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New Kinetics Methodologies Applied to Carbene Fragmentation Reactions

Robert A. Moss,*[†] Lauren A. Johnson,[†] Shunqi Yan,[†]
John P. Toscano,*[‡] and Brett M. Showalter[‡]

Department of Chemistry
Rutgers, The State University of New Jersey
New Brunswick, New Jersey 08903
Department of Chemistry, Johns Hopkins University
Baltimore, Maryland 21218

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Many alkoxychlorocarbenes (ROCCl, **1**) readily fragment.[1,2] When the "R" group affords a relatively stable carbocation, fragmentation occurs via ion pair (**2**); cf., eq 1.[1e−3]

$$\underset{\mathbf{1}}{\mathrm{RO\ddot{C}Cl}} \xrightarrow{k_{\mathrm{frag}}} \underset{\mathbf{2}}{[\mathrm{R^{+}\ OC\ Cl^{-}}]} \rightarrow \mathrm{RCl} + \mathrm{CO} + \text{other products} \qquad (1)$$

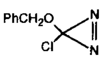
However, when R is a simple primary alkyl group (e.g., *n*-butyl), fragmentation becomes a bimolecular process driven by nucleophilic chloride attack on the carbene.[4]

We measured the rate constants (k_{frag}) of several fragmentation reactions by laser flash photolysis (LFP).[2,4,5] However, because the ROCCl generally lacked sufficiently intense UV-active chromophores, we relied on indirect kinetic monitoring of the fragmentation, making use of the pyridine ylide carbene visualization method.[6] With this method, the fragmentation itself is not *directly* observed, and the necessary dilution with pyridine, sometimes to high concentrations (e.g., 7−8 M),[7,8] can alter the solvent polarity and distort the kinetics.[9]

We are pleased to report here the first *direct* observation of carbene fragmentation, achieved by time-resolved infrared (TRIR) monitoring[10] of the appearance of CO; cf., eq 1.[11] Additionally, we disclose a second (indirect) kinetics method based on trimethoxybenzene (TMB) capture[12] of the daughter carbocations (R^+) formed from ROCCl. Together, these methods provide an unusually complete natural history of carbene fragmentation and the fate of the daughter carbocations.

We reexamined the fragmentation kinetics[5] of **1**, R = $PhCH_2$ and R = 1-adamantylmethyl ($AdCH_2$) in both MeCN (dielectric constant = 35.6) and in 1,2-dichloroethane (DCE, $\epsilon = 10.7$). The latter's dielectric constant is similar to that of pyridine ($\epsilon = 12.3$), so that changes in solvent polarity due to pyridine dilution during pyridine LFP determinations of k_{frag} are mitigated in DCE.[9]

Photolysis of 3-benzyloxy-3-chlorodiazirine (**3**) in MeCN led to benzyloxychlorocarbene (**1**, R = $PhCH_2$), which fragmented to $PhCH_2^+$ via ion pair **2**,[13] affording benzyl chloride and *N*-benzylacetamide (from $PhCH_2^+$ attack on MeCN); cf., eq 1. LFP studies using UV detection and pyridine ylide visualization[6] afford $k_{\mathrm{frag}} = 3.6 \pm 0.45 \times 10^5\ \mathrm{s}^{-1}$ (Table 1). In DCE solvent, where only $PhCH_2Cl$ is formed, the same LFP method gives $k_{\mathrm{frag}} = 6.2 \pm 0.2 \times 10^4\ \mathrm{s}^{-1}$. A small solvent effect may operate here; fragmentation is about 6 times faster in the more polar solvent, reflecting the polar transition state for conversion of **1** → **2**.[14]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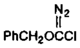
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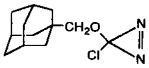
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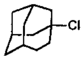
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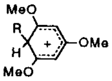
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LFP of **3** in MeCN or DCE was next monitored from 2000 to 2200 cm^{-1} by TRIR spectroscopy,[10] using 0.5 mm IR cells and $A_{355}(\mathbf{3}) = 0.5$. A TRIR spectrum averaged from 7 to 9 μs following the laser flash appears in the inset of Figure 1 (DCE experiment), where the band at 2132 cm^{-1} represents the formation of CO during fragmentation (verified with authentic CO). The time dependence of CO formation at 2132 cm^{-1} is depicted in Figure 1, where analysis of the principal growth curve gives $k = 2.9 \times 10^5\ \mathrm{s}^{-1}$ for CO formation, which we equate with k_{frag}. In MeCN ($\nu_{\max}\mathrm{CO} = 2140\ \mathrm{cm}^{-1}$) very similar results are obtained, with $k_{\mathrm{frag}} = 4.4 \times 10^5\ \mathrm{s}^{-1}$. These directly observed values (Table 1) are in reasonable agreement with the indirect LFP-UV (pyridine ylide) results. To avoid overinterpretation of our data, we do not attempt to analyze small differences between k_{frag} values determined by our three different monitoring methods.

In Figure 1, we note the rapid formation and decay of a second transient immediately after the laser pulse, a feature we attribute to (unstable) benzyloxychlorodiazomethane (**4**), formed by photoisomerization of diazirine **3**. Related diazirine to diazo isomerizations are known,[15] and our assignment is supported by a B3LYP/6-31G* calculation (gas phase, Gaussian 98, $\lambda = 1$)[16] which predicts the IR diazo band of **4** to fall at 2141.8 cm^{-1}; that is, making likely its overlap with CO.

Photolysis of 3-(1-adamantylmethoxy)-3-chlorodiazirine (**5**) in MeCN gives mainly the fragmentation products homoadamantyl chloride (**6**, 62%) and the corresponding *N*-homoadamantylacetamide (11%).[5] Again, we formulate the reaction as the fragmentation of ROCCl (R = 1-$AdCH_2$), for which LFP-UV (pyridine)

[†] Rutgers University.

[‡] Johns Hopkins University.

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Table 1. Fragmentation Kinetics of Alkoxychlorocarbenes, ROCCl[a]

method	k_{frag} (R = PhCH$_2$), s^{-1} MeCN	k_{frag} (R = PhCH$_2$), s^{-1} DCE	k_{frag} (R = AdCH$_2$), s^{-1} MeCN	k_{frag} (R = AdCH$_2$), s^{-1} DCE
LFP, UV (pyr)	$3.6 \pm 0.45 \times 10^5$	$6.2 \pm 0.2 \times 10^4$	$2.45 \times 10^{6\,b}$	$8.26 \pm 0.23 \times 10^5$
LFP, TRIR[c]	$4.4 \pm 0.03 \times 10^5$	$2.9 \pm 0.1 \times 10^5$	*d*	$3.25 \pm 0.07 \times 10^5$
LFP, UV (TMB)	$9.3 \pm 2.1 \times 10^6$	*d*	$4.2 \pm 0.4 \times 10^6$	$1.1 \pm 0.2 \times 10^6$

[a] At ambient temperature. [b] Compare, $k_{frag} = 5.2 \times 10^6$ s^{-1}; ref 5. [c] TRIR rate constants are based on averages of two to four sets of 4000 or 16000 laser shots. [d] Not measured; see text.

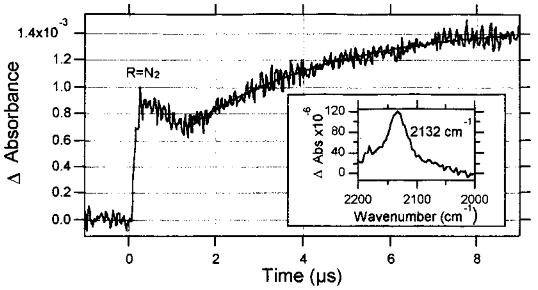

Figure 1. Intensity of CO vs time in the fragmentation of PhCH$_2$OCCl in DCE monitored at 2132 cm^{-1} by LFP-TRIR. The solid line is the calculated best fit to a single exponential for the growth of CO; $k_{frag} = 2.9 \times 10^5$ s^{-1}. The simultaneous diazoalkane formation and decay is discussed in the text. *Inset*: TRIR spectrum (2000−2200 cm^{-1}) averaged over 7−9 μs following a 355 nm laser pulse (0.5 mJ, 90 ns) applied to diazirine **3**.

affords $k_{frag} = 2.45 \times 10^6$ s^{-1}, recorded in Table 1. In DCE, the same methodology yields $k_{frag} = 8.26 \pm 0.23 \times 10^5$ s^{-1}.

LFP-TRIR kinetics were conducted on **5** as for **3**. Multiscans from 2000 to 2080 cm^{-1} in DCE tracked the time-dependent CO formation attending the fragmentation of AdCH$_2$OCCl. In DCE, $k_{frag} = 3.25 \pm 0.07 \times 10^5$ s^{-1} in reasonable agreement with the LFP-UV (pyridine) value (Table 1). In MeCN, however, persistence of the (putative) diazoalkane isomer of **5**, formed after the laser pulse, interfered with the analysis of CO production and prevented accurate determination of k_{frag}.

Pezacki et al. found that LFP of oxadiazolines generated diazoalkanes which, in the presence of (e.g.) CF$_3$COOH, very rapidly protonated to give alkyldiazonium ions, which then lost nitrogen, affording carbocations. These could be captured by TMB, yielding chromogenic cyclohexadienyl cations (**7**), which were readily observable in the UV.[12a] The additions of R$^+$ to TMB were diffusion-controlled.[12a]

LFP of **5** in MeCN or DCE containing 2.68 M TMB gave UV signals for **7** (R = homoad) at 385 nm (MeCN) or 390 nm (DCE). Analysis of the growth of **7** with time gave apparent rate constants (k_{app}) for the formation of **7**. Accepting that the addition of R$^+$ to TMB is diffusion-controlled,[12a] the rate-determining step in the ultimate formation of **7** must be the fragmentation of ROCCl to generate R$^+$. We therefore equate k_{app} with k_{frag}.[17]

We thus obtain $k_{frag} = 4.2 \pm 0.4 \times 10^6$ s^{-1} in MeCN and $1.1 \pm 0.2 \times 10^6$ s^{-1} in DCE, in reasonable agreement with the values from the UV (pyridine ylide) or TRIR methods (Table 1). Analogous LFP experiments with diazirine **3** and TMB in MeCN give signals for **7** (R = PhCH$_2$). Analysis affords k_{frag} for PhCH$_2$-OCCl as $9.3 \pm 2.1 \times 10^6$ s^{-1} (three experiments), which appears too high. However, the yield of **7** (R = PhCH$_2$) was quite low,[17] and k_{frag} here is not very reliable. In DCE, accurate data could not be obtained.

Further manipulation of the TMB data is possible.[12a] For the LFP of **5** in MeCN, a Stern−Volmer plot of 1/absorbance of **7** vs 1/[TMB] is linear ($r = 0.995$, 8 points). Assuming diffusion control for the R$^+$/TMB reaction, one can extract the lifetime of R$^+$ from the intercept and slope of the Stern−Volmer correlation.[6b,12a] We find $\tau = 2.6 \pm 0.6 \times 10^{-11}$ s for the homoadamantyl cation in MeCN/TMB. For comparison, Pezacki et al. report $\tau = 1.2 \times 10^{-10}$ s for 2-Ad$^+$ in aqueous MeCN.[12a]

Finally, we determined Arrhenius parameters for the fragmentation of 1-AdCH$_2$OCCl using both the LFP (pyridine) and LFP (TMB) monitoring methods for k_{frag}. With the former procedure, and the reaction temperature varied from −39 to 21 °C, linear correlation of ln k_{frag} versus $1/T$ gave $E_a = 3.6 \pm 0.2$ kcal/mol, log $A = 9.2 \pm 0.4$ s^{-1} (MeCN) and $E_a = 4.6 \pm 0.3$ kcal/mol, log $A = 9.3 \pm 0.6$ s^{-1} (DCE). With LFP (TMB) over −29 to 39 °C, the Arrhenius correlation in MeCN gave $E_a = 5.4 \pm 0.3$ kcal/mol, log $A = 10.6 \pm 0.4$ s^{-1}.[18] It is unclear how to interpret small differences between low E_a's measured with different monitoring methods.

Using DFT methodology, in analogy to our previous study,[14] we computed[19] the E_a's for the fragmentation of (*cis*)-1-AdCH$_2$-OCCl to the homoadamantyl cation, CO, and chloride as 4.38 (MeCN) or 5.58 (DCE) kcal/mol, in good agreement with the observed values. We have suggested that the 1-AdCH$_2$OCCl fragmentation involves a concerted ring expansion of the 1-adamantylmethyl group directly to the homoadamantyl cation.[5] The B3LYP/6-311+G** transition state, together with a B3LYP/6-31G* intrinsic reaction coordinate calculation, support this idea, although, in accord with the low activation energy, the transition state is "early." Details will appear in a full paper.

In conclusion, we have applied the mutually supportive TRIR and UV methodologies to the kinetics of ROCCl fragmentation. In the case of 1-AdCH$_2$OCCl, an unusually complete picture emerges: carbene fragmentation occurs with $k_{frag} \approx (2-4) \times 10^6$ s^{-1} (MeCN) or $\approx 3-10 \times 10^5$ s^{-1} (DCE), and $E_a \approx 3-5$ kcal/mol, log $A \approx 9.1-10.4$ s^{-1}; while the homoadamantyl cations produced by the fragmentation survive for $\sim 2 \times 10^{-11}$ s in MeCN. Applications of the multiple kinetic methodologies described here to other alkoxychlorocarbenes are in progress.

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(17) Most likely, only those carbocations that escape from the ion pair, possibly a small fraction, can react with TMB.

(18) Arrhenius experiments with k_{frag} for PhCH$_2$OCCl gave poor and relatively flat correlations, indicative of a very low E_a. The computed E_a in MeCN is 1.45 kcal/mol.[14]

(19) Single point SCI-PCM calculations were based on fully optimized B3LYP/6-311+G** gas-phase geometries, and incorporated zero-point energy and thermal corrections at the B3LYP/6-31G* level.