 due to the benzylic carbon of PhCH$_2$N=N=^{15}N.

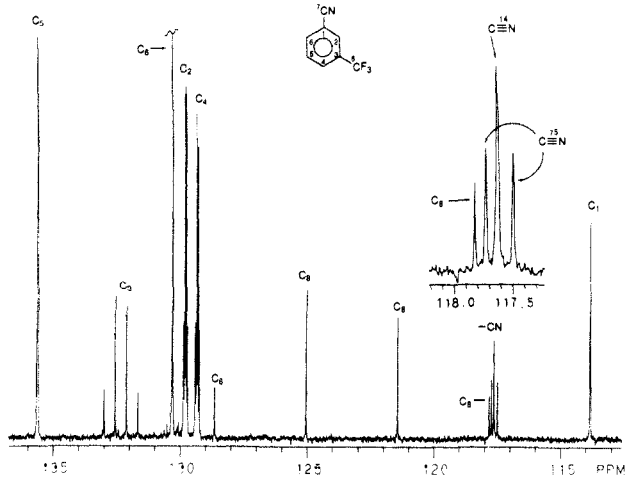
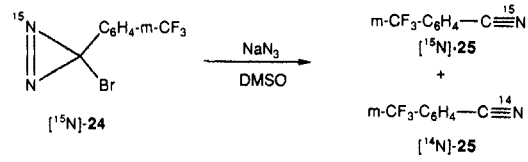


Figure 5. ^{13}C NMR spectrum of the products of reaction of [^{15}N]-**24** with $Na^+N_3^-$ in DMSO.

via the *N*-azidodiazirine, with a maximum of 1.3% of product being formed via a *C*-azidodiazirine.

The arylbromodiazirine [^{15}N]-**24**, which has an electron-withdrawing *m*-CF_3 substituent on the aromatic ring, was next examined. A procedure analogous to the preparation of [^{15}N]-**1** was used to prepare [^{15}N]-**24**. This labeled diazirine was then reacted with sodium azide in dimethyl sulfoxide. ^{15}N and ^{13}C



[^{15}N]-**24**

NMR spectra of the product, *m*-$CF_3C_6H_4CN$, are shown in Figures 4 and 5. The ^{15}N signal at δ 260.1 and the ^{13}C doublet (J_{C-N} = 17.6 Hz) at δ 117.410 reveal significant ^{15}N incorporation in the *m*-$CF_3C_6H_4CN$. Mass spectral data show that 40% of the product is ^{15}N labeled nitrile [^{15}N]-**25** while 60% of the product is unlabeled [^{14}N]-**25**. The ratio of these products deviates from the 50:50 ratio predicted from an *N*-azidodiazirine intermediate. The excess unlabeled [^{14}N]-**25** indicates that some other mechanism competes with the *N*-azidodiazirine mechanism when [^{15}N]-**24** reacts with azide ion.[14] However, this labeling study indicates that most of [^{15}N]-**24** reacts by way of mechanism 2.

All of the labeling studies reported in this paper, with either labeled diazirines or labeled azide ion, are consistent with *N*-azidodiazirines. These intermediates, which would arise via an S_N2' mechanism, allow one to bypass the diazirinium cation. The remote possibility remains that diazirinium cations such as **2** could react with azide ion at one of the ring nitrogen atoms and thereby produce **4**. However, in view of the mild conditions (room temperature or below) under which these diazirines react with nucleophiles and the fact that ions such as **2** cannot be formed readily even in the presence of silver ion, or in hexafluoroisopropyl alcohol,[7] we prefer the S_N2' mechanistic pathway for the formation of *N*-azidodiazirines.

Discussion of Previous Data in the S_N2' Framework. In light of our findings on the reaction of azide ion with arylbromodiazirines, it is necessary to address previous data that have been presented as evidence for the intermediacy of diazirinium cations. The major study presented in favor of diazirinium cation intermediates is a series of kinetic studies that attempt to support the intermediacy of the phenyldiazirinium cation.[8] It was experimentally determined that phenylbromodiazirine was substantially more reactive than the corresponding phenylchlorodiazirine, and this was presented as evidence for an ionization mechanism. While

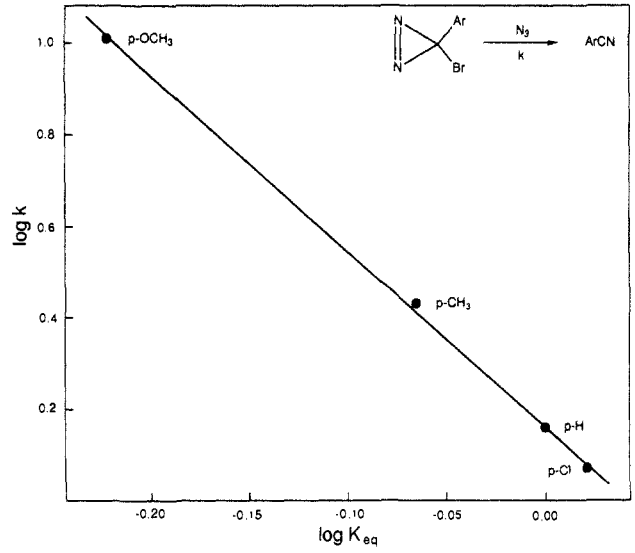
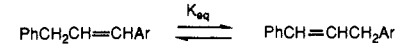


Figure 6. Plot of log *k* for the reaction of substituted arylbromodiazirines with azide vs. log K_{eq} for double-bond isomerization in 1-phenyl-3-arylpropenes.

it is true that the bromide should be more reactive than the chloride if **2** were involved, the S_N2' mechanism is also consistent with arylbromodiazirines being more reactive than arylchlorodiazirines.

The Hammett ρ^+ value was determined for the reaction of **1** and substituted analogues with azide. The value was −1. This value (the absolute value) is quite small for a mechanism involving a cationic intermediate. However, on the basis of theoretical calculations, it was suggested that the actual charge developed at the para carbon as **2** is being formed is relatively small. Therefore it was suggestd that the ρ^+ value of −1 is to be expected. We suggest the following alternative rationale for the observed substituent effect in the reaction of **1** and substituted analogues with azide ion. During the S_N2' process a carbon–nitrogen double bond develops, and this double bond is in conjunction with the aromatic ring. Therefore, we have considered the Hine alkene stability parameter[15,16] in order to account for the observed substituent effect. The equilibrium constant, K_{eq}, for the isomerization of the alkene $PhCH_2CH{=}CHAr$ (**26**) is a measure of the ability



26 **27**

of various aryl groups to stabilize a double bond. Although the number of substituents is small, Figure 6 shows that there is an excellent correlation (r = 0.9996) between literature rate data for reaction of substituted analogues of **1** with azide ion and K_{eq} for double-bond isomerization in alkene **26**. It is therefore suggested that the more rapid rate of reaction of the *p*-methoxy-substituted arylbromodiazirine with azide ion (7.1 times faster than the unsubstituted analogue) reflects the greater ability of the anisyl group to stabilize the developing carbon–nitrogen double bond in the *N*-azidodiazirine. In a similar fashion, electron-withdrawing groups on an aromatic ring decrease the stability of the developing carbon–nitrogen double bond.

It has also been found that added salts slightly increased the rate of the reaction of **1** (up to 20%) with azide in acetonitrile. This was presented as evidence for a cationic intermediate (presumably due to the normal salt effect usually seen in classic S_N1 reactions). While the salt effect could be used as evidence for a cationic intermediate, it should be kept in mind that the reaction of **1** with azide ion is bimolecular and hence not a classic S_N1 reaction. It is therefore not clear to us that reaction with azide should exhibit a normal salt effect. In support of this contention, Bordwell[17] has presented extensive evidence in a number of papers

(14) [^{15}N]-**24** reacts partially via a *C*-azidodiazirine that is proposed to arise by the $S_{RN}1$ substitution mechanism. Studies supporting this suggestion will be reported subsequently.[11]

(15) Hine, J.; Skoglund, M. J. *J. Org. Chem.* **1982**, *47*, 4766.
(16) Bushby, R. J.; Ferber, G. J. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1683.

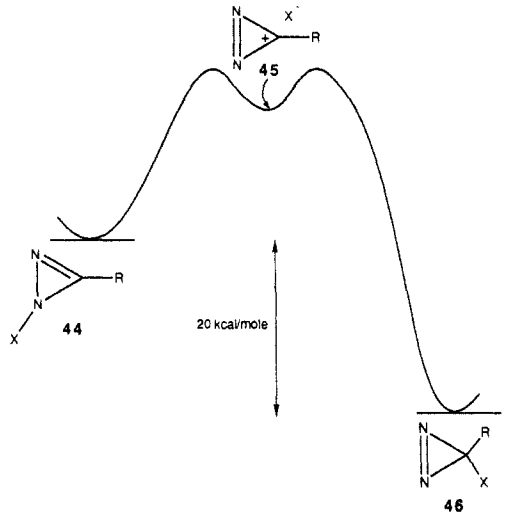
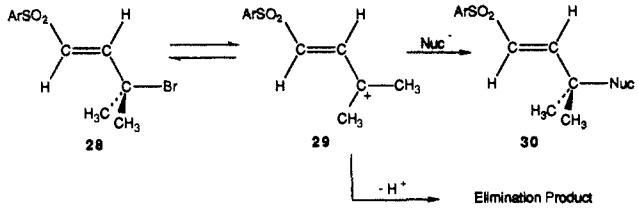


Figure 7. Proposed pathway for conversion of *N*-halodiazirines to *C*-halodiazirines.

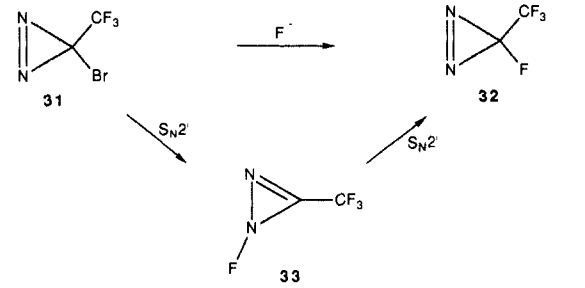
that substrate **28** reacts with nucleophiles by way of a reversibly formed ion pair. This is the same as the mechanism suggested



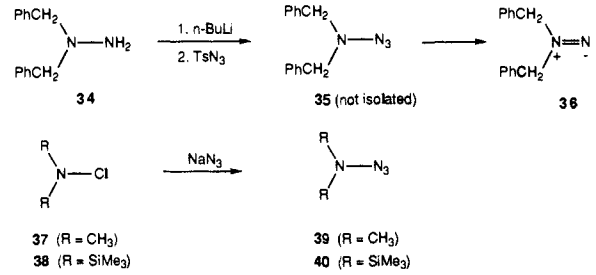
for **1**. Added salts actually suppressed rate of reaction of **28** in polar aprotic solvents such as dimethylformamide. This was attributed to the existence of the nucleophile in higher states of aggregation as added salt concentration increased. While we have no explanation for the small salt effect in the bimolecular reaction of **1** with azide, this literature precedent suggests caution in interpreting salt effects in reactions of nucleophiles with reversibly formed ion pairs.

Intermediates in Mechanism 2. Our suggestion that diazirines could react with nucleophiles by an S_N2' process is not unique. Graham suggested this as a possible mechanism in his original paper dealing with the synthesis of halodiazirines.[2] The reaction of phenylmagnesium bromide and other organometallic reagents with phenylbromodiazirine was suggested to involve initial attack of the organometallic reagent at nitrogen.[12,18] Dailey has recently reported that bromodiazirine **31** reacted quite readily with fluoride ion to give fluorodiazirine **32**.[19] On the basis of the known cation destabilizing ability of the α-CF_3 group,[20] it was suggested that **31** does not react via a cationic intermediate. Instead, it was proposed that **31** reacted by consecutive S_N2' processes to give the observed product.

Our suggested mechanism for the reaction of azide with halodiazirines involves intermediate *N*-azidodiazirines analogous to *N*-fluorodiazirine **33**. These intermediates, represented by **8**, could not be detected when the reaction is monitored by NMR spectroscopy. This type of intermediate containing four contiguous

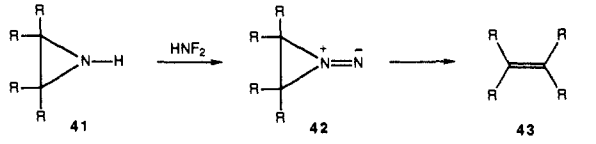


nitrogen atoms is quite unusual, although there is precedent for this type of structure in the literature. The *N*-azidoamine **35** is a suggested intermediate in the reaction of tosyl azide with the anion of dibenzylamine.[21] Intermediate **35** presumably loses



nitrogen to afford 1,1-diazene **36**. Subsequent loss of a second nitrogen leads to products derived from the benzyl radical. In contrast to **35**, explosive *N*-azidoamine **39** can be isolated,[22] and trimethylsilyl substitution stabilizes *N*-azidoamine **40** to the extent that it can actually be distilled.[23]

The suggested extrusion of nitrogen from the proposed 1,1-diazene intermediate **9** also has precedent. An analogous 1,1-diazene **42** is the proposed intermediate in the deamination of aziridine **41** with HNF_2.[24] Diazene **42** was not isolated but rapidly generated alkene **43** by loss of molecular nitrogen in an orbital symmetry allowed nonlinear cheletropic process.[25] Loss of nitrogen from 1,1-diazene **9** to give benzonitrile is analogous to the alkene forming reaction from **42**.



Diazirinium Cations in the Graham Oxidation. Computational studies suggest that diazirinium cations are high-energy intermediates.[26] Although no experimental evidence has been presented, they are suggested intermediates in the preparation of bromodiazirines and chlorodiazirines from benzamidine hydrochlorides (the Graham reaction). The proposed mechanism for the Graham reaction involves ionization of *N*-halodiazirine **44** to diazirinium cation **45**, followed by internal return to give the observed product **46** as shown in Figure 7.[27] It should be noted that ionization of **44** involves fragmentation of a N–Br or N–Cl bond, which should be much more facile than ionization of a C–Br or C–Cl bond. Computational studies place the energy difference between **44** and **46** at approximately 20 kcal/mol.[28] Therefore, the activation energy for formation of diazirinium cations from substrates such as **46** should be approximately 20 kcal/mol higher than the activation energy for ionization of the isomeric *N*-

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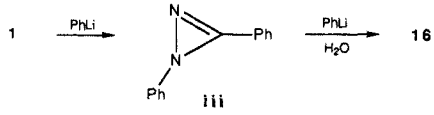
(18) The mechanism of reaction of PhLi with **1** is suggested to proceed via initial formation of **iii** and subsequent ring opening. See ref 12.



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halodiazirine. While diazirinium ions such as **45** (or **2**) may be viable intermediates from *N*-halodiazirines, they may well be bypassed in substitution reactions of **1**.

Conclusions. Studies involving the reaction of ^{15}N-labeled arylbromodiazirines with azide ion and with labeled sodium azide suggest that the nitrogen atom in the nitrile product is derived from one of the diazirine ring nitrogen atoms. *N*-Azidodiazirine intermediates, derived from attack of azide ion at nitrogen of the diazirine, are consistent with these labeling studies. These intermediates rapidly extrude two molecules of nitrogen to give benzonitrile products. Such a sequence is preferred over the previously proposed mechanism involving diazirinium cations and *C*-azidodiazirines. The previous evidence for diazirinium cations in substitution reactions of arylbromodiazirines has been reevaluated, and it is concluded that consecutive S_N2' processes more adequately account for existing data on substitution reactions of arylbromodiazirines.

Experimental Section

NMR spectra were recorded on a General Electric GN 300 spectrometer in $CDCl_3$. ^{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 with NH_4Cl (25.0 ppm) as a reference standard.[29] Mass spectra were recorded on a Finnigan MAT 8430 high-resolution spectrometer. All of the arylbromodiazirines reported in this paper were prepared with previously described procedures.[8] All of the reactions of arylbromodiazirines with azide ion were routinely shielded from room light by covering the reaction flask with foil.

Preparation of Labeled Diazirine [^{15}N]-1. Benzonitrile (1.9011 g, 0.0184 mol) was dissolved in 15 mL of anhydrous methanol, and 2.0 mL of 0.96 M sodium methoxide in methanol was added under nitrogen. The reaction mixture was stirred for 63 h at room temperature. ^{15}N-Labeled ammonium chloride (0.9688 g, 0.0183 mol; 99% ^{15}N enriched; ICN Biomedicals, Inc.) was added and the suspension stirred for 54 h at room temperature. The mixture was filtered with a Büchner funnel, and the unreacted ammonium chloride was washed with a small amount of anhydrous methanol. The filtrate was concentrated with a rotary evaporator, and the solid that formed was slurried with ether. The ether was then decanted. This procedure was carried out a total of five times in order to remove unreacted benzonitrile. The yield of ^{15}N-labeled benzamidine hydrochloride **11** was 1.2874 g (45%).

^{15}N-Labeled benzamidine hydrochloride **11** (1.287 g, 0.008 17 mol) was dissolved in 20 mL of freshly distilled dimethyl sulfoxide (DMSO), and 25 mL of hexanes was added followed by 2.92 g of NaBr. A solution of NaOBr was prepared by addition of 7.37 g of bromine to a solution of 7.57 g of NaOH in 40 mL of water at 20 °C. When all of the bromine had reacted, 3.04 g of NaBr was added and the flask was swirled to dissolve all of the NaBr. The mixture containing **11** was placed in an ice–water bath, and before the DMSO could freeze, a small amount of the freshly prepared NaOBr solution was added. The solution was allowed to cool thoroughly, and the remaining NaOBr solution was added over a 5-min period. The mixture was stirred at 0 °C for 2 h, and the organic phase was separated. The aqueous phase was extracted with two portions of ether, and the combined organic extracts were washed twice with water and then with saturated NaCl solution. The organic extract was dried over $MgSO_4$. Evaporation of the solvent gave 0.448 g of crude oil that was chromatographed on 4.9 g of silica gel and eluted with hexanes. Evaporation of solvent gave 0.280 g (17%) of diazirine [^{15}N]-**1**.

Reaction of [^{15}N]-1 with Tetrabutylammonium Azide in CH_3CN. Tetrabutylammonium azide[8,30] (1.3471 g, 0.004 73 mol) was dissolved in 5.0 mL of freshly distilled acetonitrile under nitrogen. Diazirine [^{15}N]-**1** (0.1683 g, 0.000 85 mol) was diluted with a small amount of acetonitrile and the solution added to the azide solution. The mixture was shielded from light and stirred at room temperature for 47 h. The acetonitrile was then removed with a rotary evaporator, and the residue was diluted with 12 mL of water and extracted with four portions of hexane. The organic extract was dried over $MgSO_4$. Evaporation of solvent gave 0.0434 g (49%) of benzonitrile that by ^1H NMR and gas chromatographic retention time was identical with an authentic sample of benzonitrile. The ^{15}N NMR and ^{13}C NMR spectra are shown in Figures 1 and 2. Under the same spectral conditions, unlabeled benzonitrile showed no ^{15}N signal. Mass spectral data are shown in Figure 3.

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The peak at *m/e* 104 is due to the parent peak derived from ^{15}N-labeled benzonitrile *and* the m + 1 peak derived from unlabeled benzonitrile. The amount of labeled benzonitrile (56%) was calculated from the 104/103 ratio by assuming that the m + 1 peak is 8.07% of the parent peak and that the m − 1 peak is 1.54% of the parent peak. These values were experimentally determined on a sample of unlabeled benzonitrile.

Reaction of [^{15}N]-1 with Phenylmagnesium Bromide. Diazirine [^{15}N]-**1** (0.111 g, 0.000 56 mol) was dissolved in 2 mL of anhydrous ether under nitrogen, and the solution was cooled to −50 °C. Phenylmagnesium bromide (1.0 mL of a 1.5 M solution in ether, 0.0015 mol) was added via syringe, and the mixture was allowed to warm to room temperature. After 2.5 h, the mixture was cautiously quenched with saturated ammonium chloride solution under nitrogen. The organic layer was washed with water and then saturated NaCl solution. The mixture was dried over $MgSO_4$, and the solvent was removed with a rotary evaporator. The crude crystals were slurried with hexanes to remove the biphenyl side product. The crystals obtained weighed 0.108 g; mp 136–142 °C (lit.[12] mp 145–146 °C for the ^{14}N compound). The product was dissolved in 2 mL of ether containing a small amount of CH_2Cl_2 and chromatographed on 5 g of silica gel. Elution with 2% ether in hexanes gave 0.070 g (46%) of *N,N'*-diphenylbenzamidine (**16**), mp 144–145 °C (lit.[12] mp 145–146 °C). Continued elution with increasing amounts of ether in hexanes gave an additional 0.032 g (mp 137–143 °C) of **16** that was slightly impure. The ^1H NMR spectrum and gas chromatographic retention time of the product were identical with those of an authentic sample prepared from unlabeled **1**.

The mass spectrum of unlabeled **16** showed a 100% peak at *m/e* 180 corresponding to the fragment **45** shown below. An additional peak at *m/e* 181 (14.72%) corresponds to the m + 1 peak for the fragment **45**. The mass spectrum of the product of reaction of [^{15}N]-**1** with phenylmagnesium bromide shows peak at *m/e* 180 (70.72%), 181 (100%), and 182 (13.14%). The amounts of unlabeled **45** and labeled [^{15}N]-**45** were calculated from the 180/181 ratio by assuming that the *m/e* 181 peak is 14.72% of the unlabeled **45** plus 100% of the labeled [^{15}N]-**45**. The amount of unlabeled **45** is 44%, and the amount of labeled [^{15}N]-**45** is 56%. These values correspond to 88% of monolabeled **16** and 12% dilabeled **16** if one assumes that there are no isotope effects in fragmentation of **44**.

44 **45**

Reaction of Diazirine 1 with ^{15}N-Labeled Sodium Azide. ^{15}N terminally labeled sodium azide (0.132 g of 99% terminally labeled; ICON Services, Inc.) was dissolved in 4 mL of DMSO-d_6 with gentle heating by a heat gun. The cooled azide solution was added to 0.170 g of diazirine **1**, and the mixture was stirred at room temperature for 51 h. The reaction mixture was diluted with ether, and the mixture was extracted with two portions of water. The ether extract was washed with saturated NaCl solution and dried over $MgSO_4$. Solvent removal with a rotary evaporator gave 0.045 g (57%) of benzonitrile. The mass spectrum of this product (including the 103/104 ratio) was identical with that of an authentic sample of unlabeled benzonitrile.

Reaction of *p*-Tolylbromodiazirine (22) with ^{15}N-Labeled Sodium Azide. ^{15}N terminally labeled sodium azide (0.051 g of 99% terminally labeled) was dissolved in 1.8 mL of DMSO with gentle heating by a heat gun. After the azide solution had cooled, 0.101 g of diazirine **22** was added. The mixture was stirred at room temperature for 139 h. The reaction mixture was diluted with ether and extracted with three positions of water. The ether extract was washed with saturated NaCl solution and dried over $MgSO_4$. Evaporation of solvent gave 0.048 g (80%) of *p*-methylbenzonitrile as determined by ^1H NMR spectroscopy and gas chromatographic retention time. The mass spectrum of this product (including the 117/118 ratio) was identical with that of an authentic sample of unlabeled *p*-methylbenzonitrile.

Reaction of *p*-Anisylbromodiazirine (23) with ^{15}N-Labeled Sodium Azide. ^{15}N terminally labeled sodium azide (0.053 g of 99% terminally labeled) was dissolved in 2.2 mL of DMSO-d_6. After the azide solution had cooled, 0.122 g of diazirine **23** was added. The mixture was stirred at room temperature for 42 h. The reaction mixture was diluted with ether and extracted with three portions of water. The ether extract was washed with saturated NaCl solution and dried over $MgSO_4$. Evaporation of solvent gave 0.039 g (54%) of *p*-methoxybenzonitrile as determined by ^1H NMR spectroscopy and gas chromatographic retention time. The mass spectrum of this product showed a 100% peak at *m/e* 133 corresponding to the molecular ion. An additional peak at *m/e* 134 (10.12%) corresponds to the m + 1 peak. The mass spectrum of an authentic sample of unlabeled *p*-methoxybenzonitrile showed a 100% peak at *m/e* 133 and an m + 1 peak at *m/e* 134 (9.47%).

Preparation of Labeled Diazirine [^{15}N]-**24.** 3-(Trifluoromethyl)-benzonitrile (2.983 g, 0.0172 mol) was dissolved in 17 mL of anhydrous methanol, and 1.0 mL of 1.88 M NaOMe in methanol (0.001 88 mol) was added under nitrogen. The reaction mixture was stoppered and allowed to stir for 48 h at room temperature. ^{15}N-Labeled ammonium chloride (0.9688 g, 0.0183 mol of 99.1% ^{15}N enriched; Isotech, Inc.) was added and the suspension stirred for 35 h at room temperature. The mixture was filtered, and the unreacted ammonium chloride in the filter was washed with a small amount of anhydrous methanol. The combined filtrates were concentrated with a rotary evaporator, and the crystals were slurried with ether. The ether was then decanted. This procedure was carried out a total of five times in order to remove unreacted 3-(trifluoromethyl)benzonitrile. The yield of ^{15}N-labeled 3-(trifluoromethyl)benzamidine hydrochloride was 3.0448 g (79%).

A NaOBr solution was prepared from 6.28 g of NaOH in 80 mL of water by the addition of 6.60 g of bromine. When all the bromine had reacted, 4.28 g of NaBr was added and the flask swirled to dissolve the NaBr. This solution was used immediately in the oxidation of the ^{15}N-labeled 3-(trifluoromethyl)benzamidine hydrochloride. The salt prepared above (3.044 g, 0.0135 mol) was dissolved in 40 mL of freshly distilled dimethyl sulfoxide, and 45 mL of hexanes was added followed by 3.98 g of NaBr. The mixture was placed in an ice–water bath, and before the DMSO could freeze, a small amount of the freshly prepared NaOBr solution was added. The solution was allowed to cool thoroughly, and the remaining NaOBr solution was added in portions over a 5-min period. The mixture was stirred at 0 °C for 70 min, and the organic phase was separated. The aqueous phase was extracted with two additional portions of ether, and the combined organic extracts were washed with two portions of water and with saturated NaCl solution. The organic phase was dried over $MgSO_4$, and the solvents were removed with a rotary evaporator. The residue was chromatographed on 19.6 g of silica gel and eluted with 200 mL of hexanes. The solvent was removed with a rotary evaporator, and the residue (0.456 g) was distilled (safety shield) to give 0.314 g (9%) of diazirine [^{15}N]-**24**, bp <25 °C (0.05 mm).

Reaction of [^{15}N]-**24 with Sodium Azide.** Sodium azide (0.171 g) was dissolved in 4.6 mL of DMSO. Diazirine [^{15}N]-**24** (0.231 g) was added, and the mixture was stirred at room temperature for 71 h. Ether was then added, and the mixture was extracted with two portions of water and with saturated NaCl solution. The ether solution was dried over $MgSO_4$. Solvent removal with a rotary evaporator left 0.151 g (81%) of *m*-(trifluoromethyl)benzonitrile, which was identical by ^{1}H NMR and gas chromatographic retention time with an authentic sample of *m*-(trifluoromethyl)benzonitrile. The ^{15}N NMR and ^{13}C NMR spectra are shown in Figures 4 and 5. Under the same spectral conditions, unlabeled *m*-(trifluoromethyl)benzonitrile showed no ^{15}N signal. The mass spectrum of the product shows peaks at *m/e* 171 (100%) and 172 (60.14%). Unlabeled *m*-(trifluoromethyl)benzonitrile showed peaks at *m/e* 170 (30.34%), 171 (100%), and 172 (8.96%). The ratio of [^{14}N]-**25** to [^{15}N]-**25** was calculated from the 171/172 ratio by assuming that the *m/e* 171 peak is due to unlabeled [^{14}N]-**25** and the m − 1 peak (30.34%) of labeled [^{15}N]-**25**. The peak at *m/e* 172 is due to [^{15}N]-**25** and the m + 1 peak (8.96%) of [^{14}N]-**25**.

Note Added in Proof. Since the acceptance of this manuscript, we have learned that Professor W. P. Dailey has independently carried out a study of the reaction of [^{15}N]-**1** with azide ion. We thank Professor Dailey for providing us with a preprint of his manuscript which will be published in *Tetrahedron Lett.*

Acknowledgment is made to the National Science Foundation for financial support of this research.

Registry No. 1, 4222-25-7; **1**-^{15}N, 123811-64-3; **1**-$^{15}N_2$, 123811-65-4; **7**, 100-47-0; **7**-^{15}N, 24949-34-6; **11**, 123811-70-1; **16**-^{15}N, 123811-66-5; **16**-$^{15}N_2$, 123811-67-6; **22**, 95911-62-9; **23**, 95911-61-8; **24**-^{15}N, 123811-68-7; **25**, 368-77-4; **25**-^{15}N, 123811-69-8; [N═N═^{15}N]$^-$, 33095-00-0; Bu_4NN_3, 993-22-6; CH_3-*p*-C_6H_4CN, 104-85-8; CH_3O-*p*-C_6H_4CN, 874-90-8; $^{15}NH_4Cl$, 39466-62-1; NaOBr, 13824-96-9.

A Single Crystal Molecular Structure Determination and Theoretical Calculations on Alkynyl Carboxylate Esters†

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Abstract: A single crystal molecular structure is reported for propynyl *p*-nitrobenzoate, a member of the new class of alkynyl esters. An experimentally determined C_{sp}–O bond length of 1.366 (9) Å is observed for the first time. The C≡C bond length is 1.155 (9) Å. The structural features of the ester moiety in the alkynyl ester are compared to the analogous saturated and unsaturated (vinyl, aryl) esters. Ab initio molecular orbital calculations are reported for hydroxyacetylene, ethynyl formate (**7**), propynyl formate, ethynyl acetate, vinyl formate (**10**), and methyl formate (**11**). at the 6-31G* level the most stable conformation of **7** is Z (or syn) and the calculated C≡C—O and C≡C bonds are 1.312 Å and 1.179 Å, respectively. By use of model compounds, it is estimated that the addition of correlation energy would increase these bond distances by 0.01–0.02 Å. Possible reasons for the experimental/theoretical discrepancies are discussed, and it is concluded that the theoretical values are probably closer to reality. In agreement with this conclusion, good agreement is observed between the experimental and theoretical geometries, for vinyl formate (**10**). At the 6-31G* level the calculated energies of hydrolyses for **7**, **10**, and **11** are computed to be −8.9, −4.3, and +1.5 kcal/mole, respectively. The calculated electronic structures, charge distributions, and dipole moments for acetylenic esters are also discussed.

Esters, as well as acetylenes, are ubiquitous, important, and valuable organic functionalities with a great variety of uses in mechanistic, synthetic, and bioorganic chemistry. Recently, we reported the preparation and characterization of alkynyl sulfonates,[1] **1**, alkynyl carboxylates,[2] **2**, and alkynyl phosphates,[3] **3**, which are members of the family of hitherto unknown, novel

† Dedicated to Professor Paul v. R. Schleyer on the occasion of his 60th birthday.

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§ Techion, Israel Institute of Technology.

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