Notes

β-Scission of Tertiary Alkyl Hypochlorites Promoted by Phase-Transfer Catalysis

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Tertiary alkyl hypochlorites, YZQCOCl (Y, Z = R or Ar, Q = R), are known to fragment and form ketones (YZC=O) and alkyl chlorides (QCl) when heated or subjected to photolysis in a "*β*-scission" process whose mechanism is projected to involve the corresponding tertiary alkoxy radicals (YZQCO•) as intermediates.[1] Comparable *β*-scissions have been observed in several other processes in which alkoxy radicals have been implicated.[2] Beside cleavage, alkoxy radicals, as well as alkyl radicals produced during *β*-scissions, may participate in chain-propagation steps yielding a variety of products. In addition to heat or light, *β*-scission has been induced by the action of tetraacetate−metal halides[3] and by both Ce(IV)[4] and Fe(II) ions.[5]

In the process of identifying products of oxidative decarboxylation reactions of trisubstituted acetic acids, $YZQCCO_2H$, with aqueous sodium hypochlorite and a phase-transfer catalyst, ketones, YZC=O, were isolated, along with traces of tertiary alcohols, YZQCOH.[6] Ketones detected were those expected to result from *β*-scissions of *t*-ROCl derived from these alcohols (i.e., benzophenone from triphenylmethanol), but products arising from cleaved fragments, Q, were not isolated. Furthermore, when subjected to two-phase reactions with aqueous hypochlorite in the presence of the phase-transfer catalyst, tetrabutylammonium hydrogen sulfate (TBAHS), several tertiary alcohols, including triphenylmethanol, 1,1-diphenylethanol, and 2-phenyl-2-propanol, yielded *β*-scission product ketones. These reactions were enhanced by adjusting the aqueous layer to pH ∼9, a condition observed to be propitious for efficient oxidative decarboxylation of the trisubstituted acetic acids.

Discussion

Reactions of a series of tertiary alcohols with aqueous hypochlorite at pH ∼9 have been investigated to establish a scope for TBASH catalyzed *β*-scissions and to clarify the fate of alkyl groups cleaved. Results for reactions of 2.5 mmol of substrates **1**−**7** with 70 mmol of hypochlorite and 0.59 mmol of TBASH are summarized in Table 1. Under these conditions, reactions proceeded to completion in less than 1 h at ambient temperature and gave high yields of *β*-scission ketone products. In cases where they conveniently could be detected by gas chromatography, alkyl halide products were characterized as well. "Ω-chloro" ketone products from cyclic alcohols **5**−**7** were characterized by NMR and conversion to 2,4-dinitrophenylhydrazone derivatives. Under comparable conditions except at pH ∼11, several starting alcohols, notably **3** and **7**, essentially were inert in biphasic reactions with aqueous hypochlorite and TBASH.

$$\mathrm{YZQCOH + NaOCl + TBAHS \rightarrow YZC{=}O + QCl}$$

At lower concentrations of TBASH, *β*-scission reaction times were lengthened, and evidence was found for reaction intermediates. Iodometric titration of aliquots taken from organic phases of such reactions revealed the presence of substantial quantities of alkyl hypochlorites. Moreover, in contrast to earlier studies of alkyl hypochlorite reactions in which chain decomposition was initiated thermally or with light,[1] the phase-transfer catalyst brought about *β*-scission of the intermediate alkyl hypochlorites in two-phase systems without additional heating or photolysis.

Figure 1 profiles the fate of substrate and product formed during a reaction of 2-phenyl-2-propanol (**1**) with minimal TBASH present. The 2-phenyl-2-propyl hypochlorite intermediate (**8**) was formed rapidly (<5 min). Under an air atmosphere, **8** gradually declined during an induction period of 10−15 min and then underwent rapid decomposition via *β*-scission to give acetophenone (**9**). The presence of **8** was confirmed by ^{1}H NMR analysis of a reaction of **1** in $CDCl_3$. The results of complementary GC, NMR, and titrimetric analysis are summarized in Table 2. The corresponding methyl substituents for **1**, **8**, and **9** are well resolved ($\delta = 1.59$ for **1**, $\delta = 1.70$ for **8**,[7] and $\delta = 2.6$ for **9**). Chloromethane (δ 3.02, lit.[8] δ 3.05) was also detected by ^{1}H NMR.

In reactions conducted under conditions comparable to Figure 1 but with an argon atmosphere, the inhibition period was dramatically reduced, with over 50% ketone production within 5−8 min. By contrast, with an atmos-

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Table 1. Hypochlorite-TBAHS Induced β-Scission of Tertiary Alcohols YZQC−OH + NaOCl + TBAHS → YZC=O + Q-Cl

substrate	Y	Z	Q	products[a] (%)	detected substrate	pH range
1	Ph−	Me−	Me−	acetophenone (71−80) chloromethane[b]	trace−<10%	8.6−9.4
2	Ph−	Et−	Et−	propiophenone (82−93) chloroethane[c]	trace	9.0−9.3
3	Me−	Me−	$PhCH_2-$	acetone[c] benzyl chloride (65−73)[e]	trace	8.9−9.5[d]
4	Ph−	Me−	$PhCH_2-$	acetophenone (85−98) benzyl chloride (88−98)	trace	8.7−9.3
5	Me−	$-CH_2$- - -	$-(CH_2)_4-$	7-chloro-2-heptanone (65−73) [>90][f]	trace	9.1−10.3
6	Ph-	$-CH_2$- - -	$-(CH_2)_3$-	5-chloro-1-phenyl-1-pentanone [70−90][f]	trace	8.6−9.6
7	Ph−	$-CH_2$- - -	$-(CH_2)_4-$	6-chloro-1-phenyl-1-hexanone (40−65; 80−90 in 60 min) [>90][f]	15−50% (trace−3%, 60 min)	8.6−9.2

[a] Results after 30 min unless otherwise specified. [b] Detected by NMR. [c] Undetectable under conditions employed. [d] The pH, which tended to rise, was lowered with concentrated HCl to 9.0 during reaction. [e] Benzal chloride detected also, <1%, 2% after 1 h. [f] Crude product, see the Experimental Section.

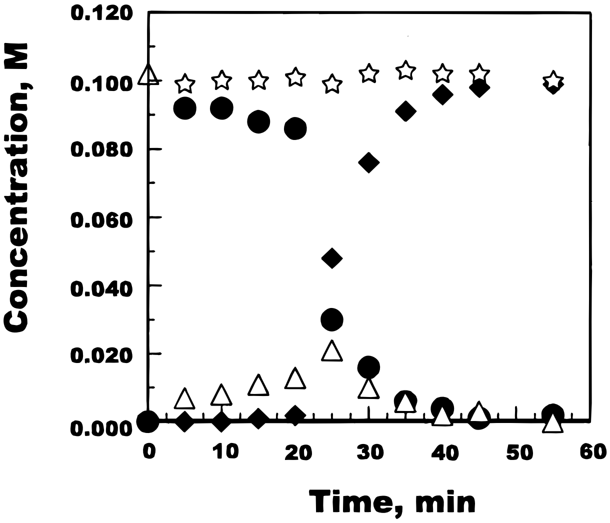

Figure 1. Reaction of 25 mL of 0.10 M **1** in CH_2Cl_2 with 100 mL of bleach at pH 9 catalyzed by 0.125 mmol of TBAHS: △ = **1**, ● = **8**, ◆ = **9**, ☆ = **1** + **8** + **9**.

Table 2. TBASH-Catalyzed Reaction of 0.099 M 2-Phenyl-2-Propanol with Bleach in $DCCl_3$

time (min)	[**1**] NMR	[**1**] GC[a]	[**8**] titrat.[b]	[**8**] NMR	[**9**] NMR	[**9**] GC	total NMR
0	0.099	0.101	0	0	0	0	0.099
60	0.034	0.031	0.065	0.064	0	0.001	0.098
180	0.029	0.035	0.064	0.064	0	0.004	0.093
600	0.018	0.015	0.057	0.059	0.026	0.028	0.103
1260	0.010	0.004	0.033	0.034	0.055[c]	0.051	0.099

[a] After KI treatment, less titrated value of **8** (see the Experimental Section). [b] No blank correction; maximum concentration of ROCl. [c] 0.032 M chloromethane also detected.

phere of O_2, nearly 100% ROCl was unreacted after 73−88 min and <5% ketone formed after 2.5 h.

The alkyl hypochlorite **8** and comparable intermediates from other alcohol precursors were found to undergo β-scission in a chromatograph injection port. To distinguish heat-promoted β-scission from that caused by TBASH, samples were treated with acidic potassium iodide, to reduce the hypochlorites to alcohols[9] before GC analysis. The results presented in Table 2 show excellent agreement among the three methods of analysis of reaction mixtures. To provide additional evidence for the alkyl hypochlorite as an intermediate in these reactions, authentic **8** was independently prepared directly from **1**.

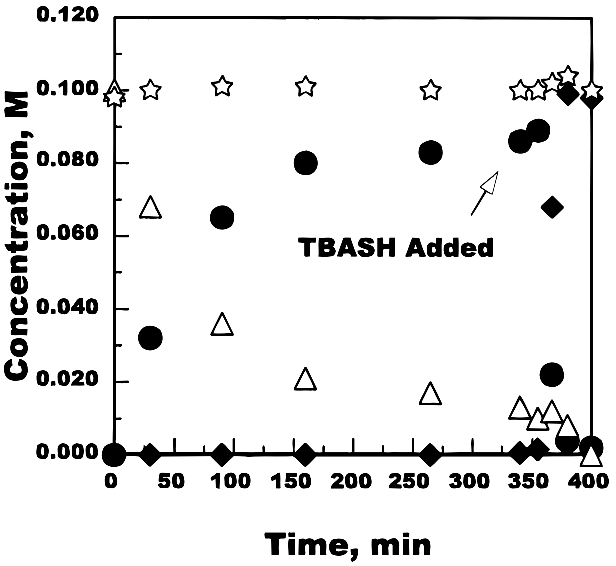

Figure 2. Addition of 0.125 mmol TBASH to a reaction mixture of 25 mL of 0.10 M **1** in CH_2Cl_2 with 100 mL of bleach at pH 9 after 345 min: △ = **1**, ● = **8**, ◆ = **9**, ☆ = **1** + **8** + **9**.

When treated with aqueous bleach in the presence of TBAHS, **8** was converted to acetophenone in 100% yield.

The phase-transfer catalyst was shown to bring about decomposition of the intermediate alkyl hypochlorite efficiently under biphasic conditions with aqueous hypochlorite. In the absence of catalyst, the alkyl hypochlorite was formed more slowly and was stable under the reaction conditions. After being stirred in dichloromethane with bleach at pH 9 for 24 h with no catalyst present, 84% of **1** was converted to **8** (as shown by titrimetry), but less than 0.3% of β-scission to acetophenone occurred. Furthermore, as shown in Figure 2, the addition of catalyst to a reaction mixture (after most of the alcohol had been converted to alkyl hypochlorite) resulted in rapid decomposition of **8** and formation of acetophenone.

Both aqueous bleach and TBAHS appeared necessary for the β-scission reaction of **8**. When the latter was dissolved in dichloromethane and mixed with TBAHS with no bleach present, no decomposition occurred after 3 h. Consequently, it is possible that the phase-transfer agent promoted formation of intermediates *either* that facilitate formation of the alkyl hypochlorite *or* that stimulate β-scission of the latter *or* both. Chlorine monoxide (Cl_2O) is illustrative of such an intermediate. An overall reaction mechanism for phase-transfer catalyst-

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[9] Fort, R.; Denivelle, L. *Bull. Soc. Chim. Fr.* **1954**, 1109.

Scheme 1

$$HOCl + OCl^- \xrightarrow{PTC} Cl_2O + OH^-$$

$$Cl_2O + YZQC\text{-}OH \rightarrow HOCl + YZQC\text{-}O\text{-}Cl$$

$$Cl_2O \rightarrow Cl\bullet + OCl\bullet$$

$$OCl\bullet + YZQC\text{-}O\text{-}Cl \rightarrow Cl_2O + YZQC\text{-}O\bullet$$

$$Cl\bullet + OCl^- \rightarrow Cl^- + OCl\bullet$$

$$YZQC\text{-}O\bullet \rightarrow YZC{=}O + Q\bullet$$

$$Q\bullet + YZQC\text{-}O\text{-}Cl \rightarrow Q\text{-}Cl + YZQC\text{-}O\bullet$$

$$Q\bullet + Cl_2O \rightarrow Q\text{-}Cl + OCl\bullet$$

$$Y, Z = R \text{ or } Ar;\ Q = R$$

induced reactions of hypochlorite with tertiary alcohols is suggested in Scheme 1, with Cl_2O potentially playing the role indicated.[10]

The stability of YZQCOCl prior to addition of the catalyst is not unexpected. Although it is generally accepted that alkyl hypochlorites undergo a rapid light-catalyzed chain decomposition, Walling and Jacknow have shown that the chain reaction is inhibited by oxygen.[11] Evidently, in a system that has a relatively low alkyl hypochlorite concentration and is not deoxygenated, chain reactions may not occur unless the initiation rate is substantially increased through the addition of the phase-transfer catalyst.

The quaternary salt may function in the traditional phase-transfer catalytic role, increasing concentration of ionic species, particularly including hypochlorite ion (OCl^-), in the organic phase to serve as a participant for several steps. Rationales for increased efficiency at pH 8−10 vs pH > 11 include the following: enhanced formation of Cl_2O, suggested as the active agent in other phase-transfer reactions of aqueous hypochlorite;[12,13] enhanced efficiency of coextraction of hypochlorous acid along with hypochlorite by catalyst at pH near the pK_a (7.5−7.6) of HOCl;[14] or by influencing efficiency of competing reactions,[12] including the chain length of radical propagating processes.

It is very important that instability of alkyl hypochlorites in nonaqueous solvents during GC analysis be recognized. Heat-induced β-scission of alkyl hypochlorites takes place readily in the inlet ports of gas chromatographs (typically > 100 °C). This is made apparent if duplicate aliquots of reaction mixtures are analyzed by GC after one is treated with KI. Alkyl hypochlorites present have been shown to react with KI and revert (be reduced) to the corresponding alcohol. This has permitted another way to estimates levels of alkyl hypochlorites.

For either GC or NMR analyses, the difference in ROH detected in reaction aliqouts before and after aqueous KI treatment corresponds nicely with the levels of ROCl observed directly by titrimetry and NMR.

Experimental Section

Materials and General Procedures. All compounds employed were secured from commercial suppliers. Aqueous hypochlorite ("5.25%") was obtained in the form of commercial Clorox bleach. In all cases, the phase-transfer catalyst (PTC) used was tetrabutylammonium hydrogen sulfate (TBAHS). All ^1H NMR spectra were recorded at 60 MHz. Gas chromatographic (GC) instruments were equipped with capillary columns and flame ionization detectors. The pH's of aqueous layers of biphasic systems were set and maintained at desired levels by addition of aqueous NaOH or HCl, and the pH was monitored with pH meters equipped with gel-filled plastic combination electrodes. Progress of reactions was followed by GC using chlorobenzene as an internal standard, which was shown to be stable to the reaction conditions and to have retention times different from both reactants and products. All reactions were conducted at ambient temperatures.

General Reactions of Tertiary Alcohols (Table 1). Substrate alcohols and chlorobenzene (2.5 mmol) were dissolved in 50 mL of CH_2Cl_2 and stirred magnetically with 100 mL (70 mmol) of hypochlorite adjusted to pH 8.8−9.3 and containing 0.20 g (0.59 mmol) of TBAHS. Reactions were conducted under conventional fluorescent lighting and analyzed by GC to determine the types and percentages of products formed. Potassium iodide (KI) workups were accomplished by treating a 0.5 mL reaction aliquots with two drops of 1 M KI in 0.5 M HCl. Under the comparable conditions, except with the aqueous phase pH ∼11 (maintained by addition of 5% aqueous NaOH), compounds **3** and **7** were found to be unreactive to bleach and TBAHS for 3 h and up to 3 days, respectively.

Ketone products from pH 9 reactions of substrates **5**−**7** were isolated from two-phase systems that did not contain an internal standard. After reactions had run for a minimum of 1 h, the CH_2Cl_2 phase was extracted six times with water, poured through fluted filter paper into a round-bottom flask, subjected to rotary evaporation, and weighed. For 7-chloro-2-heptanone: ^1H NMR (CCl_4) δ 1.5 (br m 6H), δ 2.1 (s, 3H), δ 2.4 (t, 2H), δ 3.5 (t, 2H); 2,4-dinitrophenylhydrazone (DNP), mp 94−95 °C (lit.[15] mp 95−96 °C). For 5-chloro-1-phenyl-1-pentanone: ^1H NMR ($DCCl_3$) δ 1.6 (m, ∼4H), δ 2.7 (m, ∼2H), δ 3.4 (m, ∼2), δ 7.7 (m, ∼5H); DNP mp 176−178 °C, (lit.[15] mp 76−178 °C). For 6-chloro-1-phenyl-1-hexanone: ^1H NMR ($DCCl_3$) δ 1.6 (br m, 6H), δ 2.9 (t, 2H, $J \approx 6$ Hz), δ 3.5 (t, 2H, $J \approx 6$ Hz), δ 7.7 (m, 5H); DNP mp 139.5−141 °C (lit.[15] mp 141.5−143 °C).

Reactions of 2-Phenyl-2-Propanol(1). (a) Reaction in $CDCl_3$. Analysis by ^1H NMR (Table 2). Compound **1** (0.134 g, 0.984 mmol), TBAHS (0.0191 g, 0.056 mmol), chlorobenzene (0.0552, 0.590 mmol), and *tert*-butylbenzene (0.0645 g, 0.481 mmol) were dissolved in 10 mL of $CDCl_3$. The solution was stirred with 40 mL (28 mmol) of bleach at pH 9. At intervals, aliquots of the organic layer were removed and analyzed by GC and NMR. A 0.2 mL aliquot was added to 15 mL of reagent-grade 2-propanol containing 2 mL of acetic acid and 0.25 g of NaI. The iodine was titrated to a colorless endpoint with 0.01 M sodium thiosulfate. The concentrations of the following compounds were determined from NMR by integration of the appropriate methyl signal relative to that of *tert*-butyl benzene ($\delta = 1.33$): 2-phenyl-2-propanol ($\delta = 1.60$), 2-phenyl-2-propyl hypochlorite ($\delta = 1.70$), acetophenone ($\delta = 2.60$), and chloromethane ($\delta = 3.02$). When a reaction aliquot was treated with aqueous KI, the signal at $\delta = 1.70$ disappeared, and the signal at $\delta = 1.60$ increased by a corresponding amount.

After KI treatment, levels of **1** directly measured by GC included, in addition to unreacted starting material, some alcohol due to reduction of **8** by KI. Direct GC analyses of aliquots (no KI treatment) resulted in significant thermal decomposition of **8**. For Table 2 and Figures 1 and 2, concentrations of unreacted starting material were determined by subtracting the titrimetri-

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[10] Chlorine monoxide is known to react with alcohols to form ROCl; see: Anbar, M.; Ginsburg, D. *Chem. Rev.* **1954**, *54*, 925 and references therein. Other radical species, such as chlorine atoms, also may participate in chain propagation steps analogous to those shown in Scheme 1.

[11] Walling, C.; Jacknow, B. B. *J. Am. Chem. Soc.* **1960**, *82*, 6108.

[12] Fonouni, H. E.; Krishnan, S.; Kuhn, D. G.; Hamilton, G. A. *J. Am. Chem. Soc.* **1983**, *105*, 7672.

[13] Dneprovskii, A. S.; Eliseenkov, E. V. *Russ. J. Org. Chem.* **1994**, *30*, 235.

[14] Abramovici, A.; Neuman, R.; Sasson, Y. *J. Mol. Catal.* **1985**, *29*, 291. The pK_a of HOCl reported therein is 7.53; elsewhere it is cited as 7.58.

[15] Wilt, J. W.; Hill, J. W. *J. Org. Chem.* **1961**, *26*, 3523.

cally determined concentrations of **8** from alcohol levels in KI-treated aliquots.

(b) Reactions in CH_2Cl_2 (Figures 1 and 2). Except as noted below, illumination was minimized by operating either in a darkened room or in a hood with covered window. The general procedure for tertiary alcohols was followed using 2.5 mmol of **1** in 25 mL of CH_2Cl_2 and 0.125 mmol of TBASH. The catalyst was added either at the beginning of the reaction (Figure 1) or after 345 min (Figure 2). Aliquots were taken periodically, and reactions were subjected to fluorescent room lighting for short sampling periods. The concentration of **8** was determined by iodometric titration, and a blank correction equivalent to 0.005 M hypochlorite, determined by titration of an aliquot taken from a reaction without alcohol, was used. The concentrations of **1** and **9** after KI treatment were measured by GC. The concentration of **1** present prior to KI treatment were calculated as described in (a) above.

Conditions equivalent to Figure 1, except for exposure to intense incandescent lighting, gave essentially the same results as displayed in Figure 1. Experiments conducted comparable to Figure 1, except for use of an argon atmosphere resulted in rapid formation of ketone product; use of an oxygen atmosphere almost eliminated ketone formation for a period of hours (see Discussion).

(c) Reaction in CH_2Cl_2 without TBAHS. A 25 mL solution of 0.103 M **1** was stirred with 100 mL of bleach at pH 9. Iodometric titration showed 81% of **1** converted to **8** after 6 h and 90% after 24 h. GC analysis after 24 h indicated only a 0.9% conversion of **1** to **9**.

1-Methyl-1-phenethyl Hypochlorite (8). The method of Walling and McGuinness[1a] was modified. A solution of 2-phenyl-2-propanol (409 mg, 3.00 mmol) in CH_2Cl_2 (15 mL) was cooled in an ice bath, and aqueous hypochlorite (15 mL, 10 mmol) at pH 7.5 was added with stirring. After the solution was stirred for 25 min in the ice bath in the dark, the layers were separated, and the organic layer was washed two times with 10% aqueous sodium carbonate and dried over anhydrous sodium sulfate. Iodometric titration indicated an alkyl hypochlorite concentration of 0.20 M. An aliquot of the alkyl hypochlorite solution and chlorobenzene was diluted to 25 mL. This solution was treated with 100 mL of bleach at pH 9 containing 0.140 mmol of TBASH. The reaction progress was followed by titrimetry and GC, and **9** was formed in proportion to the loss of **8**.

For ^1H NMR analysis, **8** was prepared as above from 15 mL of a 0.40 M solution of **1** in CCl_4 treated with 30 mL of bleach at pH 7.5. Iodometric titration of this solution gave a hypochlorite concentration of 0.36 M. Analysis by ^1H NMR (CCl_4) gave δ 1.53 (s, 0.5 H), δ 1.63 (s, 5.3 H), δ 7.37 (s, 5 H). Calculations using the relative areas of the two methyl signals indicated that the sample was 91% alkyl hypochlorite and 9% alcohol.

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