Tetrahedron Letters 51 (2010) 5615–5617

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

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

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ARTICLE INFO

Article history:
Received 20 July 2010
Revised 17 August 2010
Accepted 19 August 2010
Available online 25 August 2010

Keywords:
Hypochlorite
Hydroperoxyacetal
Chloroperoxide
Fragmentation
Ester

ABSTRACT

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

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1. Introduction

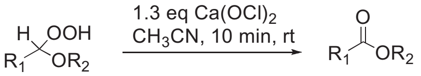
Hydroperoxyacetals, readily available intermediates,[1] are substrates for a number of useful fragmentations, including Fe(II)-mediated cleavage to alkoxy radicals,[1c,2] heterolytic C–O bond migrations of tertiary peresters, or persulfonates (Criegee rearrangement),[3] and the base-promoted dehydration 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 $Ca(OCl)_2$, *t*-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 $Ca(OCl)_2$ (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 CH_3OH/CH_2Cl_2; however the reaction in CH_2Cl_2, THF, or toluene was limited by the solubility of $Ca(OCl)_2$. The dehydration proved compatible with a free primary alcohol (entry 4) or a chloroethyl acetal (entry 8). Little reaction was observed with aq NaOCl.

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 CH_2Cl_2 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 equiv) quantities of *t*-BuOCl (entries 5 and 8), although the reactions now required 15 min for completion.

Table 1
Fragmentation of hydroperoxyacetals with $Ca(OCl)_2$



Entry	Substrate	R^1	R^2	Product	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	$(CH_2)_2OH$	**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	$(CH_2)_2Cl$	**2h**	82% (92)

[a] Isolated yields on 0.5 mmol or (5 mmol) scale.

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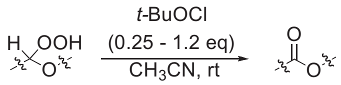
doi:10.1016/j.tetlet.2010.08.068

Table 2
Fragmentation of hydroperoxyacetals with *t*-BuOCl



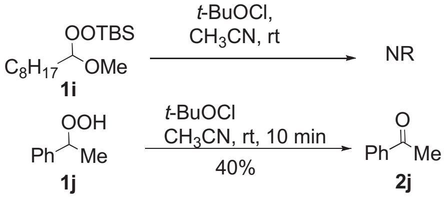
Entry	Substrate	*t*-BuOCl (equiv)	*t* (min)	Product	Yield[a] (%)
1	**1a**	1.2	10	**2a**	77
2[b]	**1a**	1.2	10	**2a**	77
3[c]	**1a**	1.2	10	**2a**	79
4[d]	**1a**	1.2	10	**2a**	84
5	**1a**	0.25	15	**2a**	78
6	**1b**	1.2	10	**2b**	85
7	**1d**	1.2	10	**2d**	84
8	**1e**	0.25	15	**2e**	85
9	**1h**	1.2	10	**2h**	84

[a] Isolated yields on 0.5 mmol scale.
[b] Protected from light (Al foil over flask).
[c] CH$_2$Cl$_2$ as solvent.
[d] Added HOAc (⩾2 equiv).

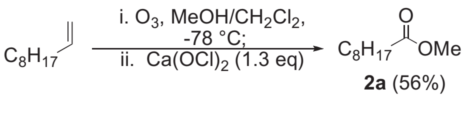
No reaction was observed between *t*-BuOCl and a silylated hydroperoxyacetal (**1i**, Scheme 1). However, a secondary hydroperoxide (**1j**)[11] underwent rapid dehydration; the low yield likely reflects product volatility. Dehydration of secondary allylic hydroperoxides (not shown) required excess *t*-BuOCl 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).

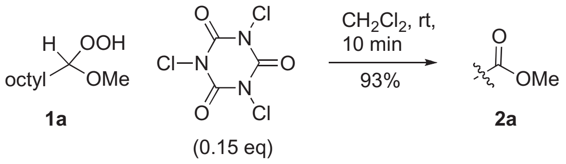
The fragmentation is likely to involve the initial formation of chloroperoxides, species previously prepared only in tertiary systems.[12] The intermediacy of ROOCl is consistent with the lack of reaction of silylated hydroperoxyacetal **1i**. In an effort to access chloroperoxides with reagents other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



Scheme 1. Substrates other than hydroperoxyacetals.



Scheme 2. Application in tandem with ozonolysis.



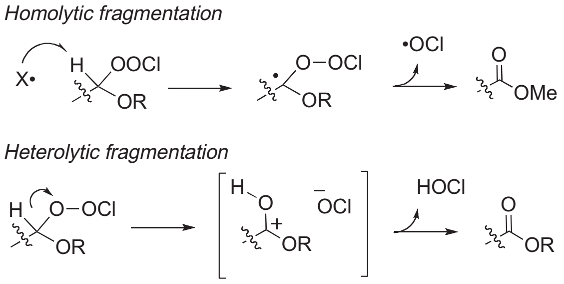
Scheme 3. Dehydration with trichloroisocyanuric acid.

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).

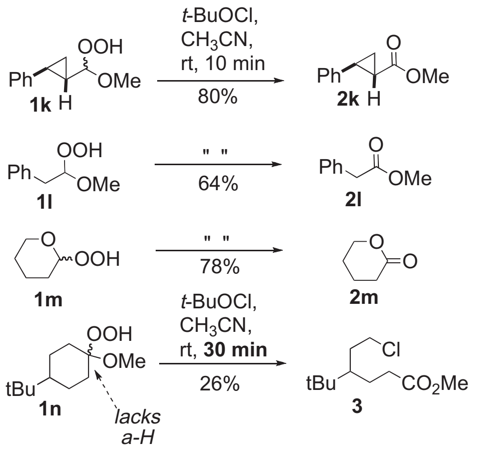
Chloroperoxides are reported to undergo homolytic scission to generate ROO$^{\cdot}$ and Cl$^{\cdot}$.[12,13] For this reason, we initially hypothesized the dehydrations involved a radical chain initiated by abstraction of the acetal C–H; the resulting carbon radical would be expected to fragment to the product ester and a propagating radical ($^{\cdot}$OCl). However, the dehydrations were insensitive to the presence or the absence of visible light and did not occur in the presence of PhI(OTFA)$_2$, a reagent known to promote peroxyl 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



Scheme 4. Mechanistic possibilities.



Scheme 5. Additional substrates.

reagents can have a strong influence on rearrangements to electron-deficient oxygen. The proposed mechanism predicts the 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]

Acknowledgments

This research was funded by NSF (CH-0749916) and the Nebraska Research Initiative and conducted in facilities remodeled with support from NIH (RR016544-01). NMR spectra were acquired, in part, on spectrometers purchased with NSF support (MRI 0079750 and CHE 0091975). We thank Dr. Chris Schwartz and Professor Stephen DiMagno for helpful discussions.

Supplementary data

^{1}H and ^{13}C NMR spectra for **1a**–**i**, **1k**–**n**, **2a**–**l**, **2k**–**m**, **3**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.068.

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8. Typical procedure for reactions with $Ca(OCl)_2$: To a flame-dried 8 mL vial equipped with stirbar and screw-top septa cap containing technical grade $Ca(OCl)_2$ (1.3 equiv, 1.0 mmol, 143 mg of 65% reagent) is added CH_3CN (2 mL). A solution of the hydroperoxy acetal (1.0 equiv, 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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