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Fragmentation of chloroperoxides: hypochlorite-mediated dehydration of hydroperoxyacetals to esters

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Abstract

Hypochlorites efficiently dehydrate hydroperoxyacetals to furnish the corresponding esters. The reaction, which can be accomplished with stoichiometric $\text{Ca}(\text{OCl})_2$ or with catalytic amounts of $t\text{-BuOCl}$, appears to involve formation and heterolytic fragmentation of secondary chloroperoxides, species not previously described in solution chemistry.

Keywords

Hypochlorite; Hydroperoxyacetal; Chloroperoxide; Fragmentation; Ester

1. Introduction

Hydroperoxyacetals, readily available intermediates,¹ are substrates for a number of useful fragmentations, including Fe(II)-mediated cleavage to alkoxy radicals,^{1c,2} heterolytic C–O bond migrations of tertiary peresters or persulfonates (Criegee rearrangement),³ and the base-promoted dehydration of hydroperoxyacetals or derived peresters or persulfonates.^{1c,4–5} In the course of investigations into the addition of oxygen nucleophiles to ozonolysis-derived carbonyl oxides,⁶ we observed the rapid dehydration of secondary hydroperoxyacetals in the presence of commercial bleach.⁷ We now report that $\text{Ca}(\text{OCl})_2$, $t\text{-BuOCl}$, and trichloroisocyanuric acid mediate the rapid heterolytic dehydration of hydroperoxyacetals through the apparent intermediacy of secondary chloroperoxides, species whose solution chemistry has not been previously described.

2. Results and Discussion

Most of the substrates employed in this study were prepared via ozonolysis of alkenes in the presence of an alcohol. ^{1a} Addition of $\text{Ca}(\text{OCl})_2$ (1.3 equiv) to CH_3CN solutions of hydroperoxyacetals **1a–h** furnished esters **2a–h** (Table 1) after evaporation of solvent and filtration through a short silica column.^{7,8} The reaction could also be conducted in $\text{CH}_3\text{OH}/\text{CH}_2\text{Cl}_2$; however reaction in CH_2Cl_2 , THF, or toluene was limited by solubility of $\text{Ca}(\text{OCl})_2$. The dehydration proved compatible with a free primary alcohol (entry 4) or a chloroethyl acetal (entry 8). Little reaction was observed with aq. NaOCl.

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Supplementary Material

¹H and ¹³C NMR spectra for **1a–i**, **1k–n**, **2a–I**, **2k–m**, **3**.

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Comparable yields were available with *t*-BuOCl (Table 2).⁹ Reactions, although conducted for the same duration as for Ca(OCl)₂ were now complete within 1 min (TLC).¹⁰ The rate and yield were not affected by protection from laboratory light (entry 2), use of CH₂Cl₂ as solvent (entry 3), or the presence of acid (entry 4). However, the presence of methanol slowed reactions considerably (not shown). Dehydration could be conducted with catalytic (0.25 eq) quantities of *t*-BuOCl (entries 5 and 8), although the reactions now required 15 min for completion.

No reaction was observed between *t*-BuOCl and a silylated hydroperoxyacetal (**1i**, Scheme 1). However, a secondary hydroperoxide (**1j**)¹¹ underwent rapid dehydration; the low yield likely reflects product volatility. Dehydration of secondary allylic hydroperoxides (not shown) required excess *t*-BuOCl and furnished the expected α,β -unsaturated ketones as mixtures with significant amounts of byproducts lacking unsaturation.

The fragmentation can be combined with alkene ozonolysis to afford a convenient one-pot synthesis of esters (Scheme 2).

The fragmentation is likely to involve initial formation of chloroperoxides, species previously prepared only in tertiary systems.¹² The intermediacy of ROOCl is consistent with the lack of reaction of silylated hydroperoxyacetal **1i**. In an effort to access chloroperoxides with reagents other than hypochlorites, we discovered that commercially available trichloroisocyanuric acid promotes the dehydrative fragmentation as or more efficiently than *t*-BuOCl (Scheme 3).

The conversion of the chloroperoxides to esters could in principle proceed through either homolytic or heterolytic pathways (Scheme 4), and several additional experiments were conducted to discriminate between these possibilities (Scheme 5).

Chloroperoxides are reported to undergo homolytic scission to generate ROO• and Cl•.¹²⁻¹³ For this reason, we initially hypothesized the dehydrations involved a radical chain initiated by abstraction of the acetal C-H; the resulting carbon radical would be expected to fragment to the product ester and a propagating radical (•OCl). However, the dehydrations were insensitive to the presence or absence of visible light and did not occur in the presence of PhI(OTFA)₂, a reagent known to promote peroxy radical formation.¹⁴ Perhaps most convincingly, dehydration of **1k**, a hydroperoxyacetal substrate incorporating a fast radical clock (Scheme 5), proceeded with no detectable formation of ring-opened products.¹⁵

The potential role of alkoxy radicals was probed with hydroperoxyacetals **1l** and **1m**¹⁶ (Scheme 5); the α -oxygenated alkoxy radicals derived from either substrate would be expected to readily undergo β -scission.¹⁷ However, both **1l** and **1m** undergo dehydration with no signs of radical cleavage. In contrast, a hydroperoxyketal unable to dehydrate (**1n**) undergoes a much slower (30 min) reaction to furnish chloroalkanoate **3**, the product of alkoxy radical cleavage.

The results support fragmentation through the heterolytic pathway illustrated in Scheme 4, presumably through a mechanism analogous to Criegee or Hock fragmentation (activation of hydroperoxides by protonation or Lewis acid complexation).^{3,18} The specificity for migration of hydrogen relative to Ph or Bn (**1j**, **1l**) under nonbasic conditions is interesting. However, as has recently been demonstrated for Baeyer-Villiger rearrangements of alkoxybromanes derived from hemiacetals,¹⁹ the nature of the activating reagents can have a strong influence on rearrangements to electron-deficient oxygen. The proposed mechanism predicts regeneration of HOCl,²⁰ and is consistent with the high conversion obtained in the presence of substoichiometric *t*-BuOCl or trichloroisocyanuric acid. The results may be of relevance to atmospheric decomposition of primary chloroperoxides.²¹

3. Conclusions

We have developed a new fragmentation of hydroperoxyacetals to esters based upon heterolytic fragmentation of intermediate chloroperoxides.

CAUTION: While we experienced no hazards in the course of this work, any preparative work with peroxides should be conducted with an awareness of the potential for spontaneous and exothermic decomposition reactions.²²

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

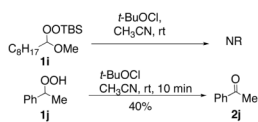
Acknowledgments

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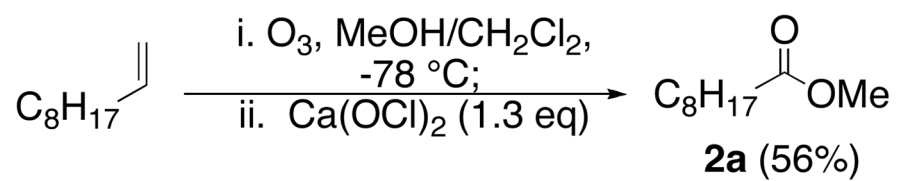
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8. Typical procedure for reactions with $\text{Ca}(\text{OCl})_2$: To a flame-dried 8 mL vial equipped with stirbar and screw-top septa cap containing technical grade $\text{Ca}(\text{OCl})_2$ (1.3 eq, 1.0 mmol, 143 mg of 65% reagent) is added CH_3CN (2 mL). A solution of the hydroperoxy acetal (1.0 eq, 0.50 mmol) in CH_3CN (1 mL) is added as a single portion via syringe. The reaction is stirred vigorously for 10 min at which time the partially heterogeneous solution is filtered through a short plug of silica. The reaction vial is rinsed with a small amount of CH_2Cl_2 and this solution is also filtered through the silica plug. The silica plug is rinsed with another small portion of CH_2Cl_2 and the filtrate is concentrated.
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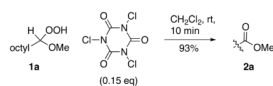
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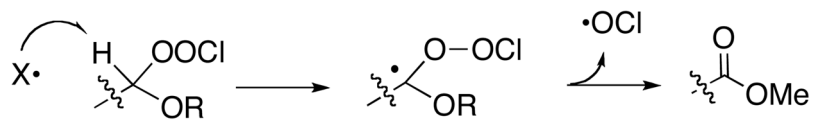
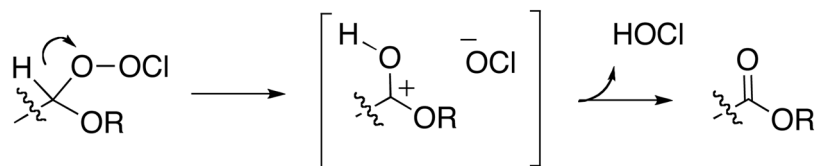
Scheme 1.
Substrates other than hydroperoxyacetals

**Scheme 2.**

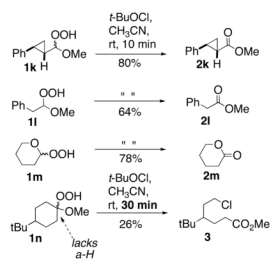
Application in tandem with ozonolysis



Scheme 3.
Dehydration with trichloroisocyanuric acid.

Homolytic fragmentation*Heterolytic fragmentation*

Scheme 4.
Mechanistic possibilities



Scheme 5.
Additional substrates

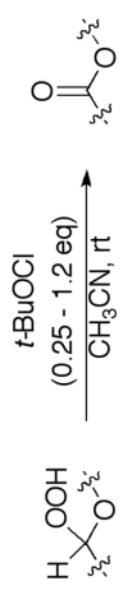
Table 1

Fragmentation of hydroperoxyacetals with $\text{Ca}(\text{OCl})_2$

Entry	Subs.	R ¹	R ²	Prod.	Yield ^a
1	1a	octyl	Me	2a	75% (91)
2	1b	octyl	Et	2b	86% (90)
3	1c	octyl	i-Pr	2c	83% (93)
4	1d	octyl	(CH ₂) ₂ OH	2d	83% (86)
5	1e	AcO(CH ₂) ₈	Me	2e	85% (93)
6	1f	BnO(CH ₂) ₃	Me	2f	81% (94)
7	1g	Ph(CH ₂) ₂	Me	2g	80% (93)
8	1h	octyl	(CH ₂) ₂ Cl	2h	82% (92)

^aIsolated yields on 0.5 mmol or (5 mmol) scale.

Table 2

Fragmentation of hydroperoxyacetals with *t*-BuOCl


Entry	Substrate	<i>t</i> -BuOCl (eq)	t (min)	Product	Yield ^a
1	1a	1.2	10	2a	77%
2 ^b	1a	1.2	10	2a	77%
3 ^c	1a	1.2	10	2a	79%
4 ^d	1a	1.2	10	2a	84%
5	1a	0.25	15	2a	78%
6	1b	1.2	10	2b	85%
7	1d	1.2	10	2d	84%
8	1e	0.25	15	2e	85%
9	1h	1.2	10	2h	84%

^a Isolated yields on 0.5 mmol scale.^b Protected from light (Al foil over flask).^c CH₂Cl₂ as solvent.^d Added HOAc (≥ 2 eq)