

Ionic and radical fragmentations of alkoxyhalocarbenes – a perspective

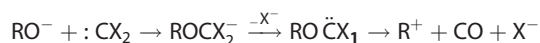
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Fragmentations of secondary or tertiary alkoxyhalocarbenes in polar solvents generate carbocations as components of ion pairs. A variety of carbocations can be produced including acyclic, alicyclic, benzyl, bridgehead, cyclopropyl, cyclopropylcarbinyl, and norbornyl examples. Laser flash photolysis (LFP) studies provide kinetics and activation parameters for the carbene fragmentations, which are orders of magnitude faster, and require considerably reduced activation energies, compared to analogous solvolytic carbocation-generative processes. In some cases, the time required for solvent and anion equilibration of the ion pairs can be estimated. In nonpolar solvents, the gas phase, or cryogenic matrices, homolytic carbene fragmentation may, in certain cases, supplant heterolytic fragmentation. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: carbenes; carbocations; ion pairs; radicals

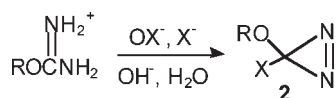
INTRODUCTION

In the 1950s, Hine^[1] and Skell^[2] discovered that alkoxides and dihalocarbenes reacted to form alkoxyhalocarbenes, ROX, **1**. When R was a secondary or tertiary alkyl group, ROX fragmented to R⁺ with the loss of CO and X⁻ (X = Cl or Br).



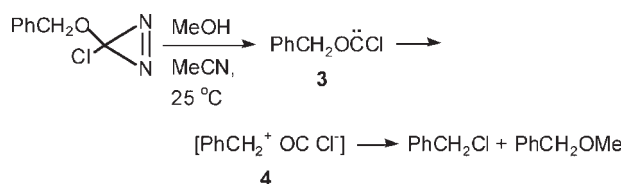
Subsequent deprotonation of R⁺ under the strongly basic reaction conditions afforded alkenes. The fragmentation of alkoxyhalocarbenes is of intrinsic mechanistic interest, but the presence of strong base limits mechanistic interrogation; neither carbenes nor carbocations will long survive the reaction conditions.

In 1965, Graham reported that the hypohalite oxidation of amidines gave halodiazirines and, in the case of alkyl isoureas, alkoxyhalodiazirines (**2**), could be obtained.^[3] Next, Smith and Stevens found that methoxychlorocarbene (MeOCCl) and isobutoxychlorocarbene (*i*-BuOCCl) formed upon thermolyses of **2** with R = Me or *i*-Bu, and X = Cl.^[4]



Alkoxyhalocarbenes could thus be generated under neutral conditions in a variety of solvents; the scope and mechanisms of their reactions could be examined.

An early example is the fragmentation of benzyloxychlorocarbene, **3**, which yields benzyl chloride in MeCN at 25 °C.^[5] In MeCN–MeOH mixtures, both benzyl chloride and benzyl methyl ether form, the yield of the ether increasing to a maximum of ~60% in undiluted methanol. Remarkably, about 40% of benzyl chloride persists in methanol, suggesting that the fragmentation of **3** transits ion pair **4** which can



either collapse to form benzyl chloride or react with methanol to give the methyl ether.^[5] The persistence of the chloride product requires either that the ion pair be 'tight' or that the fragmentation proceeds (in part) by a S_Ni mechanism. The tight ion pair alternative is consistent with the polar solvent, and with the stereochemical evidence: fragmentation of chiral α -deuteriobenzyloxychlorocarbene in MeCN affords α -deuteriobenzyl chloride with 60–80% net retention.^[6] Substantial (but incomplete) retention would be expected in the collapse of ion pair **4**.

Alkoxyhalocarbenes reside at an intersection of carbene, cation, elimination, and substitution (S_N1, S_N2, S_Ni) chemistry. Fragmentations of ROX afford many of the iconic carbocations of physical organic chemistry, as well as ion pairs that contain these cations. In several cases, homolytic fragmentations give rise to radical pairs, while, in other instances, S_Ni fragmentations preempt both heterolytic and homolytic reaction channels.

We have discussed the S_N2 chemistry of primary alkoxychlorocarbenes (RCH₂OCCl) elsewhere,^[7] and we recently reviewed S_Ni fragmentations of ROCCl in this journal.^[8] Now, we focus on

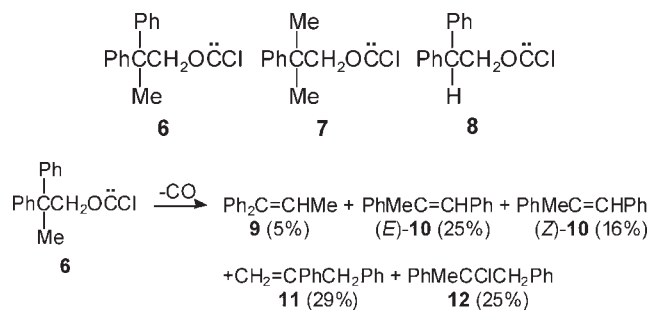
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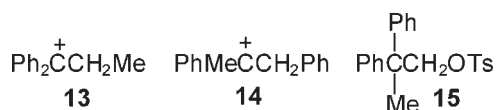
the ion pair and radical pair fragmentations of these protean species. An earlier review summarized the chemistry through 1999^[9] so that this 'Perspective' examines the period 2000–2007.

CATIONS AND ION PAIRS

Many carbocations can be accessed by carbene fragmentation and their chemistry can be studied by both kinetics and product formation. Acyclic systems are exemplified by the fragmentations of carbenes **6–8**, each generated by photolysis of the appropriate alkoxychlorodiazirine.^[10,11] Fragmentation of carbene **6**

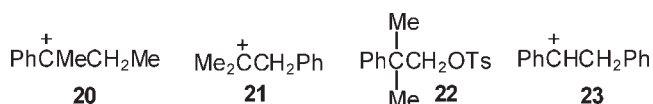


gives products **9–12** in the indicated pro-rated yields, *cf.*, Scheme 1.^[10] (Not all of **6** fragments; 48% of the carbene is captured by HCl and 5% by water.) Alkene **9** stems from 1,2-Me migration, which accompanies the fragmentation of **6**, and yields the 1,1-diphenylpropyl cation (**13**), which loses a proton. Alkenes **10** and **11** result from 1,2-Ph migration, concerted with fragmentation of **6**, which gives 1,2-diphenyl-2-propyl cation **14**, again followed by proton loss. Chloride **12** results from chloride ion return to cation **14**. Clearly, 1,2-Ph migration is preferred to 1,2-Me migration during fragmentation of **6**; the statistically

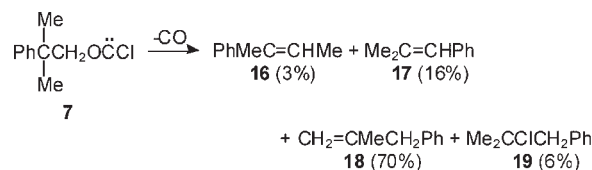


corrected Ph/Me migratory aptitude is $\sim 9.5:1$. For comparison, formolysis of 2,2-diphenylpropyl tosylate (**15**), which corresponds to fragmentation of carbene **6**, gives only 1,2-Ph migration, affording alkene (*E*)-**10** in 77% yield.^[12] The carbene fragmentation is less selective than the formolysis.

Similar considerations attend the fragmentation of neophylchlorocarbene **7** in CDCl_3 to products **16–19**; *cf.*, Scheme 2.^[10] Alkene **16** arises by 1,2-Me migration accompanying the fragmentation of **7**, giving the 2-phenyl-2-butyl cation, **20**, followed by deprotonation. Alkenes **17** and **18** represent competitive 1,2-Ph migration to cation **21**, followed by proton loss, while chloride **19** stems from collapse of **21** with chloride anion.



The production distribution, corrected for the 2:1 Me/Ph ratio of carbene **7**, indicates a Ph/Me migration advantage of $\sim 61:1$.



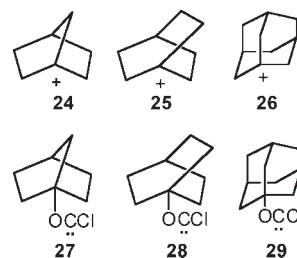
Scheme 2.

Although this is a substantial dominance, it is exceeded in the formolysis of neophyl tosylate **22**, where the Ph/Me migration ratio is $\sim 286:1$.^[13] Related 1,2-Ph migration occurs in the fragmentation of carbene **8**, where the products are very largely derived from proton loss or chloride collapse of the rearranged 1,2-diphenylethyl cation **23**.^[11]

Rate constants for the fragmentations of carbenes **6–8** were measured by laser flash photolysis (LFP) using the pyridine ylide visualization method.^[10,11,14] At 25 °C in dichloroethane (DCE), k_{frag} was $9.9 \times 10^5 \text{ s}^{-1}$ for **6**, $2.0 \times 10^6 \text{ s}^{-1}$ for **7**, and $4.6 \times 10^5 \text{ s}^{-1}$ for **8**. Activation energies for the fragmentations were very low, ranging from 1.2 kcal/mol for **7** to 2.1 kcal/mol for **6** in DCE.^[10] For carbene **8** in MeCN, E_a was 1.5 kcal/mol.^[11] Values for ΔS^\ddagger were quite negative (-24 to -28 e.u.), presumably reflecting solvent restriction during the polar, heterolytic fragmentations, and perhaps rotational restrictions connected with phenyl migration. Were it not for the very negative ΔS^\ddagger , the carbene would fragment too rapidly for the competitive trapping by pyridine which is essential to the kinetics methodology.^[14]

The computed activation energy for the fragmentation of a simple primary alkoxychlorocarbene, for example, $\text{CH}_3\text{CH}_2\text{OCCl}$, is 17.9 kcal/mol in simulated methanol,^[15] so that the much lower E_a 's measured for the fragmentations of primary analogues **6–8** argue that the migrations of Ph or Me groups must be *concerted* with fragmentation. The dominance of Ph over Me migration in the fragmentations of **6** or **7** is weaker than in the corresponding formolysis reactions, where E_a is much larger.

The low activation energy associated with carbene fragmentation suggests that bridgehead cations should be accessible by this route. Indeed 1-norbornyl (**24**), 1-bicyclo[2.2.2]octyl (**25**), and 1-adamantyl (**26**) cations, paired with Cl^- , arise upon fragmentations of ROCCl precursors **27–29**.^[16] Rate constants for the carbene fragmentations were determined by LFP in DCE with pyridine ylide UV visualization (**27** and



28), or by time resolved infrared monitoring of released CO (**29**).^[17] The measured values ($3.3 \times 10^4 \text{ s}^{-1}$ for **27**, $1.5 \times 10^5 \text{ s}^{-1}$ for **28**, and $5.9 \times 10^5 \text{ s}^{-1}$ for **29**) are many orders of magnitude greater than the analogous solvolysis rate constants. For example, acetolysis at 70 °C of the tosylates corresponding to **27–29** occur with $k_{\text{HOAc}} = 1.15 \times 10^{-11} \text{ s}^{-1}$, $2.09 \times 10^{-5} \text{ s}^{-1}$, and $1.02 \times 10^{-1} \text{ s}^{-1}$, respectively.^[18] The fragmentation of **27** to **24** at ambient temperature occurs 3×10^{15} times more rapidly than the acetolysis of 1-norbornyl tosylate at 70 °C.^[16] Moreover, the classical

10^{10} kinetic difference between the solvolysis of 1-adamantyl and 1-norbornyl tosylates^[18,19] is reduced to a factor of only 18 for carbene fragmentation.^[16]

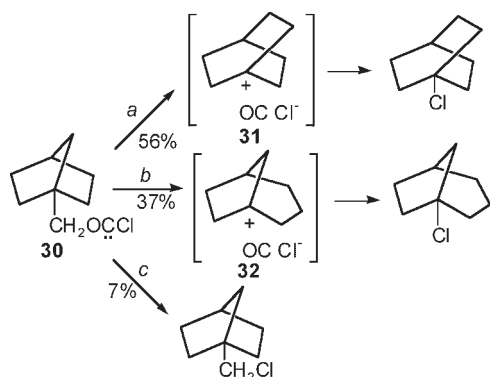
These striking differences in kinetics trace back to activation energies. We find E_a values of 9.0 and 4.4 kcal/mol for the fragmentations of **27** and **28** in DCE, which contrast with ΔH^\ddagger values of 27.8 kcal/mol for the acetolysis of 1-norbornyl triflate and 26.2 kcal/mol for the acetolysis of 1-bicyclo[2.2.2]octyl brosylate.^[18]

The chemistry of **24–26**, as generated from **27** to **29**, accords with expectations: in DCE, the cations collapse with their chloride counterions to give the bridgehead chlorides. In DCE–MeOH mixtures, both bridgehead chlorides and methyl ethers are obtained by partition of the ion pair between return and solvolysis.^[16]

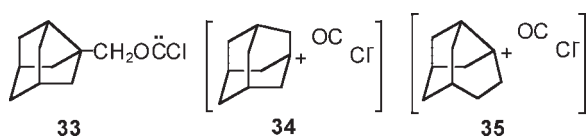
Bridgehead carbocations can also be generated by ring expansion coupled to carbene fragmentation.^[20] Thus, appropriate diazine photolysis in DCE affords 1-norbornylmethoxychlorocarbene **30**, which fragments with ring expansion to either is the bicyclo[2.2.2]octyl cation, **31**, or (b) the bicyclo[3.2.1]octyl cation, **32**, both as ion pairs with chloride anion, *cf.*, Scheme 3.^[20]

Fragmentation of **30** in DCE occurs with an aggregate $k_{\text{frag}} = 7.7 \times 10^5 \text{ s}^{-1}$, $E_a = 5.1 \text{ kcal/mol}$, and $\Delta S^\ddagger = -17 \text{ e.u.}$ The partition between short-bridge (a) and long-bridge (b) expansion is 56:37, but the latter is favored by a statistical factor of 2. Therefore, short-bridge expansion to **31** is intrinsically three times superior to long-bridge expansion to **32**.^[20] In DCE, ion pairs **31** and **32** collapse to the appropriate chlorides. These are accompanied by a small quantity of unrearranged chloride (path c) which may arise by competing S_N2 attack^[7] of chloride ion on carbene **30**.^[20]

Analogous results attend the fragmentation of 3-noradamantylmethoxychlorocarbene **33**, where the short-bridge expansion yields adamantyl ion pair **34**, while long-bridge expansion affords ion pair **35**, in a statistically adjusted ratio of 4.8:1.^[20] In DCE, ion pairs **31**, **32**, **34**, and **35** give only the anticipated chlorides, but in methanol, mixtures of the chlorides and the corresponding methyl ethers are formed.



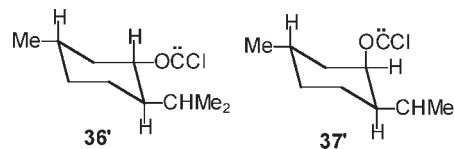
Scheme 3.



The ion pair lifetimes must be comparable to the diffusion that removes chloride and affords the fully solvated cation. Moreover, ion pair **31** generated by fragmentation-ring expansion of

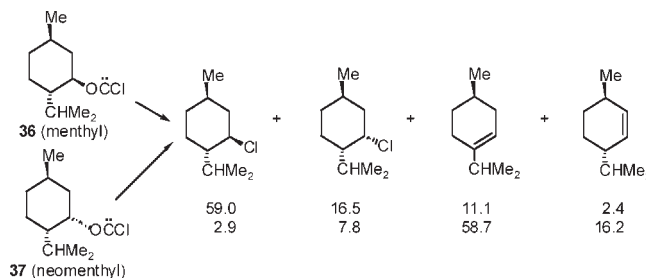
carbene **30** (Scheme 3) in methanol is *not* identical to the 'same' ion pair generated by the direct fragmentation of carbene **28**: the bicyclo[2.2.2]octyl RCl/ROME product ratio is 2.5 from carbene **30**, but only 0.39 from carbene **28**.^[20] The ion pair's fate, collapse with chloride or reaction with methanol, depends on its carbene parent; the rates of the product-forming reactions must be comparable to solvent/counterion equilibration of the ion pairs. From carbocation trapping experiments with trimethoxybenzene^[7,17,21] we estimate the lifetimes of the cations in Scheme 3 as $\sim 70 \text{ ps}$ in DCE.^[20]

Alicyclic systems provide for simultaneous study of the stereochemistry of fragmentation-initiated substitution reactions and competing elimination reactions. For example, fragmentations of menthylmethoxychlorocarbene **36** and neomenthylmethoxychlorocarbene **37** in polar solvents transit short-lived ion pairs that yield largely distinct, stereochemically retained substitution products from **36**, and elimination products from **37**; *cf.*, Scheme 4.^[22] In DCE, fragmentation of **36**, where the carbenic moiety is equatorial (**36'**), gives mainly the return (substitution) product, menthyl chloride with retention, along with lesser amounts of the inverted return product, neomenthyl chloride, and the elimination products, 3- and 2-menthene. Substitution (Cl^- return) dominates elimination (loss of HCl) by 5.6:1, and there is 56% net retention in the return process. In contrast, fragmentation of **37**, where the carbenic moiety is axial (**37'**), leads mainly to elimination (substitution/elimination = 0.14); there is only a minor return pathway, again with net retention.^[22]

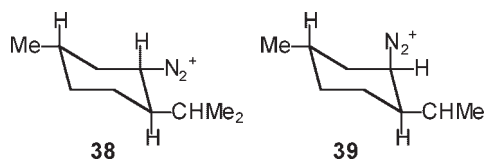


Very similar results are obtained in other polar solvents such as acetonitrile and dioxane. These reactions proceed via tight ion pairs in which the cations retain a 'memory' of their carbenic origins. In the ion pair derived from **37** (**37'**), the chloride ion likely accepts a proton during the elimination process.

There is a close analogy between both product type and product distribution in the fragmentations of **36** and **37** and of the corresponding diazonium ions, **38** and **39**, derived from the aqueous nitrous acid deaminations of menthylamine and neomenthylamine, respectively.^[23] The diazonium ions may be paired

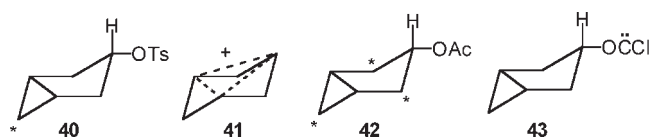


Scheme 4.

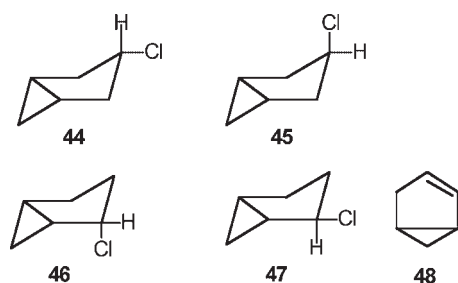


with anions that are hydrogen-bonded to water molecules. The parallel between carbene fragmentation, in which CO is lost, and deamination, in which N₂ departs, was first noted by Skell and Starer;^[2] results with the menthyl and neomenthyl species **36–39** are paradigmatic examples.^[22]

Solvolytic reactions of tosylate or triflate substrates often involve significant intramolecular assistance from neighboring σ - or π -electrons. A classic case is the acetolysis of *cis*-3-bicyclo[3.1.0]hexyl tosylate, **40**, where the 4,5-cyclopropyl σ -bond assists tosylate ionization, leading to formation of the trishomocyclopropenyl cation, **41**. This intermediate affords acetate **42** with stereochemical retention, rate acceleration relative to the axial epimer of substrate **40**, and scrambling of a C-2 label over carbons 2,4, and 6.^[24]

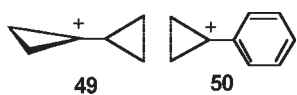


However, given the very low activation energy needed for carbene fragmentation, σ -bond assistance can be 'disconnected,' and its consequences mitigated. Thus, fragmentation of *cis*-3-bicyclo[3.1.0]hexyloxylchlorocarbene, **43**, in DCE leads to chlorides **44** (30%) and **45** (9%) by chloride return, chlorides **46** (17%) and **47** (13%) by 1,2-hydride shift followed by chloride return, and alkene **48** by elimination.^[25] In contrast to the chemospecific and stereospecific solvolysis of **40**, fragmentation of **43** largely bypasses cation **41**, proceeding instead via a bicyclo[3.1.0]hexyl chloride ion pair that collapses to **44** and **45**, undergoes 1,2-hydride shift followed by chloride return to **46** or **47**, or loses HCl to yield **48**.



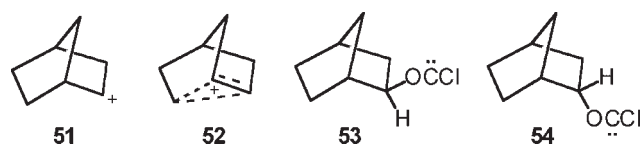
LFP studies give $E_a = 2.4$ kcal/mol for the fragmentation of carbene **43**,^[25] whereas ΔH^\ddagger for the acetolysis of **40** is 24.1 kcal/mol.^[24] And, k_{frag} for **43** is unaccelerated at $7.5 \times 10^4 \text{ s}^{-1}$ (compared to $k_{\text{frag}} = 8.7 \times 10^4 \text{ s}^{-1}$ for cyclopentylloxylchlorocarbene, both at 25 °C in DCE). Label scrambling is suppressed in the conversion of carbene **43** to chloride **44**: scrambling of a d_2 label at C-2 of **43** occurs to only 9% in CDCl₃ or 15% in CD₃CN,^[25] whereas scrambling is complete in the acetolysis of **40**.^[24]

Cyclopropyl cations such as **49** and **50** can also be generated by fragmentation of the appropriate ROCCl. Stabilized by electron-releasing α -substituents, these cations collapse with their chloride counterions yielding significant quantities of ring-preserved cyclopropyl products.^[26]



Several heuristic cations

The 2-norbornyl cation, **51**, is an especially sensitive indicator of intramolecular σ -bond delocalization. When **51** is solvolytically generated from *exo*-2-norbornyl tosylate, electron density diverted from the C-1 to C-6 σ -bond helps to stabilize the developing positive charge at C-2.^[27,28] Consequences of delocalization, in which C-1, C-2, and C-6 comprise a 3-center, 2-electron



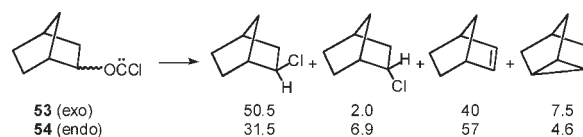
bonding array (**52**), include rate and activation energy advantages of *exo*- over *endo*-2-norbornyl solvolytic substrates and stereospecific formation of *exo*-solvolysis products.

Given the reduced activation energy for carbene fragmentation, relative to solvolysis, we anticipate a reduced demand for σ -bond delocalization during fragmentation. The kinetic disparity between *exo*- and *endo*-2-norbornyloxylchlorocarbene fragmentations should be minimized, and memory effects should appear in the respective product distributions. These expectations are fulfilled.^[28] Although acetolysis of the 2-norbornyl brosylate epimers leads to an *exo/endo*-rate advantage of 350 (1610, corrected for internal return),^[29] fragmentations in DCE of *exo*- and *endo*-2-norbornyloxylchlorocarbenes, **53** and **54**, occur with $k_{\text{frag}} = 7.2 \times 10^4 \text{ s}^{-1}$ and $8.7 \times 10^4 \text{ s}^{-1}$; the *exo* > *endo*-kinetic advantage for the 2-norbornyl brosylate solvolysis is lost in the fragmentations of **53** and **54**.^[28]

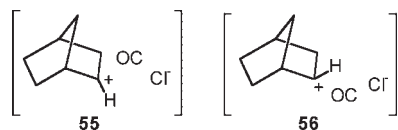
In the acetolysis of the 2-norbornyl tosylates, $\Delta G^\ddagger_{\text{exo}} = 22.6$ kcal/mol, while $\Delta G^\ddagger_{\text{endo}} = 27.1$ kcal/mol, yielding a 4.5 kcal/mol advantage for the *exo*-isomer.^[29] We could not obtain reliable experimental activation parameters for the fragmentations of **53** and **54** ($E_a < 4$ kcal/mol), but computed values at the B3LYP/6-31G* level in simulated MeCN solvent (SCI-PCM model) lead to $\Delta G^\ddagger_{\text{exo}} = 2.60$ kcal/mol and $\Delta G^\ddagger_{\text{endo}} = 2.87$ kcal/mol; the *exo*-advantage in solvolysis disappears in carbene fragmentation.^[28]

Product distributions from the fragmentations of carbenes **53** and **54** in DCE appear in Scheme 5; the distributions are nearly identical in acetonitrile.^[28] In the acetolysis of *exo*- or *endo*-norbornyl arenesulfonates, both isomers afford the *exo*-acetate product because both reaction pathways intersect at delocalized cation **52**, which leads only to *exo*-product.^[29] The fragmentations of **53** and **54**, however, are much less specific and are origin-dependent: the *exo*-carbene gives mainly *exo*-chloride and norbornene, while the *endo*-carbene yields mainly norbornene with a lesser quantity of *exo*-chloride. More *endo*-chloride (~7%) forms from the *endo*-carbene than from its *exo*-isomer (2%); the *exo/endo*-product ratio is ~25 from *exo*-carbene **53**, but only ~4.6 from *endo*-carbene **54**.

The product results suggest the formation of distinct ion pairs (e.g. **55** from **53** and **56** from **54**, which retain some memory of their parent carbene. The cationic portions of these ion pairs could

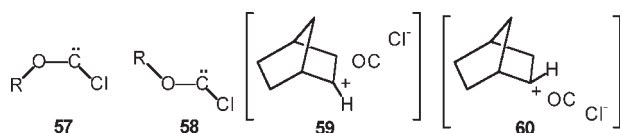


Scheme 5.



delocalize to **52** (i.e., become 'nonclassical') on the vibrational time scale, or ion pair recombination could compete with evolution to the delocalized cation.

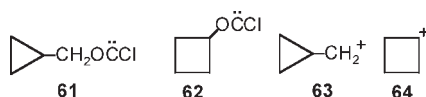
In the presence of added methanol, *exo*-norbornyl methyl ether is formed from either **53** or **54**, largely at the expense of the norbornene product.^[28] In undiluted methanol, the ether yields are 22% from **53** and 28% from **54**, but the yields of the *exo*- and *endo*-chlorides are only marginally reduced. Ion pairs **55** and **56** probably collapse efficiently to the chlorides, even in methanol, while related ion pairs might be the progenitors of the norbornyl ether and norbornene products. For example, ion pairs **55** and **56** derive from *cis*-isomers (**57**) of carbenes **53** and **54**, but *trans*-isomers (**58**) can also exist^[9] because rotation about the central O—C bond of ROCCl is opposed by a barrier of ~15–18 kcal/mol due to partial double bond character.^[15,30] *Trans*-isomers of *exo*-**53** and *endo*-**54** could give ion pairs **59** and **60**, respectively, which would be interceptable by methanol.^[28,31] Moreover, minor variations in ion pair organization can account



for the extensive norbornene formation via proton transfer from C-3 to Cl⁻ within the ion pairs.^[28]

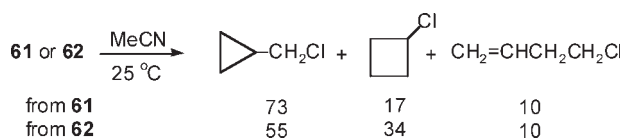
Consequences of the low activation energies required for ROCCl fragmentation are thus apparent with *exo*- and *endo*-2-norbornyloxylchlorocarbenes, where the dramatic, isomer-dependent differences in solvolytic processes are subverted. Further instructive examples are found in the fragmentations of cyclopropylmethoxychlorocarbene **61** and cyclobutoxychlorocarbene **62**.^[32,33]

In MeCN, fragmentations



of **61** ($k_{\text{frag}} = 7.6 \times 10^5 \text{ s}^{-1}$) and **62** ($k_{\text{frag}} = 7.1 \times 10^5 \text{ s}^{-1}$), lead to tight, distinct ion pairs which collapse to different distributions of cyclopropylcarbiny, cyclobutyl, and allylcarbiny chlorides; *cf.*, Scheme 6.^[33] Interconversions within these ion pairs of cyclopropylmethyl cation (**63**) and cyclobutyl cation (**64**) must be competitive with ion pair collapse to the RCl products, although the collapse process dominates so that more cyclobutyl chloride forms from **62** than from **61**.^[33]

In contrast, when cations **63** or **64** are generated in a 'free' solvated state by the aqueous nitrous acid deamination of the corresponding amines, rapid 1,2-C rearrangements interconvert



Scheme 6.

these cations, scramble labeled carbon atoms within them, and afford cyclopropylmethanol, cyclobutanol, and 3-butanol in a typical distribution of 52:44:4.^[34,35] Here, there is no 'memory' of the initial precursor; distinct ion pairs are not involved, only an equilibrating mixture of cations **63** and **64** or their delocalized equivalents.^[36]

Label scrambling due to CH₂ group interchange also occurs when cations **63** and **64** arise from fragmentations of carbenes **61** and **62**; *cf.*, Scheme 6. From carbene **61** fragmenting to cation **63** in MeCN, CH₂ interchange is 27–36% complete,^[32] considerably less than the 72% of interchange observed for cation **63** in water.^[34] Presumably, the difference is due to the tight ion pair generated from the carbene.

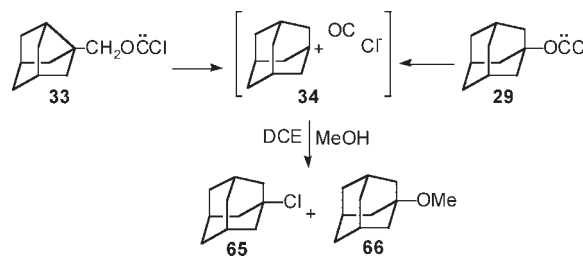
Remarkably, the same extent of interchange occurs when **61** fragments in *cyclohexane*, and the product distribution in hydrocarbon solvent resembles that obtained in MeCN.^[37] Can carbene fragmentation generate ion pairs in hydrocarbon solvents? Detailed spectroscopic studies in Ar matrices, as well as extensive computational examination, reveal that both **61** and **62** decay to CO and the chloride products of Scheme 6 via transient hydrogen-bonded cation chloride complexes with significant ion pair character, even in nonpolar solvents.^[37] Radical intermediates do not form from **61** or **62** in cryogenic Ar matrices; the fragmentations are heterolytic. However, flash vacuum pyrolytic generation of **61** at 365 °C in the gas phase appears to access a radical reaction channel.^[38] Further discussion of homolytic fragmentations appears below.

Solvent and counterion equilibration of ion pairs

The dynamics of ion pair solvation and evolution are currently of interest.^[39–41] Focusing on the fragmentation of ROCCl, we ask two questions: (1) has the ion pair formed by fragmentation equilibrated with the surrounding solvent, and (2) how long does this process take? Answers to these questions are illustrated by experiments in the 1-adamantyl and 3-homoadamantyl systems.^[42]

Consider the generation of the 1-adamantyl cation chloride anion pair **34** in a DCE–MeOH mixture by both ring expansion-fragmentation of 3-noradamantylmethoxychlorocarbene **33**^[20] and also by direct fragmentation of 1-adamantylmethoxychlorocarbene **29**.^[16] *cf.*, Scheme 7.^[42] Ion pair **34** can either collapse with chloride to form 1-adamantyl chloride **65**, or be captured by methanol to yield the corresponding methyl ether **66**. When we track the ether/chloride product ratio [**66**]:[**65**] as a function of the mole fraction of methanol in the MeOH–DCE solvent, we obtain the data shown in Fig. 1.

Ring expansion-fragmentation of **33** and direct fragmentation of **29** each produce ion pairs that track the concentration of methanol, and their ROME/RCl product ratios, [**66**]:[**65**], display



Scheme 7.

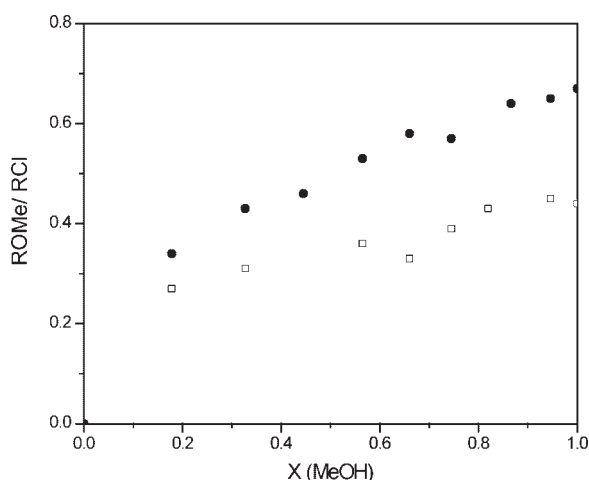


Figure 1. Product ratio [66]:[65] from the fragmentations of carbenes **29** and **33** (Scheme 7) in MeOH–DCE *versus* χ_{MeOH} . Key: ● from carbene **29**; □ from carbene **33**^[42]

similar dependencies on [MeOH]. Nevertheless, these dependencies are *not* identical, and the final product ratios in pure methanol also differ: [66]:[65] is 0.64 by direct fragmentation but 0.43 by ring expansion.^[42] The intermediate ion pairs from carbenes **33** or **29** are similar but not identical; there is a residual memory of ion pair origin, suggesting that product formation must be competitive with R^+Cl^- reorganization within ion pair **34**.

The 3-homoadamantyl cation (in **67**) is 4.2 kcal/mol more stable than the 1-adamantyl cation (in **34**) in the gas phase.^[43] This increased stability translates into an increased lifetime that permits ion pair **67** to become pathway independent. Consider Scheme 8, which is analogous to Scheme 7 (above). Here, ion pair **67** forms either by ring expansion-fragmentation of carbene **68**, or by direct fragmentation of carbene **69**. In MeOH–DCE, mixtures of 3-homoadamantyl chloride **70** and the corresponding methyl ether **71** are formed.^[42] The dependence of the resulting ROME/RCI product ratio, [71]:[70], on [MeOH] appears in Fig. 2. Equivalence of ion pair **67** from either generative pathway is now achieved; the products are formed from solvent and counterion equilibrated ion pairs.

Figure 3 depicts the B3LYP/6-31G(d) transition state for the fragmentation of carbene **69**, and the resulting ion pair **67** from an IRC calculation on the transition state optimized in simulated methanol by the PCM method.^[42] Note the apparent H-bonding between the chloride anion and the protons on the carbon atoms

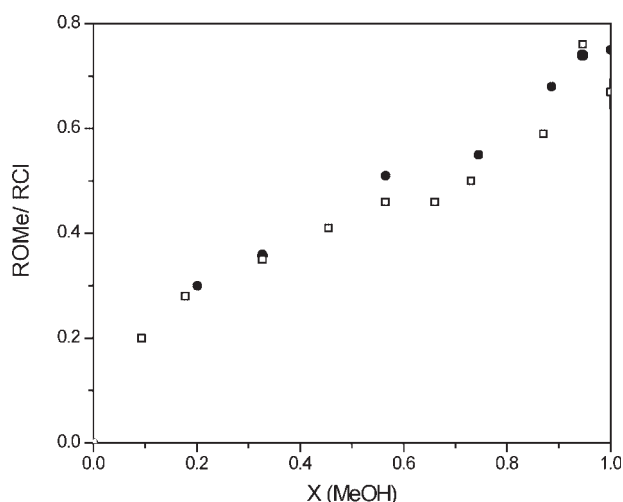
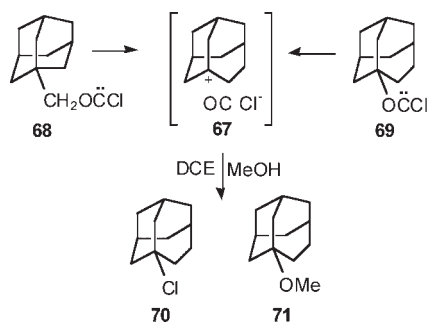


Figure 2. Product ratio [71]:[70] from the fragmentations of carbenes **68** and **69** (Scheme 8) in MeOH–DCE *versus* χ_{MeOH} . Key: ● from carbene **69**; □ from carbene **68**^[42]

flanking the cationic center. Given the small separation of the cation and anion (4.16 Å), the ion pair is likely of the ‘intimate’ or contact variety.^[44,45] Analogous computational studies of the ring expansion-fragmentation of carbene **68** lead to an ion pair that is almost identical (C^+Cl^- separation = 4.18 Å) to the ion pair depicted in Fig. 3.^[42] Presumably, these ion pairs become truly identical more rapidly than they collapse or react with methanol.

What is the lifetime of ion pair **67**? An estimate can be obtained as follows:^[42] LFP generation of carbene **68** in the presence of 1,3,5-trimethoxybenzene (TMB) in MeCN gives a UV signal for adduct **72** (R = 3-homoadamantyl) at 385 nm.^[17,21] A Stern–Volmer correlation of the inverse absorbance of **72** at 385 nm *versus* $1/[\text{TMB}]$ is linear.

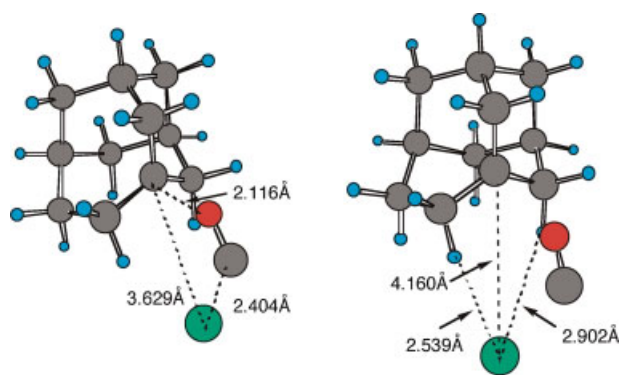
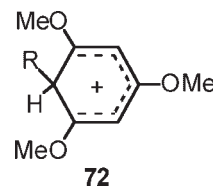


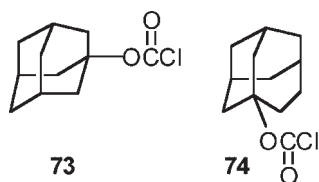
Figure 3. (Left) B3LYP/6-31G(d) transition state for the fragmentation of carbene **69**. (Right) Optimized ion pair from an IRC calculation on the transition state. (Reprinted with permission from Reference^[42]; copyright, 2004, American Chemical Society).

Assuming diffusion control for reaction of the trappable homoadamantyl cation with TMB, we can extract the cation's lifetime from the slope and intercept of the Stern–Volmer correlation.^[21,42,46] This yields an estimated lifetime of 20–30 ps for the 3-homoadamantyl cation that is trappable by TMB in MeCN.^[42] It seems reasonable to identify the trappable cation as part of a solvent-separated ion pair^[44,45] derived from an intimate ion pair which resembles **67** (Scheme 8). The polarities of MeCN and MeOH are similar, suggesting that 20–30 ps is also the time required for evolution of ion pair **67** to its solvent-separated form in MeOH–DCE. This also provides an upper limit for the time needed for solvent equilibration of the initial ion pairs arising from carbenes **68** and **69**.

For comparison, the diphenylmethyl cation chloride anion contact ion pair undergoes solvent separation in MeCN in 65 ps, and collapse to benzhydryl chloride in 92 ps.^[39] The longer time-scale, relative to **67**, can be attributed to the increased stability of the diphenylmethyl cation *versus* the homoadamantyl cation.^[43]

Solvent equilibration of **67** in methanol is roughly in balance with ion pair decay, so that a decrease in cation stability and lifetime (to the 1-adamantyl cation) leads to the precursor-dependent, non-equilibrated situation illustrated in Scheme 7 and Fig. 1. An even greater disparity between the Cl[−]/MeOH selectivities of ring expansion-fragmentation or direct fragmentation ion pairs occurs with the even less stable bicyclo[2.2.2]octyl chloride ion pair, **31**, derived either from carbenes **30** or **28**.^[42]

Independent entries to ion pairs analogous to **34** and **67** are available by fragmentations of chloroformates **73** and **74**, respectively.^[47] Kevill *et al.*^[48,49] provided strong evidence that the fragmentation



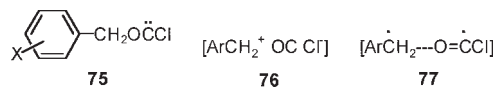
of (e.g.) **73** in polar solvents proceeds with the loss of CO₂ through adamantyl cation chloride anion pairs. We can thus verify the results displayed in Figs 1 and 2 by obtaining the ROME/RCI product distributions as a function of [MeOH] from the fragmentations of **73** and **74** in MeOH–DCE mixtures. Indeed, the [66]:[65] product ratios from the fragmentation of chloroformate **73** strongly diverge from those obtained from carbene **29**; the 1-adamantyl cation chloride anion pairs from each source differ,^[47] just as they do when they derive from carbenes **33** and **29** (Scheme 7).^[42] In contrast, the [71]:[70] product ratios from fragmentations of chloroformate **74** and carbene **69** are identical within experimental error, indicating that solvent-equilibrated 3-homoadamantyl chloride ion pairs arise from each precursor,^[47] as they do from carbenes **68** or **69**.^[42]

HOMOLYTIC CARBENE FRAGMENTATION

The fragmentation of (*cis*) benzyloxychlorocarbene **3** in polar solvents is reasonably understood as a heterolytic process passing through a polar transition state to tight ion pair **4**.^[5,6,9,15,17] However, in nonpolar solvents or in cryogenic matrices, carbene **3** can, in part, homolytically fragment to the benzyl and COCl radicals; these can be detected by UV and IR spectroscopy in Ar

matrices at 12 K.^[50] Products of the homolytic pathway include benzyl chloride, after loss of CO from [•]COCl and recombination of the chloride atom and the benzyl radical, as well as phenacyl chloride (PhCH₂COCl) by direct recombination of the benzyl and chlorocarbonyl radical pair.^[50] *Trans*-benzyloxychlorocarbene is particularly apt to access the homolytic reaction channel in pentane solvent or in Ar matrices.^[50]

Further evidence for homolytic fragmentation comes from a study of substituted benzyloxychlorocarbenes **75**.^[51] Absolute rate constants for the fragmentations of **75** in DCE at 25 °C,



determined by LFP, appear in Table 1. A correlation of log *k*_{frag} *versus* the Hammett σ⁺ constants of the aryl substituents (X) is V-shaped,^[51] suggesting a 'change of mechanism' as X morphs from an electron donating to an electron withdrawing group. A consistent explanation posits heterolytic fragmentation of **75** to ion pair **76** when X is electron donating (Me, Ph). However, when X is electron withdrawing (*m*-Cl, CF₃, NO₂) and would destabilize ArCH₂⁺, the fragmentation transition state assumes radical character as depicted in **77**. Computational studies support the view that radical cleavage of **75** becomes increasingly competitive, and ultimately superior to heterolytic fragmentation, as X becomes more electron withdrawing.^[51] Experimentally, in homolytic fragmentations of PhCH₂OCOCH₂Ar at 110 °C, the competitive formation of ArCH₂[•] over PhCH₂ is favored by electron withdrawing substituents on Ar.^[52]

Importantly, freely diffusing ArCH₂[•] and Cl (or COCl) radicals do not form in the fragmentations of **75** at ambient temperatures. Even in cumene solvent, no radical abstraction products are observed.^[51] If transition state **77** does lead to radical pairs, a strict cage effect must operate, CO is lost,^[53] and ArCH₂Cl forms by recombination.

Homolytic fragmentation of the related allyloxychlorocarbene occurs in hydrocarbon (but not polar) solvents;^[54] *cf.*, Scheme 9. Photochemical generation of labeled carbene **78**, in 90:10 DCE/CDCl₃ gives only allyl chloride isotopomers **82** and **82'** in a 66:34 ratio, consistent with heterolytic cleavage of **78** to an allylic cation chloride anion pair.^[54] However, in a cyclohexane-*d*₁₂/pentane solvent, we obtain **81** (42%), **81'** (19%), **82** (26%), and **82'** (13%). Thermal generation of **78** at 25 °C affords a similar product distribution, but with somewhat reduced label rearrangement. These results suggest initial homolytic fragmentation to allyl/

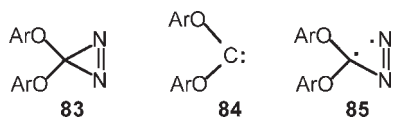
Table 1. Rate constants for fragmentation of ArCH₂OCCl^a

X in 75	<i>k</i> _{frag} (s ^{−1})	σ ⁺
<i>p</i> -Me	2.6 × 10 ⁵	−0.31
<i>p</i> -Ph	8.3 × 10 ⁴	−0.17
H	6.0 × 10 ⁴	0.00
<i>p</i> -Cl	5.2 × 10 ⁴	0.11
<i>m</i> -Cl	1.3 × 10 ⁵	0.37
<i>p</i> -CF ₃	2.1 × 10 ⁶	0.61
<i>p</i> -NO ₂	6.3 × 10 ⁶	0.79

^a In DCE at 25 °C. See Reference^[51] for errors and precision of kinetic data.

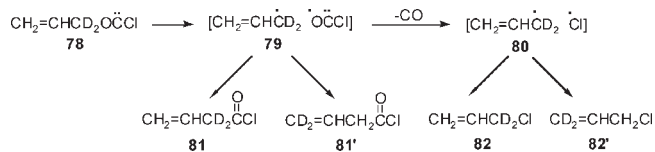
COCl radical pair **79**, which either recombines to give 3-butenoyl chlorides **81** and **81'** or loses CO to give allyl/Cl radical pair **80** and thence its products, allyl chlorides **82** and **82'**.^[54] Computational studies indicate that, among several alternatives, initial homolysis of **78** and **79** is the energetically preferred pathway for carbene **78** *in vacuo*, and presumably in a hydrocarbon solvent.^[54]

Related homolytic β -fragmentations of allylmethoxycarbenes to allyl/methoxycarbonyl radical pairs,^[55] and of benzyloxy-methoxycarbene to a benzyl/methoxycarbonyl radical pair^[56] are known. Note, in this context, the apparent α -fragmentation of diaryloxy-carbenes to aryloxy radicals.^[57] Photolysis of diaryloxy-diazirines **83** generates not only diaryloxy-carbenes **84** (and expected products), but also aryloxy radicals (ArO \cdot). These can be visualized by LFP-UV spectroscopy and trapped by H-donors like

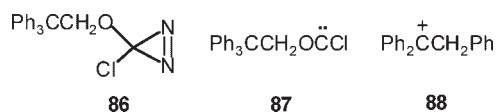


α -tocopherol or ascorbic acid 6-palmitate.^[57] Thermolysis of diazirines **83**, however, gives only products of carbene **84**; aryloxy radical products are absent. This suggests that the radicals arise by α -scission of *photoexcited* diazirines **83**, represented here as ring-opened diazirinyl diradicals **85**.^[58]

An example of the heterolytic fragmentation of a diazirine excited state is also known: simple cleavage ($\sim 75\%$) of photoexcited 2,2,2-triphenylethoxychlorodiazirine, **86**, affords triphenylethoxychlorocarbene **87**, while simultaneous cleavage and fragmentation ($\sim 25\%$) leads directly to

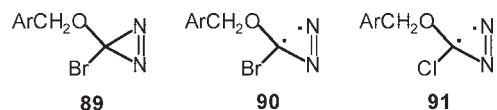


Scheme 9.



triphenylethyl cation **88**.^[59] In parallel, carbene **87** undergoes fragmentation and 1,2-phenyl migration to cation **88**.^[59]

Finally, photolytic (but not thermal) decomposition of 3-arylmethoxy-3-bromodiazirines **89** gives arylmethyl radicals (ArCH $_2$) in CDCl $_3$ at ambient temperature. These radicals can be detected by LFP-UV spectroscopy and intercepted by H-donors such as 1,4-cyclohexadiene.^[60] Thermal decomposition of **89** does not yield radicals; only ArCH $_2$ Br is obtained via the fragmentation of the carbene, even in the



presence of 1,4-cyclohexadiene. Radical reactions are also not observed upon analogous photolysis of (e.g.) benzyloxychlorodiazirine, where the generation of PhCH $_2$ OCCl and its heterolytic fragmentation to PhCH $_2$ Cl take precedence.^[5]

It seems likely that a photoexcited state of **89** (e.g., **90**) undergoes homolytic fragmentation to ArCH $_2$. The stronger C—Cl bond of chloro analog **91** is more resistant to homolysis than the C—Br bond of **90**; excited state **91** therefore yields the ArCH $_2$ OCCl carbene by nitrogen loss, while **90** both loses nitrogen to ArCH $_2$ OCCl and homolytically fragments to ArCH $_2$.^[60]

CONCLUSIONS

Fragmentations of secondary or tertiary alkoxyhalocarbenes in polar solvents generate carbocations as components of ion pairs. A variety of carbocations can be produced including acyclic, alicyclic, benzyl, bridgehead, cyclopropyl, cyclopropylcarbinyl, and norbornyl examples. LFP studies provide kinetics and activation parameters for the carbene fragmentations, which are orders of magnitude faster and require considerably reduced activation energies, compared to analogous solvolytic carbocation-generative processes. In some cases, the time required for solvent and anion equilibration of the ion pairs can be estimated. In nonpolar solvents, the gas phase, or cryogenic matrices, homolytic carbene fragmentation may, in certain cases, supplant heterolytic fragmentation.

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