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Chlorofluorocarbene: First UV Observation of a Dihalocarbene in Solution

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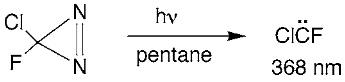
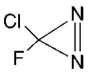
ABSTRACT



Chlorofluorocarbene (ClCF), generated by laser flash photolysis of chlorofluorodiazirine, absorbs at 368 nm in pentane. Absolute rate constants are reported for ClCF additions to several alkenes and pyridine. ClCF is less reactive toward alkenes than CCl_2, and it does not react rapidly with oxygen. Pertinent computational studies are included.

In the development of laser flash photolysis (LFP) for the study of halocarbenes in solution, halodiazirines have been the essential carbene precursors.[1] Diazirine precursors for ArCX, RCX, ArOCX, and ROCX, where X = F, Cl, or Br, are available via the Graham hypohalite oxidation of amidines or isouronium salts,[2] coupled (when X = F) with the diazirine exchange reaction.[1,3] However, dihalodiazirines, and thus dihalocarbenes, were unavailable by this methodology until 2005, when we successfully prepared chlorofluorodiazirine (**1**).[4] A parallel preparation of dichlorodiazirine (**2**) soon followed.[5]



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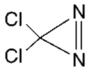

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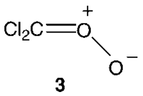
$Cl_2C{=}\overset{+}{O}{-}O^-$

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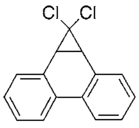
Photolyses of **1** and **2** generated ClCF and CCl_2,[4,5] but LFP experiments with **2** did not reveal the absorption signature of CCl_2, calculated at 492 nm (in simulated heptane).[6] No UV−vis signals were observed under nitrogen, while a transient absorption observed at 465 nm in pentane under air was assigned to dichlorocarbene carbonyl oxide **3**.[6] CCl_2 and ClCF have been photoextruded from hydrocarbon precursors **4**[7] and **5**,[8] respectively, but LFP experiments did not afford UV−vis spectra of the carbenes; only spectra of their pyridinium ylides were obtained.



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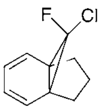

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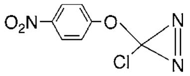

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Here, we report an improved synthesis of chlorofluorodiazirine, the UV spectrum of ClCF in solution as obtained by LFP of diazirine **1**, absolute rate constants for the reactions of ClCF with several olefins, the failure of ClCF to react with oxygen, and a computational study of the latter reaction.

Diazirine **1** was first prepared by the reductive defluorination−cyclization of a trifluoroamidine precursor,[9,10] but

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[1] Moss, R. A. *Acc. Chem. Res.* **2006**, *39*, 267.
[2] Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.
[3] Moss, R. A. In *Chemistry of Diazirines*; Liu, M.T.H., Ed.; CRC Press: Boca Raton, FL, 1987; Vol. 1, p 99f.
[4] Moss, R. A.; Chu, G.; Sauers, R. R. *J. Am. Chem. Soc.* **2005**, *127*, 2408.
[5] Chu, G.; Moss, R. A.; Sauers, R. R. *J. Am. Chem. Soc.* **2005**, *127*, 14206.
[6] Moss, R. A.; Tian, J.; Sauers, R. R.; Ess, D. H.; Houk, K. N.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **2007**, *129*, 5167.
[7] Chateauneuf, J. E.; Johnson, R. P.; Kirchoff, M. M. *J. Am. Chem. Soc.* **1990**, *112*, 3217.
[8] Tippmann, E. M.; Platz, M. S. *J. Phys. Chem. A* **2003**, *107*, 8547.

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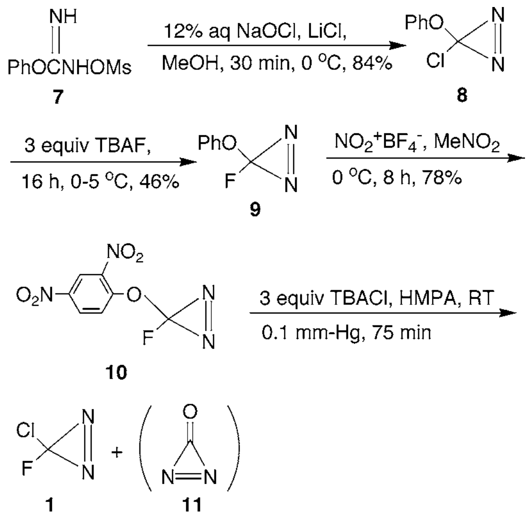
that precursor was inconvenient and explosive. We reported that the reaction of *p*-nitrophenoxychlorodiazirine (**6**) with tetrabutylammonium (TBA) fluoride provided diazirine **1** and diazirinone.[4] Now we describe a related, but more efficient and reproducible, preparation of **1** (cf. Scheme 1).

Scheme 1



N-Methanesulfonyloxy-*O*-phenylisourea (**7**)[11] was oxidized to phenoxychlorodiazirine (**8**)[12] by NaOCl in methanol. The diazirine, purified by flash chromatography, was obtained in 84% yield.[13] Diazirine **8** was converted to phenoxyfluorodiazirine (**9**) by exchange with "molten" TBAF,[14] and the fluorodiazirine was dinitrated to 2,4-dinitrophenoxyfluorodiazirine (**10**) with nitronium tetrafluoroborate in nitromethane. Diazirine **10** was slowly added to a solution of 3-fold excess anhydrous TBACl in HMPA under a vacuum at 25 °C. Chlorofluorodiazirine **1** distilled out and was trapped in 1 mL of pentane or CDCl$_3$ at 77 K. After dilution with an additional 1 mL of solvent, we obtained solutions of **1** with $A = 1.6-2.0$ at 356 nm.

The diazirine exchange reaction which converts **10** to **1** most likely proceeds via a double S$_N$2′ mechanism,[1] in which an initial S$_N$2′ attack of Cl$^-$ at diazirine N leads to the loss of 2,4-dinitrophenoxide and the generation of a *N*-chloroisodiazirine. The latter is then converted to **1** by a second S$_N$2′ attack of Cl$^-$ at carbon. (The process is analogous to the conversion of 2,4-dinitrophenoxychlorodiazirine to dichlorodiazirine by TBACl.[6]) A competitive *ipso* attack of Cl$^-$ on the 2,4-dinitrophenoxy moiety of **10** presumably leads to diazirinone (**11**), which subsequently fragments to nitrogen and carbon monoxide (within 5 min at rt).[4]

Chlorofluorodiazirine was identified by its UV spectrum in pentane (see Supporting Information, Figure S-1) which displayed absorption peaks at 356, 351, 344, 339, 334, 329, 324, and 320 nm, in excellent agreement with the published (gas phase) spectrum.[9] Diazirine **1** also afforded a ^{19}F NMR resonance at δ −104.8 (CFCl$_3$, CDCl$_3$).

LFP[6] of diazirine **1** ($A_{356} = 0.5$ in pentane) affords a weak absorption at 368 nm (Figure 1) which we assign to ClCF. The spectrum is *identical* under nitrogen or oxygen. There is no evidence for rapid reaction of ClCF with oxygen, in contrast to the behavior of CCl$_2$.[6] The 368 nm absorption accords with the reported UV specrum of ClCF at 340−390 nm obtained by photolysis of CH$_2$ClF or CD$_2$ClF in Ar matrices at 14 K.[15,16]

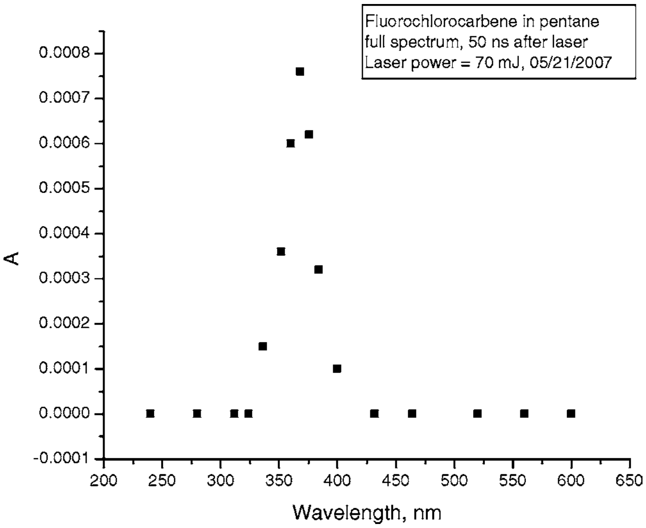


Figure 1. LFP UV spectrum of ClCF under nitrogen. The spectrum is unchanged under oxygen.

The computed absorption of ClCF is at 365 nm (Table 1), in excellent agreement with experiment. For CCl$_2$, ClCF, and CF$_2$, the percent contribution of the HOMO−LUMO excitation to the lowest carbene excited state is nearly constant at 75%. The doubly occupied in-plane σ lone pair and the formally vacant 2p orbitals on C are the primary contributors to these two molecular orbitals, so that a $\sigma \rightarrow$ p designation for the excitation appears appropriate. Note that the computed oscillator strength (*f*) of ClCF is 3 times that of CCl$_2$. Given that the observed absorbance of ClCF is very weak (Figure 1), it is perhaps not surprising that we were unable to observe the absorbance of CCl$_2$ under comparable LFP conditions.[6]

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(10) Mitsch, R. A. *J. Org. Chem.* **1968**, *33*, 1847.

(11) Fedé, J.-M.; Jockusch, S.; Lin, N.; Moss, R. A.; Turro, N. J. *Org. Lett.* **2003**, *5*, 5027.

(12) Moss, R. A.; Perez, L. A.; Wlostowska, J.; Guo, W.; Krogh-Jespersen, K. *J. Org. Chem.* **1982**, *47*, 4177.

(13) See the Supporting Information for experimental details.

(14) (a) Cox, D. P.; Moss, R. A.; Terpinski, J. *J. Am. Chem. Soc.* **1983**, *105*, 6513. (b) Moss, R. A.; Terpinski, J.; Cox, D. P.; Denney, D. Z.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1985**, *107*, 2743.

(15) Smith, C. E.; Milligan, D. E.; Jacox, M. E. *J. Chem. Phys.* **1971**, *54*, 2780.

(16) A reviewer has noted that the ClCF absorption is surprisingly narrow for a HOMO to LUMO carbene band. At its base, it spans ~100 nm. In comparison, the HOMO to LUMO absorption of MeCCl in pentane solution spans ~200 nm (Moss, R. A.; Tian, J.; Sauers, R. R.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **2007**, *129*, 10019). There are very few HOMO−LUMO bands of carbenes in solution to afford further comparisons. Note that we do not observe diazirine bleaching in Figure 1; only about 0.1% of the diazirine is destroyed per laser pulse.

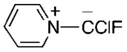
Table 1. Computed Absorptions of Dihalocarbenes[a]

carbene	λ (nm)	f
CCl_2	491.9	0.004
ClCF	365.0	0.012
CF_2	267.4	0.040

[a] Calculations are TD-PBEPBE/6-311+G(d)//PBEPBE/6-311+G(d) in simulated heptane (pentane). For details, see the Supporting Information.

Tippmann and Platz did not detect the UV absorbance of ClCF upon LFP extrusion of the carbene from precursor **5**,[8] although they did observe an extremely weak signal at ~365 nm in Freon-113 (see the inset in Figure 1 of ref 8). This was assigned to a triene valence isomer of **5** (with a computed absorbance at 285 nm),[8] although a better assignment would now appear to be ClCF, which absorbs at 368 nm in pentane (Figure 1). In any event, diazirine **1** is clearly a more efficient progenitor of ClCF than diene **5**.

LFP of **1** in the presence of 0.65 mM pyridine in pentane led to pyridine ylide **12** with a maximum at 464 nm (see Figure S-2 in the Supporting Information). A value of 406 nm ($f = 0.286$) was computed for this absorption at the TD-PBEPBE/6-311+G(d) level (details appear in the Supporting Information). A comparable UV spectrum, though with a less well-defined maximum, was obtained for **12** via LFP of **5** with pyridine in Freon-113.[8] From a correlation of k_{obs} for the formation of **12** vs the concentration of pyridine in pentane, we obtain $k_f = 2.0 \times 10^{10}$ $M^{-1}s^{-1}$ for the capture of ClCF by pyridine (Supporting Information, Figure S-3),[17] in reasonable accord with $k_f = 8.0 \times 10^9$ $M^{-1}s^{-1}$ reported for this reaction in cyclohexane.[8]



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The UV absorbance of ClCF is too weak for accurate direct kinetics studies. Therefore we used the pyridine ylide method[18] to determine absolute rate constants for addition of ClCF to several alkenes. The rate of formation of ylide **12** in pentane is accelerated by the addition of an alkene at a constant concentration of pyridine. A correlation of the observed rate constants for the formation of **12** vs [alkene] is linear, and its slope gives k_{add} for the addition of ClCF to the alkene.

An example, the addition of ClCF to tetramethylethylene (TME), appears in Figure 2, where $k_{add} = 1.2 \times 10^9$ $M^{-1}s^{-1}$, about 10 times faster than the value obtained with precursor **5** in Freon-113.[8,19] Similarly, we determined k_{add} for ClCF additions to trimethylethylene, cyclohexene, and 1-hexene.

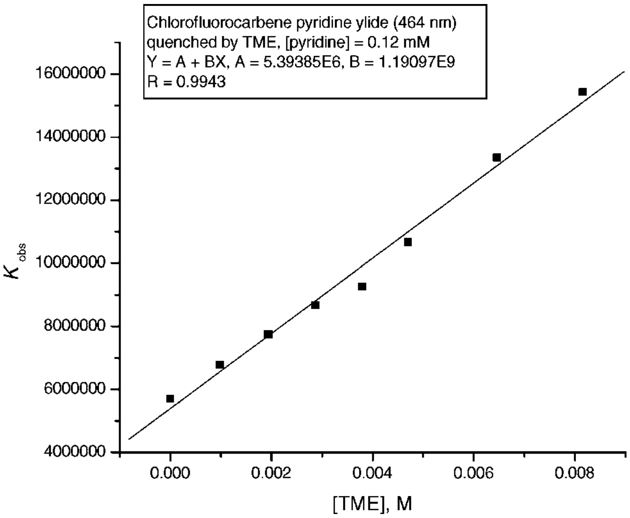

Figure 2. LFP determination of k_{add} for the addition of ClCF to tetramethylethylene: k_{obs} for the formation of **12** vs [TME].

In all cases, we maintained constant concentrations of pyridine (0.12 mM) and diazirine ($A_{356} = 0.5$) in pentane at 25 °C. Rate constants are collected in Table 2, and the correlations from which they derive appear in Supporting Information Figures S-4–S-6.[21]

Table 2. Rate Constants for Additions of Carbenes to Alkenes[a]

alkene	k_{ClCF} ($M^{-1}s^{-1}$)[b]	k_{CCl2} ($M^{-1}s^{-1}$)[c]	k_{CCl2} ($M^{-1}s^{-1}$)[d]
$Me_2C{=}CMe_2$	1.2×10^9	4.7×10^9	(3.8×10^9)
$Me_2C{=}CHMe$	3.8×10^8	2.5×10^9	(2.2×10^9)
cyclohexene	2.7×10^7	6.4×10^7	(3.5×10^7)
$CH_2{=}CHC_4H_9$	1.1×10^7	1.8×10^7	(1.1×10^7)

[a] In pentane, 25 °C, [pyridine] = 0.12 mM; $A_{diazirine} = 0.5$. [b] LFP of diazirine **1**; see text and Figures 1 and Supporting Information Figures S-4–S-6. [c] LFP of dichlorodiazirine; see Supporting Information Figures S-7–S-10. [d] Rate constants in parentheses are from LFP of precursor **4**; see ref 7.

For comparison, we measured k_{add} for additions of CCl_2 to the same alkenes. The carbene was generated by LFP of dichlorodiazirine[6] under conditions identical to those employed for ClCF. The new CCl_2 data appear in Table 2 (and in Supporting Information Figures S-7–S-10).[21] Also included in Table 2 are analogous CCl_2 rate constants obtained from LFP experiments with precursor **4**.[7] The two sets of CCl_2 data are comparable, although the diazirine-derived rate constants are slightly larger.

The absolute rate constants of Table 2 generally accord with expectations.[22] Thus, ClCF (like CCl_2[7]) reacts as an electrophile with the four alkenes: alkene reactivity increases with increasing alkyl substitution. Moreover, CCl_2, less

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(17) From the *Y*-intercept of this correlation, we derive a lifetime of ~0.2 μs for ClCF in pentane under our reaction conditions.

(18) Jackson, J. E.; Soundararajan, N.; Platz, M. S.; Liu, M. T. H. *J. Am. Chem. Soc.* **1988**, *110*, 5595.

(19) GC spiking experiments and ^1H, ^{13}C, and ^{19}F NMR comparisons with an authentic sample[20] showed that the appropriate cyclopropane was produced when diazirine **1** was photolyzed in tetramethylethylene.

(20) Dolbier, W. R., Jr.; Burkholder, C. R. *J. Org. Chem.* **1990**, *55*, 589.

(21) We estimate the errors in the rate constants at 10–15%. All of the correlation constants (*r*), from which the rate constants derive, are ≥0.99.

stabilized than ClCF by its substituents,[22] reacts more rapidly than ClCF with each alkene. We defer more detailed scrutiny of comparative ClCF−CCl_2 selectivity, as that analysis is preferably grounded in more precise alkene relative reactivity data[22] rather than in the absolute rate constants with wide dynamic ranges collected in Table 2.

As indicated above, ClCF does not react rapidly with oxygen, whereas CCl_2 does.[6] Computational studies provide a rationale for this contrast. Calculations at the PBE/6-311+G(d) level find no barrier to the formation of a triplet CCl_2−O_2 complex in an energetically favorable reaction ($\Delta H = -15.1$ kcal/mol, $\Delta G = -7.0$ kcal/mol). This complex can subsequently undergo intersystem crossing to the singlet dichlorocarbene carbonyl oxide **3** with a low activation energy (∼1.8 kcal/mol), favorable geometric factors, and significant spin−orbit coupling.[6] Indeed, intermediate **3** may well have been detected by LFP at 465 nm.[6] However, analogous PBE/6-311+G(d) calculations detect a small kinetic barrier for the formation of a triplet ClCF−O_2 complex ($\Delta H^{\ddagger} = 0.9$ kcal/mol, $\Delta G^{\ddagger} = 8.0$ kcal/mol). Moreover, the reaction is not very favorable ($\Delta H = -5.9$ kcal/mol, $\Delta G = 2.1$ kcal/mol).[23] Computational details appear in the Supporting Information.

In conclusion, we have obtained the first UV spectrum of a dihalocarbene (ClCF) in solution (368 nm) and measured the absolute rate constants of its addition reactions with several alkenes. ClCF is a moderately selective electrophilic carbene, and as anticipated, it is less reactive toward alkenes than CCl_2. In contrast to CCl_2, ClCF does not rapidly react with oxygen. Computational studies rationalize this difference and support our assignment of the carbene's UV absorbance.

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Supporting Information Available: Preparations of **1**, **8**, **9**, and **10**; Figures S-1−S-10; and computational details (optimized ground state geometries, absolute energies, and excited-state data). This material is available free of charge via the Internet at http://pubs.acs.org.

OL701804M

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[22] (a) Moss, R. A. In *Carbene Chemistry From Fleeting Intermediates to Powerful Reagents*; Bertrand, G., Ed.; Dekker-Fontis: New York, 2002; pp 57f. (b) Moss, R. A. *Acc. Chem. Res.* **1989**, *22* 15. (c) Moss, R. A. *Acc. Chem. Res.* **1980**, *13*, 58.

[23] At the B3LYP/6−311+G(d) level, the barriers for the formation of the ^{3}ClCF−O_2 and $^3CCl_2$−O_2 complexes are $\Delta G^{\ddagger} = 15.8$ and 11.7 kcal/mol, respectively, whereas the respective free energies of reaction are $\Delta G = 4.2$ and −3.8 kcal/mol.