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Solvent-Equilibrated Homoadamantyl Chloride Ion Pairs from Chloroformate or Oxachlorocarbene Fragmentations

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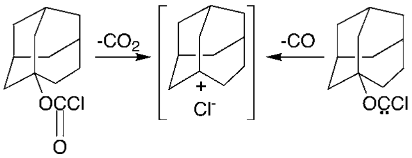
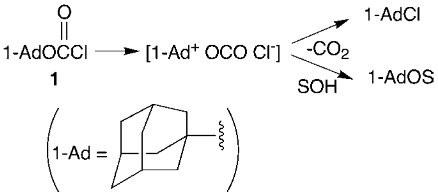
ABSTRACT



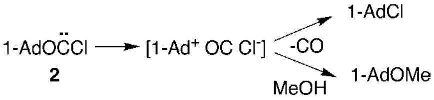
Fragmentations of 3-homoadamantyl chloroformate and 3-homoadamantyloxychlorocarbene produce identical ion pairs as product-determining intermediates.

Kevill, Kyong, et al. present strong evidence that the fragmentation of 1-adamantyl chloroformate (**1**) in hydroxylic solvents proceeds with loss of carbon dioxide to adamantyl chloride ion pairs, which then give adamantyl chloride (1-AdCl) by ion pair collapse or 1-AdOS by solvolysis; cf. Scheme 1.[1,2] This process closely resembles the fragmentation of 1-adamantyloxychlorocarbene (**2**) in (for example) methanol, where an analogous ion pair, there formed with the expulsion of carbon monoxide, similarly affords 1-AdCl by ion pair return or 1-AdOMe by ion pair solvolysis; cf. Scheme 2.[3,4]

Scheme 1



Scheme 2



Despite the overall similarities, the ion pairs of Schemes 1 and 2 are not identical: Kevill notes that the [1-AdOMe]/[1-AdCl] product ratio from the fragmentation of chloroformate **1** in methanol is 2.9,[2] whereas this ratio is only 0.67 from carbene **2**.[3b] The [1-Ad$^+$Cl$^-$] ion pair from the carbene is more likely to undergo chloride return, while the ion pair from the chloroformate prefers solvolysis to 1-AdOMe. Either a higher-energy, shorter-lived carbocation forms from carbene **2**, or there is less steric hindrance to chloride return when CO, rather than CO$_2$, is the ejected molecule.[2]

Moreover, it is likely that one or both of the ion pairs of Schemes 1 and 2 are not solvent- and anion-equilibrated and therefore exhibit precursor "memory" and different

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[1] Kevill, D. N.; Kyong, J. B.; Weitl, F. L. *J. Org. Chem.* **1990**, *55*, 4304.

[2] Kyong, J. B.; Yoo, J.-S.; Kevill, D. N. *J. Org. Chem.* **2003**, *68*, 3425.

[3] (a) Moss, R. A.; Ge, C.-S.; Maksimovic, L. *J. Am. Chem. Soc.* **1996**, *118*, 9792. (b) Moss, R. A.; Zheng, F.; Fedé, J.-M.; Sauers, R. R. *Org. Lett.* **2002**, *4*, 2341.

[4] Moss, R. A.; Zheng, F.; Fedé, J.-M.; Johnson, L. A.; Sauers, R. R. *J. Am. Chem. Soc.* **2004**, *126*, 12421.

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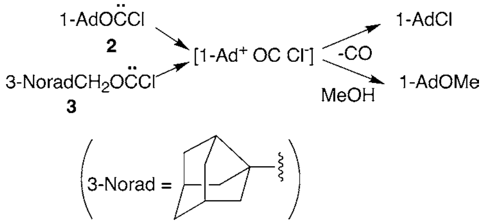
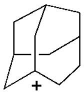
product distributions.[4] We recently reported that the [1-Ad$^+$-Cl$^-$] ion pairs generated in methanol by the direct fragmentation of carbene **2** or the ring expansion−fragmentation of 3-noradamantylmethoxychlorocarbene (**3**) lead to divergent [1-AdOMe]/[1-AdCl] product ratios; cf. Scheme 3.[3b,4] The ratio was ~0.43 from carbene **3** but 0.67 from carbene **2**. In our view, the [1-Ad$^+$Cl$^-$] ion pair is not sufficiently stable to live long enough to achieve anion and solvent cage equilibration and to "forget" its precursor, whether that be chloroformate **1** or carbenes **2** or **3**.

Scheme 3



However, the 3-homoadamantyl (3-Homoad) cation (**4**) is ~4 kcal/mol more stable than the 1-adamantyl cation (**5**) in the gas phase.[5,6] If the solution lifetimes of the [R$^+$Cl$^-$] ion pairs parallel the stabilities of R$^+$, then [3-Homoad$^+$Cl$^-$] will be longer-lived than [1-Ad$^+$Cl$^-$] and could achieve solvent equilibration and precursor independence. Indeed, [3-Homoad$^+$Cl$^-$] ion pairs generated *either* by direct fragmentation of carbene **6** or by ring expansion−fragmentation of 1-adamantylmethoxychlorocarbene (**7**) exhibit identical partition between Cl$^-$ return and MeOH solvolysis across a broad range of methanol concentrations in dichloroethane (DCE); in pure methanol, the [3-HomoadCl]/[3-HomoadOMe] distribution is ~0.71 from either source.[4] We estimate that 20−30 ps is required for solvent and anion equilibration of the [3-Homoad$^+$Cl$^-$] ion pairs.[4]



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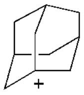

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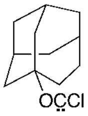

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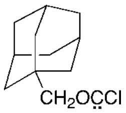

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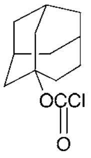
These results clearly predict that, in contrast to the divergent Cl$^-$/MeOH selectivities of the [1-Ad$^+$Cl$^-$] ion pairs from chloroformate **1** and carbene **2**, the selectivities associated with the ion pairs formed from 3-homoadamantyl chloroformate (**8**) and 3-HomoadOCCl (**6**) should be *identical*. Here we present an experimental test of this proposition, as well as related computational studies of the relevant ion pairs.



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3-Homoadamantanol[7] was converted in 79% yield to the corresponding chloroformate (**8**)[8] with triphosgene and pyridine in ether/benzene. The chloroformate was characterized by ^{1}H and ^{13}C NMR spectroscopy, as well as by IR spectroscopy (see Supporting Information). Similarly, 1-adamantyl chloroformate[1,9] was prepared from 1-adamantanol using triphosgene in place of phosgene.

The decomposition of **8** (to 3-HomoadCl) in benzene at 15 °C was monitored by IR spectroscopy relative to an ethyl acetate standard, measuring the integrated intensity of the chloroformate's carbonyl absorbance (1776 cm^{-1}) against that of EtOAc (1739 cm^{-1}) at 5−10 min intervals; cf. Figure S1 in Supporting Information. From a correlation of ln(relative intensity at 1776 cm^{-1}) vs time, we obtained $k = 2.56 \times 10^{-4}$ s^{-1} for the decay of **8** (Figure S2, Supporting Information), corresponding to a half-life of ~45 min. The decomposition of **8** is therefore 465 times faster than the analogous reaction of its 1-adamantyl relative ($k = 5.51 \times 10^{-7}$ s^{-1} in benzene at 14.6 °C).[9] This is reasonable, given that the fragmentation of **8** transits the more stabilized[5] homoadamantyl cation.

Fragmentations of chloroformates **1** and **8** were carried out in MeOH−DCE mixtures at 20 °C. The fragmentation of **1** was followed by IR, monitoring the decrease in carbonyl absorption at 1783 cm^{-1} over 3 days. With the more reactive **8**, fragmentation was complete in 2 h. In each case, the major products were RCl and ROMe, readily identified by capillary GC and GC-MS comparisons with authentic materials (see Supporting Information). The chlorides and ethers can be attributed to collapse or methanolysis of [R$^+$Cl$^-$] ion pairs (see, for example Scheme 1). These products were accompanied by minor quantities of 1-AdOH (2−3.5% from **1**) or 3-HomoadOH (4−8% from **8**), which may have arisen by adventitious hydrolysis of the chloroformates (followed by loss of CO$_2$).

Tables S1 and S2 (Supporting Information) detail the capillary GC product distributions from the fragmentations of **1** and **8** at each of 7 MeOH mole fractions in DCE. Ratios of [ROMe]/[RCl] were determined from the product distributions and corrected for relative detector response. In the case of chloroformate **8**, traces of 3-HomoadCl formed during preparation and manipulation. ^{1}H NMR analysis permitted the quantitation of this "preexisting" chloride so that the fragmentation product mixture could be corrected for it by subtraction from the chloride component.[10]

Figure 1 illustrates the dependence of the [1-AdOMe]/[1-AdCl] product ratio from the fragmentation of chloroformate

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(5) (a) Abboud, J.-L. M.; Alkorta, I.; Davalos, J. Z.; Müller, P.; Quintanilla, E.; Rossier, J.-C. *J. Org. Chem.* **2003**, *68*, 3786. (b) Abboud, J.-L. M.; Herreros, M.; Notario, R.; Lomas, J. S.; Mareda, J.; Müller, P.; Rossier, J.-C. *J. Org. Chem.* **1999**, *64*, 6401. (c) Abboud, J.-L. M.; Alkorta, I.; Davalos, J. Z.; Müller, P.; Quintanilla, E. *Adv. Phys. Org. Chem.* **2002**, *37*, 57.

(6) This corresponds to the free energy difference associated with chloride exchange between 1-Ad$^+$ and 3-Homoad$^+$ in the gas phase and reflects the intrinsic gas-phase stabilities of the carbocations.

(7) Farcasiu, D.; Jähme, J.; Rüchardt, C. *J. Am. Chem. Soc.* **1985**, *107*, 5717.

(8) Gerzon, K.; Krumkalns, E. V. U.S. Patent 3,369,041, 1968.

(9) Kevill, D. N.; Weitl, F. L. *J. Am. Chem. Soc.* **1968**, *90*, 6416.

(10) Control experiment established that 3-HomoadCl was not solvolyzed to 3-HomoadOMe after 12 h in MeOH at 25 °C.

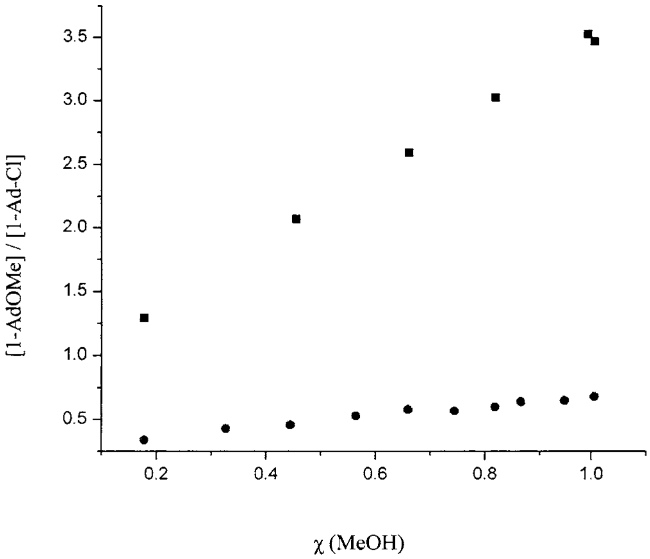


Figure 1. Product ratio [1-AdOMe]/[1-AdCl] from fragmentations of chloroformate **1** (Scheme 1) and carbene **2** (Scheme 2) in MeOH/DCE vs χ_{MeOH}; cf. Table S1 in Supporting Information (for **1**) and Table S4 in Supporting Information of ref 4 (for **2**). Key: ■ from chloroformate **1**; ● from carbene **2**.

1 on the mole fraction of MeOH in DCE. This correlation is compared with analogous data for the fragmentation of 1-adamantyloxychlorocarbene (**2**).[4] The dependences of the ether/chloride product ratios on χ_{MeOH} are clearly very different. Chloride return dominates the carbene fragmentation, whereas methanolysis holds sway over the chloroformate decomposition. The detailed studies summarized in Figure 1 underscore Kevill's conclusion[2] that the fragmentations of **1** and **2** do not transit identical ion pair intermediates. The results are consistent with our suggestion that [1-Ad$^+$Cl$^-$] ion pairs are too short-lived to achieve the anion and solvent cage equilibration required for precursor independence.[4]

Figure 2 compares the dependences of the [3-HomoadOMe]/[3-HomoadCl] product ratios from the fragmentations of chloroformate **8** and carbene **6** on χ_{MeOH} in MeOH–DCE solutions. Within experimental error (±0.04), the product ratios for the two reactions are very similar across the entire range of methanol mole fractions and effectively independent of the precursor, chloroformate **8** or carbene **6**. The results have two important consequences: they provide strong support for Kevill's formulation of tertiary-alkyl chloroformate decomposition as an ion pair process[1,2] and they bolster our previous contention that the fragmentation of homoadamantyloxychlorocarbene (**6**), but not that of adamantyloxychlorocarbene (**2**), occurs via a counterion- and solvent-equilibrated ion pair as the product-determining intermediate.[4]

Scheme 4 summarizes the key result: both chloroformate **8** and carbene **6** fragment to [3-Homoad$^+$Cl$^-$] ion pair **9**, which either collapses to chloride **10** or is diverted by methanol to ether **11**. The same ion pair is formed from either precursor, so that the product ratio [**11**]/[**10**] is precursor-independent.

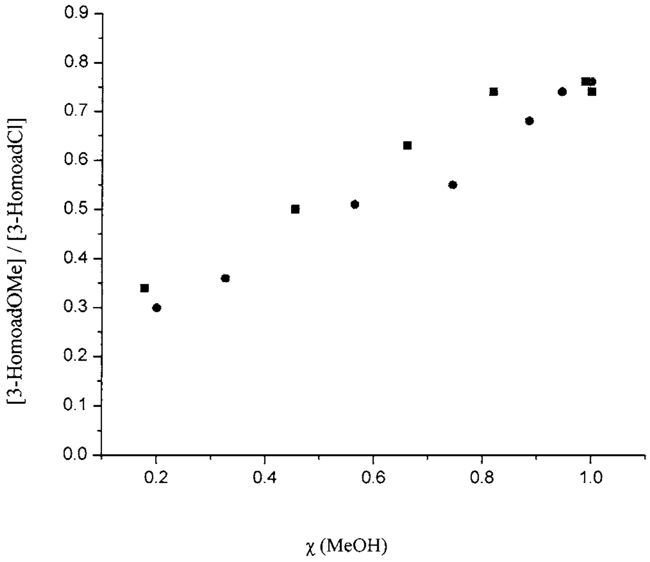
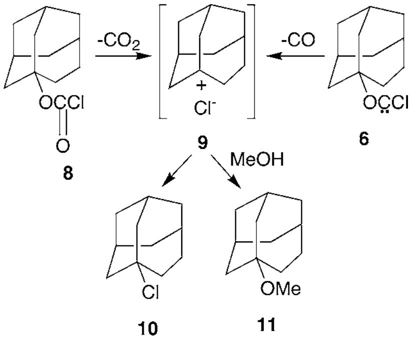


Figure 2. Product ratio [3-HomoadOMe]/[3-HomoadCl] from the fragmentations of chloroformate **8** and carbene **6** (see Scheme 4) in MeOH/DCE vs χ_{MeOH}; cf. Table S2 in Supporting Information (for **8**) and Table S6 in Supporting Information of ref 4 (for **6**). Key: ■ from chloroformate **8**; ● from carbene **6**.

Computational studies were carried out for the fragmentations of chloroformates **1** and **8**. All structures were fully optimized by analytical gradient methods using the Gaussian98 and Gaussian03 suites[11a] and density functional (DFT) calculations at the 6-31G(d) level, with the exchange potentials of Becke[11a,b] and the correlation functional of Lee, Yang, and Parr.[11a,c] Activation energies were corrected for zero-point energy differences (ZPVE, unscaled) and thermal effects at 298.150 K. Vibrational analyses established the nature of stationary points as either energy minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency). Solvation simulations used the polarized continuum model (PCM) methodology.[11a]

The transition state (TS) computed for the fragmentation of chloroformate **1** (Figure S3a in Supporting Information; Δ*H** (298 K) = 26.9 kcal/mol in vacuo) was subjected to an intrinsic reaction coordinate (IRC) calculation, followed

Scheme 4



by PCM optimization in simulated methanol, affording the ion pair depicted in Figure 3a. Similarly, fragmentation of chloroformate **8** was computed to traverse the TS shown in Figure S3b (Supporting Information, $\Delta H^* = 21.4$ kcal/mol in vacuo). An IRC calculation and optimization in methanol yielded the ion pair shown in Figure 3b. The lower activation enthalpy calculated for the 3-Homoad chloroformate vs 1-Ad chloroformate reflects the 4 kcal/mol greater stability of 3-Homoad$^+$ vs 1-Ad$^+$ in the gas phase at 331 K.[5,6]

The chloroformate-derived ion pairs of Figure 3 can be compared with the corresponding ion pairs computed for the fragmentations of carbenes **2** and **6** (Figures 6 and 5 in ref 4). All four ion pairs are similar and feature H-bonding between the chloride anion and the C−H bonds that flank the cationic carbon atom. In the [1-Ad$^+$Cl$^-$] case, the C−H···Cl$^-$ separations are 2.71 Å from chloroformate **1** and 2.80 Å from carbene **2**,[4] while the accompanying C$^+$···Cl$^-$ separations are 4.10 and 4.28 Å, respectively, all in simulated methanol. For the [3-Homoad$^+$Cl$^-$] ion pairs, the C−H···Cl$^-$ separations are 2.38 and 2.82 Å from chloroformate **8** and 2.54 and 2.90 Å from carbene **6**. The related C$^+$···Cl$^-$ separations are 3.86 and 4.16 Å, respectively.

The computed ion pairs are not identical in either case, although the experimentally observed MeOH/Cl$^-$ selectivity is comparable in the [3-Homoad$^+$Cl$^-$] reactions (Scheme 4). The residual differences in the computed ion pair geometries may reflect the presence of CO_2 (from the chloroformate precursors) as opposed to CO (from the carbene precursors). We also note that the PCM method used to optimize the ion pairs in methanol does not employ actual solvent molecules and cannot replicate methanol−chloride H-bonds. However, the computational study strongly supports ion pairs as the product-determining intermediates in the fragmentations of chloroformates **1** and **8** (and carbenes **2** and **6**). Furthermore, experiment demonstrates that the ion pairs derived from 3-homoadamantyl chloroformate and 3-homoadamantyloxychlorocarbene behave as solvent- and anion-equilibrated species in methanolic solution, in keeping with predictions based on previous results.[4]

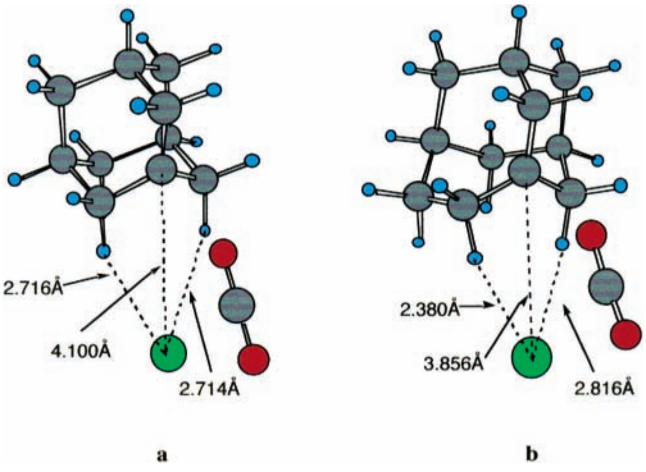


Figure 3. (a) Optimized ion pair from the fragmentation of chloroformate **1** from an IRC calculation on the TS shown in Figure S3a (Supporting Information) using B3LYP/6-31G(d) in simulated methanol with the PCM.[11] (b) Optimized ion pair from the fragmentation of chloroformate **8** from an IRC calculation on the TS shown in Figure S3b using B3LYP/6-31G(d) in simulated methanol (PCM).[11]

Acknowledgment. We are grateful to the National Science Foundation for financial support and to the National Center for Supercomputing Applications for allocation of computer time on the IBM pseries 690 (Grant CHE 030060). We thank Professor Dennis N. Kevill for helpful correspondence.

Supporting Information Available: Synthetic procedures, Tables S1 and S2 of product distributions for chloroformates **1** and **8**, and Figures S1−S3. This material is available free of charge via the Internet at http://pubs.acs.org.

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