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Dichlorodiazirine: A Nitrogenous Precursor for Dichlorocarbene

Gaosheng Chu, Robert A. Moss,* and Ronald R. Sauers*

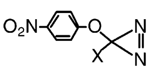
Department of Chemistry and Chemical Biology, Rutgers, The State University of New Jersey,
New Brunswick, New Jersey 08903

Received August 25, 2005; E-mail: moss@rutchem.rutgers.edu; sauers@rutchem.rutgers.edu

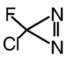
Given its central role in the history[1] and practice[2] of carbene chemistry, it is remarkable that we still lack a suitable diazo or diazirine precursor for dichlorocarbene (CCl$_2$). The carbene can be photoextruded from the CCl$_2$ adducts of styrene,[3a] 1,4-dihydronaphthalene,[3b] indane,[3c] or phenanthrene,[4] but these procedures perforce also generate aromatic byproducts which can interfere with spectroscopic studies of CCl$_2$.[4] A nitrogenous precursor is therefore desirable.

Chlorination of diazomethane with *tert*-butyl hypochlorite at −100 °C gives monochlorodiazomethane, which thermally decomposes above −40 °C.[5] However, attempts to prepare dichlorodiazomethane by further chlorination lead to rapid nitrogen loss, even at −100 °C.[5,6] Difluorodiazirine[7] and chlorofluorodiazirine[8] are available from "shatteringly explosive" fluorinated nitrogenous intermediates,[9] but extension of this chemistry to dichlorodiazirine is neither trivial nor inviting.

Recently, we reported that the reaction of fluoride with 3-*p*-nitrophenoxy-3-chlorodiazirine (**1**) followed three competitive pathways: F/Cl exchange yielding 3-*p*-nitrophenoxy-3-fluorodiazirine (**2**), F/aryloxy exchange leading to 3-fluoro-3-chlorodiazirine (**3**), and a remarkable ipso attack on the *p*-nitrophenyl moiety affording diazirinone (**4**).[10] If the reaction of **1** and chloride were to follow an analogous course, dichlorodiazirine could be obtained. We are pleased to report the success of this approach and to document the preparation of dichlorodiazirine (DCD), the first nitrogenous precursor for dichlorocarbene.



1, X=Cl; **2**, X=F



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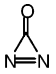

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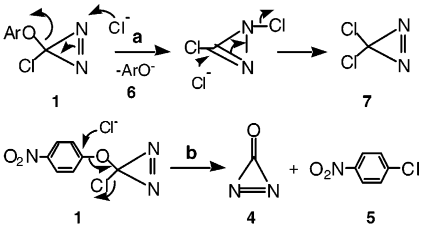
As "proof of principle", diazirine **1**[10] was reacted with excess tetrabutylammonium chloride (TBACl) in CD$_3$CN at 25 °C for 1 week in the absence of light. ^{1}H NMR monitoring revealed the slow disappearance of **1** and a concomitant build up of *p*-chloronitrobenzene (**5**) and *p*-nitrophenol (**6**) in a ratio of 7:3. The formation of products **5** and **6** suggests that the reaction of **1** and Cl$^-$ proceeds analogously to that of **1** and F^{-10} (cf. Scheme 1).

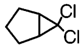
Scheme 1



Here, S$_N$2′ attack of Cl$^-$ at diazirine N (path a) leads to the ejection of *p*-nitrophenoxide (later protonated to **6**) and, via a second S$_N$2′ attack of Cl$^-$ on an intermediate isodiazirine, to the formation of dichlorodiazirine (**7**, DCD).[11]

Competitively, ipso attack of Cl$^-$ on the *p*-nitrophenyl moiety of **1** (path b) affords diazirinone (**4**) and product **5**.

We did not verify the formation of diazirinone,[12] but the generation of DCD is supported by the following observations. Repetition of the **1**/TBACl reaction in the presence of cyclopentene gave CCl$_2$ adduct **8**,[13] as well as **5** and **6** (in a 6:4 ratio). The yields of **8** and **6** were comparable.



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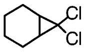

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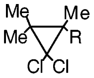

10, R=Me;
11, R=H

Analogous experiments with added cyclohexene, tetramethylethylene, or trimethylethylene afforded the expected CCl$_2$ adducts **9**−**11**.[13]

To further substantiate the intermediacy of CCl$_2$, we determined the relative reactivities[14] for the dichlorocyclopropanations of tetramethylethylene versus cyclohexene and tetramethylethylene versus trimethylethylene by running the **1**/TBACl reaction in the presence of known quantities of the paired alkenes. GC product analysis led to k_{rel} values of 56.5 and 2.17, respectively, in excellent agreement with k_{rel} = 53.7 or 2.28 for CCl$_2$ generated from chloroform and potassium *t*-butoxide.[15] The olefinic capture of CCl$_2$ from the reaction of diazirine **1** and TBACl implies the prior formation of DCD (Scheme 1, path a), which gradually decomposes to CCl$_2$ during the week-long reaction.[16] Definitive evidence is supplied by the *isolation* of DCD.

A key problem is the low nucleophilicity of chloride, which necessitates the lengthy reaction time of diazirine **1** with TBACl. We find that a more reactive chloride source is provided by a 1.1:1.0:1.6 blend of TBACl, CsCl, and the ionic liquid 1-butyl-3-methylimidazolium chloride (mp 55 °C).[17] Combination of this mixture with diazirine **1** in a little dry HMPA, followed by warming to 40−50 °C under vacuum at 1 mm·Hg, produces a melt from which DCD distills into a cold trap containing pentane at −70 °C over 6−7 h. (Chloride ion is present in >10-fold excess relative to diazirine **1** in the melt; see Supporting Information for details.)

In pentane, DCD exhibits a broad, weak UV absorbance at 310−390 (λ_{max} 339) nm, a stronger absorbance at ~260 nm (see Supporting Information), and an IR band at 1560 cm^{-1}. These features are attributable to the diazirine moiety and disappear upon photolysis at 350 nm. UV monitoring indicates that DCD is moderately stable at 25 °C in the dark: about 10% of decomposition occurs after 13 h. B3LYP/6-311+G(2d,p) calculations[18−20] predict λ_{max} values of 240 and 361 nm for DCD, and E_a = 28 kcal/mol for cleavage to CCl$_2$ and N$_2$, in fair agreement with experiment.[21]

DCD is expected to be an efficient progenitor of CCl$_2$. Indeed, photolysis of DCD in the presence of cyclohexene leads to dichloronorcarane **9**.[13] Even more convincing is laser flash pho-

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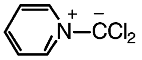

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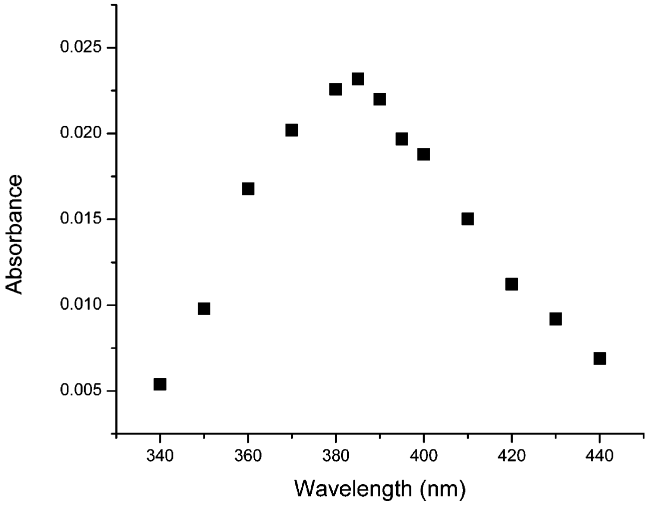

Figure 1. The transient absorption of ylide **12** formed after the laser flash photolysis of DCD in 0.4 M pyridine in pentane. The spectrum was recorded 200 ns after the laser pulse at 351 nm.

tolysis of DCD in 0.4 M pyridine/pentane, whereupon the known UV spectrum of the pyridinium dichloromethyl ylide **12** is observed with $\lambda_{\max} = 387$ nm (lit.,[4] 390 nm); see Figure 1.

With the obtention of DCD, a practical nitrogenous precursor of dichlorocarbene, various spectroscopic and absolute kinetics investigations become possible. Indeed, preliminary laser flash photolysis experiments with DCD in pentane at room temperature reveal a transient absorbing at 480−520 nm, consistent with the absorbance at 440−560 nm attributed to (matrix isolated) dichlorocarbene.[22] Further reports will appear in due course.

Acknowledgment. This paper is dedicated to the memory of Professor Gerhard L. Closs. We thank the National Science Foundation for financial support, and the National Center for Computer Applications for time on the IBM P Series 690 (to R.R.S.).

Supporting Information Available: Experimental procedure for DCD, complete ref 19, UV spectrum of DCD, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Ejection of Cl^- from **1** is degenerate and leads back to the initial diazirine.
(12) The very slow rate of the **1**/TBACl reaction, coupled with the instability of **4**,[10] makes the detection of diazirinone impossible under these conditions.
(13) This product was identified by ^1H NMR, GC, and GC−MS comparisons to an authentic sample.
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(16) A control experiment was performed to rule out the formation of CCl_2 by reaction of *p*-nitrophenoxychlorocarbene (ArOCCl, from thermolysis of **1**) with chloride ion. Photolysis of **1** with excess TBACl and cyclopentene in 1:2 MeCN/THF led to adducts of ArOCCl and cyclopentene, as well as $ArOCHCl_2$, but *not* to CCl_2 adduct **8**. Moreover, the adducts of ArOCCl and cyclopentene were *not* converted to **8** when stirred with excess TBACl for 5 days at 25 °C.
(17) For anion nucleophilicity in ionic liquids, see: Landini, D.; Maia, A. *Tetrahedron Lett.* **2005**, *46*, 3961 and references therein.
(18) All structures were fully optimized by analytical gradient methods using the Gaussian 03 suite[19] and density functional (DFT) calculations at the 6-311+G(2d,p) level, the exchange potentials of Becke[20a] and the correlation functional of Lee, Yang, and Parr.[20b] Activation energies were corrected for zero-point energy differences (ZPVE, unscaled) and thermal effects at 298.150 K. Vibrational analyses established the nature of all stationary points as either energy minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency).
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