temperature. The maroon solution was filtered, and the filtrate was extracted with an equal volume of ether. The organic layer was discarded. After the aqueous layer was acidified with glacial acetic acid, it was extracted twice with equal volumes of ether. The ether layers were combined to yield crude **5**. Purification was achieved by sublimation at 115° (0.1 mm). The yield varied from 50 to 70% and the compound melted at 155–158° (reported[16] mp 159–160°).

Pyrazinetetracarboxylic Acid (6) from 1-Hydroxyphenazine (5).—**5** (100 mg) was oxidized to **6** as described for **2**, in 70% yield.

Registry No.—**2**, 2538-68-3; **3**, 85-66-5; DL-shikimic acid, 138-59-0.

Acknowledgment.—This work was supported by Grant AI09598, National Institutes of Health.

δ-Chloro Alcohols and Tetrahydrofurans from Primary and Secondary Alkyl Hypochlorites[1]

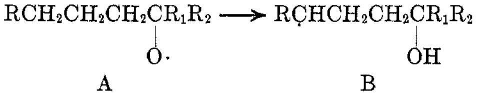
CHEVES WALLING* AND DOUGLAS BRISTOL

Department of Chemistry, University of Utah, Salt Lake City, Utah 84112

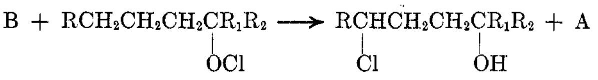
Received April 11, 1972

The photodecomposition of primary and secondary alkyl hypochlorites in the presence of *cis*- or *trans*-dichloroethylene and similar chloro olefins which act as chlorine atom traps leads to greatly improved yields of δ-chloro alcohols (or tetrahydrofurans after treatment with base). Yields of 50–90% are obtained from a number of hypochlorites, and the method appears to offer substantial advantages over lead tetraacetate oxidations and other more complex techniques for carrying out intramolecular alkoxy radical reactions.

Tertiary alkyl hypochlorites containing a side chain of at least four carbons are readily converted to δ-chloro alcohols on irradiation or treatment with a free-radical source[2,3] *via* a sequence involving intramolecular hydrogen abstraction. The reaction has been



$$\underset{\mathbf{A}}{\mathrm{RCH_2CH_2CH_2\underset{\displaystyle O\cdot}{C}R_1R_2}} \longrightarrow \underset{\mathbf{B}}{\mathrm{R\underset{\cdot}{C}HCH_2CH_2\underset{\displaystyle OH}{C}R_1R_2}} \qquad (1)$$



$$\mathrm{B} + \mathrm{RCH_2CH_2CH_2\underset{\displaystyle OCl}{C}R_1R_2} \longrightarrow \mathrm{R\underset{\displaystyle Cl}{C}HCH_2CH_2\underset{\displaystyle OH}{C}R_1R_2} + \mathrm{A} \qquad (2)$$

much less successful with primary and secondary hypochlorites, presumably because of competing steps initiated by α-hydrogen attack.

$$\mathrm{X\cdot + RCH_2OCl \longrightarrow HX + R\dot{C}HOCl} \qquad (3)$$

$$(\mathrm{X = Cl,\ RCH_2O\cdot})$$

$$\mathrm{R\dot{C}HOCl \longrightarrow RCHO + Cl\cdot} \qquad (4)$$

$$\mathrm{HCl + RCH_2OCl \longrightarrow RCH_2OH + Cl_2} \qquad (5)$$

$$\mathrm{Cl_2 + 2RCH_2OH \longrightarrow 2RCHO + 2HCl} \qquad (6)$$

$$\mathrm{Cl_2 + RH \longrightarrow RCl + HCl} \qquad (7)$$

In short, molecular chlorine is introduced into the system, and is continually regenerated *via* eq 5–7, making the reaction no longer intramolecular and specific. In fact, the aldehydes produced are chlorinated further to acid chloride, which ends up largely as ester.

$$\mathrm{RCHO + Cl_2 \longrightarrow RCOCl + HCl} \qquad (8)$$

$$\mathrm{RCOCl + RCH_2OH \longrightarrow RCOOCH_2R + HCl} \qquad (9)$$

Modest yields of δ-chloro alcohols have only been obtained under special conditions (the presence of $NaHCO_3$ and reflux under reduced pressure) designed to remove HCl and thus prevent eq 5.[2,4]

Adventitious chlorine sometimes complicates the reactions of tertiary hypochlorites by similarly introducing chlorine atom chains, but here the effect can be largely eliminated[5] by adding olefins with strong electron-withdrawing groups which are inert toward alkoxy radicals but act as chlorine atom traps.

$$\mathrm{Cl\cdot + CHCl{=}CCl_2 \longrightarrow CHCl_2\dot{C}Cl_2} \qquad (10)$$

$$\mathrm{CHCl_2\dot{C}Cl_2 + ROCl \longrightarrow CHCl_2CCl_3 + RO\cdot} \qquad (11)$$

This paper describes application of the same technique to the intramolecular chlorination of long-chain primary and secondary hypochlorites, and demonstrates that the reaction can be made to give high yields of δ-chloro alcohols (or, subsequently, tetrahydrofurans), making it a remarkably simple and specific synthetic procedure.

Results

Initial experiments were carried out with *n*-butyl hypochlorite, irradiated under N_2 or in sealed, degassed tubes, and are summarized in Table I. In the absence of a chlorine atom trap yields are low and erratic and a wide spectrum of products is produced. In the presence of trichloroethylene, yields of 4-chloro-1-butanol rise to 50–60%, and the remaining products are quite cleanly 1-butanol, butyl butyrate, and pentachloroethane, giving overall material balances of 90–100%. Since the stoichiometry of the ester-forming reaction should be eq 12, a small amount of random chlorination

$$\mathrm{4RCH_2OCl + 2C_2HCl_3 \longrightarrow RCOOCH_2R + 2ROH + 2C_2HCl_5} \qquad (12)$$

must be taking place as well. In the presence of olefin, base appears to have no further beneficial effect, and yields decrease only slightly when the temperature is raised from 0 to 50°.

In Table II the reaction is extended to 1-pentyl hypochlorite and several radical traps investigated. Yields are higher than in Table I, presumably because of the greater reactivity of secondary hydrogens in the intramolecular process, and *cis*- or *trans*-dichloroethylene appear to be the most efficient chlorine atom

---

[1] Support of this work by a grant from the National Science Foundation is gratefully acknowledged.

[2] C. Walling and A. Padwa, *J. Amer. Chem. Soc.*, **83**, 2207 (1961); **85**, 1597 (1963).

[3] F. D. Greene, *et al.*, *ibid.*, **83**, 2196 (1961); *J. Org. Chem.*, **28**, 55 (1963).

[4] E. L. Jenner, *ibid.*, **27**, 1031 (1962).

[5] C. Walling and J. A. McGuinness, *J. Amer. Chem. Soc.*, **91**, 2053 (1969).

TABLE I

PHOTODECOMPOSITION OF *n*-BUTYL HYPOCHLORITE IN THE PRESENCE OF TRICHLOROETHYLENE

			Products[b]					Balance, %	
[ROCl]	$[C_2HCl_3]$/ [ROCl]	Conditions[a]	4-Chloro-1-butanol	1-Butanol	Ester	Butanal	C_2HCl_5	RO	Cl
1.7	0[c]	$NaHCO_3$, N_2	18.1	32	19.2	8		77.3	18.1
0.62	0	$NaHCO_3$, N_2	7.3	25.2	11.4	1.6		45.5	7.3
0.62	6.0	$NaHCO_3$, N_2	46.4	37.1	11.1		41.2	94.6	87.6
0.79	5.0	$NaHCO_3$, N_2	46.8	36.6	11.8		43.6	95.2	90.4
0.79	5.0	$NaHCO_3$, N_2	45.9	36.3	11.8		42.6	94.0	88.5
0.74	5.0	$NaHCO_3$	59.6	32.4	8.6		38.2	100.6	97.8
0.74	5.0		60.7	33.2	9.0		40.6	102.9	101.3
0.39	5.0	$NaHCO_3$	58.9	31.7	6.1		36.0	96.7	94.5
0.37	5.0		59.6	32.5	6.3		36.9	98.4	96.5
0.88	4.8	50°	50.7	33.7	7.6		40.2	92.0	90.9
0.88	4.8	50°	50.9	33.1	7.5		39.3	91.5	90.2
0.74	5.0	−3°, dark	19.6	20.3	14.9		54.5	54.8	74.2

[a] In 1,1,2-trichlorotrifluoroethane at 0° in sealed, degassed tubes unless indicated. N_2 indicates experiments in flasks under N_2. [b] By glc analysis, based on hypochlorite. [c] Reference 2.

TABLE II

EFFECT OF OLEFINS ON THE PHOTODECOMPOSITION OF *n*-PENTYL HYPOCHLORITE[a]

			Yield, %	
[ROCl]	Olefin	Olefin/ ROCl	4-Chloro-1-pentanol	1-Pentanol
	None[c]		35.6[b]	27
1.3	*cis*-CHCl=CHCl	1.0	68.0 ± 4.6	22.5 ± 1.1
0.934		5.0	83.5 ± 2.8	12.8 ± 1.4
0.923		5.0	75.0 ± 1.5[b]	
1.17	*trans*-CHCl=CHCl	2.0	60.9 ± 0.5[b]	
1.06		3.5	69.0 ± 1.3[b]	
0.923		5.0	74.6 ± 1.2[b]	
0.549		15.0	78.5 ± 0.8[b]	
0.934	$CH_2=CCl_2$	5.0	70.1 ± 3.3	14.1 ± 0.1
1.30	C_2HCl_3	1.0	58.6 ± 2.3	23.9 ± 0.9
0.934		5.0	70.8 ± 0.3	20.5 ± 0.3
0.934	C_2Cl_4	5.0	73.2 ± 3.9	23.2 ± 1.1
0.934	Cyclohexane	5.0	49.6 ± 0.2	

[a] Duplicate runs at 0° in CCl_4. [b] Determined as 2-methyltetrahydrofuran after treatment of product with KOH in ethanol. [c] Reference 2.

traps. Most of the remaining hypochlorite is recovered as 4-pentanol, although other products were only examined in the trichloroethylene experiments which yielded 5-10% C_2HCl_5 and under 1% ester.

Table III summarizes additional experiments in which δ-chloro alcohols were either isolated or converted to the corresponding tetrahydrofurans. Results with two secondary hypochlorites are comparable to those in Tables I and II, reactions involving attack on secondary hydrogen giving the highest yields. Also included are three preparatory-scale experiments, which show quite satisfactory isolated yields although no attempt was made to optimize isolation procedures. The poorer yield of 4-chloro-1-pentanol compared with 2-methyltetrahydrofuran, however, was shown to arise from the former's decomposition to the furan during vacuum distillation.

Discussion

Our results show clearly that chlorine radical traps such as dichloroethylene lead to substantial improvements in the conversion of primary and secondary hypochlorites to the corresponding δ-chloro alcohols or tetrahydrofurans. Hypochlorite decompositions are only one of a number of techniques for carrying out intramolecular reactions of alkoxy radicals; others include nitrite photolysis, alcohol oxidation by lead tetraacetate, and the use of iodine in the presence of base or lead tetraacetate.[6] Perhaps the simplest of these is the use of lead tetraacetate, developed by Mihailovic,[7,8] which leads directly to the corresponding tetrahydrofuran. A comparison with our results is given in Table IV. Admittedly, yields are not strictly comparable since some of ours are based on glc analysis and quantitative conversion of alcohol to hypochlorite is assumed. On the other hand, the major by-product in the hypochlorite reaction is starting alcohol, which can readily be recycled, making the reaction in principle almost quantitative. In view of this, the simplicity of the procedures and the low cost of reagents, we suggest that our technique may prove the method of choice for conversion of many alcohols to either δ-chloro alcohols or furans.

Experimental Section

Materials unless noted were commercial reagents, distilled and purity checked by glc before use. Authentic 4-chloro-1-butanol was prepared by treating tetrahydrofuran with gaseous HCl in the presence of BF_3 etherate. Authentic 4-chloro-1-pentanol was obtained from 1-pentyl hypochlorite as described below.

Hypochlorites were prepared by the procedure of Walling and McGuinness[5] by reaction of the appropriate alcohol in chlorocarbon solvent with 2 equiv of acetic acid and commercial sodium hypochlorite (Clorox) at 0°. They were used without isolation after drying. Concentrations of hypochlorite solutions were determined by iodimetry, and conversions were quantitative since solutions showed no -OH absorption by ir nor extraneous nmr peaks. However, material losses on the small scale involved limited yields to 80-90%. Primary hypochlorite solutions were stable cold in the dark in halocarbon solvent, but secondary hypochlorites and primary hypochlorites in the presence of olefins decomposed slowly and so such solutions were used at once.

Decompositions.—Except for initial experiments carried out under N_2, decompositions were carried out in sealed, degassed tubes,[2] placed in thermostats and irradiated by a 40-W incandescent lamp at a distance of 30 cm for twice the time (*ca.* 60 min) for disappearance of the hypochlorite color. Products were analyzed by glc using internal standards added after reaction. Conversion of δ-chloro alcohols to tetrahydrofurans was accomplished by refluxing reaction mixtures briefly with 1.5 equiv of 5% alcoholic KOH.

Preparative Scale Experiments. 4-Chloro-1-pentanol.—A mixture of 105 ml of 2 *M* 1-pentyl hypochlorite in CCl_4 and 1.01 *M* *cis*-dichloroethylene was photolyzed at 0° and concentrated on a

---

[6] K. Heusler and J. Kalvoda, *Angew. Chem.*, **76**, 518 (1964).

[7] V. M. Micovic, R. I. Mamuzic, D. Jeremic, and M. L. Mihailovic, *Tetrahedron*, **20**, 2279 (1964).

[8] M. L. Mihailovic and Z. Cekovic, *Synthesis*, 209 (1970).

TABLE III

PHOTODECOMPOSITION OF ADDITIONAL HYPOCHLORITES

[ROCl]	*M*	[Olefin]	*M*	Yield, % Chloro alcohol	 Tetrahydrofuran	 Alcohol
1-Pentyl	1.16	*cis*-$C_2H_2Cl_2$	5.8	34[a]		
	1.12	*cis*-$C_2H_2Cl_2$	5.6		50[a]	
4-Phenyl-1-butyl	0.888	*cis*-$C_2H_2Cl_2$	4.44		56[a]	
2-Pentyl	1.15	*trans*-$C_2H_2Cl_2$	2.3		25.7 ± 0.4	43.5 ± 0.3
	0.91		4.55		40.1 ± 1.8	36.6 ± 1.8
	0.536		7.94		49.1	21.6
2-Hexyl	0.885	*cis*-$C_2H_2Cl_2$	4.43		89.0 ± 0.4[b]	6.7 ± 0.5
	0.663		6.63		82.7 ± 2.3[b]	5.3 ± 0.1

[a] Isolated product in preparative-scale experiments. [b] Equimolar mixture of cis and trans isomers.

TABLE IV

CONVERSION OF ALCOHOLS TO TETRAHYDROFURANS

Alcohol (or hypochlorite)	Yield, % ROCl	 $Pb(OAc)_4$[a]
1-Butyl	60	20
1-Pentyl	75	43
2-Pentyl	49	9.5
2-Hexyl	89	41
4-Phenyl-1-butyl	56	40–49
2-Methyl-2-pentyl	80[b]	10

[a] Reference 8. [b] Reference 2. No radical trap is required in the case of *tert*-hypochlorites.

rotary evaporator. Three vacuum distillations of the residue yielded 34% product, bp 67–68° (4 mm). The purity by glc was >95% and ir and nmr spectra consistent with the structure. The major impurity was 2-methyltetrahydrofuran formed during distillation and accounting for the low yield.

2-Methyltetrahydrofuran.—1-Pentyl hypochlorite (0.530 mol) (2 *M* solution in Freon-113) and 2.65 mol of *trans*-dichloroethylene were photolyzed at 0°. One-half of the reaction mixture was refluxed with 0.53 mol of 2,6-lutidine for 1 hr. Two fractional distillations yielded 11.7 g (51%) of 2-methyltetrahydrofuran, bp 68–70° (648 mm), purity by glc >98%. The other half of the reaction mixture was refluxed for 1 hr with 200 ml of 15% KOH in propylene glycol. Distillation yielded 11.1 g (49%) of 2-methyltetrahydrofuran.

2-Phenyltetrahydrofuran.—A mixture of 30.5 ml of 1.33 *M* 4-phenyl-1-butyl hypochlorite and 0.204 mol of *cis*-dichloroethylene was photolyzed at 0° (3 hr). The product was refluxed overnight with 91 ml of 5% KOH in methanol. Water was added and the mixture was extracted with three portions of ether. Fractional distillation yielded 3.36 g (56%) of 2-phenyltetrahydrofuran, bp 105–107.5° (15 mm), ir and nmr spectra consistent with structure. A higher boiling fraction (1.05 g) contained 59% of the furan by glc, indicating a total yield of 66%.

Registry No.—*n*-Butyl hypochlorite, 5923-22-8; *n*-pentyl hypochlorite, 35042-28-5; 4-chloro-1-pentanol, 35096-45-8; 2-methyltetrahydrofuran, 96-47-9; 2-phenyltetrahydrofuran, 16133-83-8.

Photosensitized Oxidation of Dialkyl Disulfides[1]

ROBERT W. MURRAY* AND SOHAN L. JINDAL

Chemistry Department, University of Missouri—St. Louis, St. Louis, Missouri 63121

Received May 1, 1972

Dialkyl disulfides are photooxidized in the presence of methylene blue sensitizer to the corresponding thiosulfinates. Quenching experiments indicate that singlet oxygen is the oxidant. A mechanism for the reaction, involving an adduct between the disulfide and singlet oxygen as an intermediate, is proposed. The implications of these results for the photodynamic effect are discussed.

By a variety of ways and particularly through the work of Foote and coworkers,[2] it has been amply demonstrated that the Kautsky[3,4] mechanism for photosensitized oxidation is a valid mechanism. According to this mechanism the photooxygenation occurs with excited singlet molecular oxygen as the oxidant. This demonstration has important implications both for organic chemistry and biological chemistry. In biological chemistry, photosensitized oxidation leading to pathological effects in organisms has been known as photodynamic action. Foote[5] and Hastings and Wilson[6] have pointed out that in some cases photodynamic action may also involve singlet oxygen. Indeed, Foote[7] has demonstrated that β-carotene efficiently quenches singlet oxygen and has suggested that the function of carotenoid pigments is to provide protective action against photodynamic damage.

In addition to photosensitization, a number of other methods for producing singlet oxygen have been described. Included are the reaction of sodium hypochlorite and hydrogen peroxide,[8] the use of a radiofrequency discharge in gaseous oxygen,[9,10] the reaction of bromine and hydrogen peroxide,[11] the decomposition of alkaline solutions of peracids,[11] the decomposition of photoperoxides,[12,13] the self-reaction of *sec*-butylperoxy

---

[1] Presented in part at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 12–17, 1971; *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **16**, A72 (1971).

[2] C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968).

[3] H. Kautsky and H. de Bruyn, *Naturwissenschaften*, **19**, 1043 (1931).

[4] H. Kautsky, *Trans. Faraday Soc.*, **35**, 216 (1939).

[5] C. S. Foote, *Science*, **162**, 963 (1968).

[6] J. W. Hastings and T. Wilson, "Photophysiology," V. A. C. Giese, Ed., Academic Press, New York, N. Y., in press.

[7] C. S. Foote, Y. C. Chang, and R. W. Denny, *J. Amer. Chem. Soc.*, **92**, 5216 (1970).

[8] C. S. Foote and S. Wexler, *ibid.*, **86**, 3879 (1964).

[9] E. J. Corey and W. C. Taylor, *ibid.*, **86**, 3881 (1964).

[10] A. M. Winer and K. D. Bayes, *J. Phys. Chem.*, **70**, 302 (1966).

[11] E. McKeown and W. A. Waters, *J. Chem. Soc. B*, 1040 (1966).

[12] H. H. Wasserman and J. R. Scheffer, *J. Amer. Chem. Soc.*, **89**, 3073 (1967).

[13] A. M. Trozzolo and S. R. Fahrenholtz, *Ann. N. Y. Acad. Sci.*, **171**, 61 (1970).