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Synthesis and Reactions of Chloroalkene Epoxides

Stanley A. Kline,* Jerome J. Solomon, and Benjamin L. Van Duuren

Laboratory of Organic Chemistry and Carcinogenesis, Institute of Environmental Medicine, New York University Medical Center, New York, New York 10016

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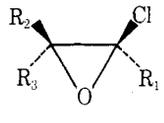
The chloroalkene epoxides, vinyl chloride oxide (**1**), trichloroethylene oxide (**2**), tetrachloroethylene oxide (**3**), *cis*- and *trans*-1-chloropropene oxide (**4** and **5**), and *cis*- and *trans*-1,3-dichloropropene oxide (**6** and **7**), were synthesized from their respective chloroalkenes via either autooxygenation (in the case of **2** and **3**) or *m*-chloroperbenzoic acid oxidation (in the case of **1** and **4–7**). Dichlorobenzene was a byproduct in the synthesis of both **6** and **7**. In the case of **6**, its formation was determined to be a result of a bimolecular reaction involving an intermediate in the synthesis of **6**. Kinetics of hydrolysis at pH 7.4 and 37 °C were determined for compounds **2–7**. Kinetics of thermal decomposition in dilute hydrocarbon solution were determined for compounds **2**, **4**, **5**, and **7**. The hydrolysis and thermolysis rates are discussed with respect to structure and mechanism of product formation.

Halogenated alkenes are widely employed as insecticides, industrial monomers, as solvents, and for other uses. Vinyl chloride has been shown to be carcinogenic to animals and man.[1] Trichloroethylene has been shown to be carcinogenic to mice.[1] These compounds and others including *cis*- and *trans*-1,3-dichloropropene are potent mutagens.[2] Vinyl chloride and trichloroethylene have been shown to bind covalently to cellular macromolecules.[3] This binding requires metabolic oxidation of the compounds and there is some evidence which suggests that epoxides may be intermediates involved in the binding.[4] Such epoxides have been proposed as potential activated carcinogenic intermediates[5] based on their structural similarity to known epoxide and chloroether carcinogens.[6] We have undertaken the synthesis and characterization of a number of such epoxides including vinyl chloride oxide (**1**), trichloroethylene oxide (**2**), tetrachloroethylene oxide (**3**), *cis*- and *trans*-1-chloropropene oxide (**4** and **5**), and *cis*- and *trans*-1,3-dichloropropene oxide (**6** and **7**). We determined and compared the rates and products of hydrolysis of these epoxides at physiological conditions. In addition, we have carried out thermal degradations of several of these epoxides and determined the rate of degradation and the nature of the products formed.



1, $R_1 = R_2 = R_3 = H$
2, $R_1 = H$; $R_2 = R_3 = Cl$
3, $R_1 = R_2 = R_3 = Cl$
4, $R_1 = R_3 = H$; $R_2 = CH_3$
5, $R_1 = R_2 = H$; $R_3 = CH_3$
6, $R_1 = R_3 = H$; $R_2 = CH_2Cl$
7, $R_1 = R_2 = H$; $R_3 = CH_2Cl$

Trichloroethylene oxide (**2**), synthesized by the autooxidation of trichloroethylene,[7] has been previously characterized in this laboratory.[8] Frankel et al.[9] had reported the synthesis of tetrachloroethylene oxide (**3**) by the chlorine-initiated photooxygenation of tetrachloroethylene. We modified this procedure by eliminating the chlorine initiator (which was found to catalyze the decomposition of the product) and allowing the reaction to go to completion. In this way the yield was improved and the purification of the product was greatly simplified.

Kirrman and co-workers synthesized 1-chloropropene oxide via dehydrohalogenation of 1,1-dichloro-2-hydroxypropane.[10] They obtained an unseparated mixture of cis and trans epoxides in low yield. Pure **4** and pure **5** were obtained in excellent yield by the *m*-chloroperbenzoic acid (*m*-CPBA) oxidation of the respective *cis*- and *trans*-1-chloropropenes. The NMR spectrum of each of the pure compounds was superimposable on the NMR spectrum of the mixture obtained by the method of Kirrman.

cis- and *trans*-1,3-dichloropropene oxide (**6** and **7**) were likewise synthesized by the *m*-CPBA oxidation of the corresponding alkenes. NMR, IR, and mass spectra of the major products were consistent with two possible structures, i.e., the assigned epoxide structure (A) or the cyclic ether (B). Incremental addition of the lanthanide shift reagent Eu(fod)^{TM} to compound **6** moved the chemical shifts of the methine (CH_2) protons (H(b), assigned on the basis of peak shape and integration) at a rate slower than that of either of the other protons H(a) or H(c) (Table I). The lanthanide reagents are known to

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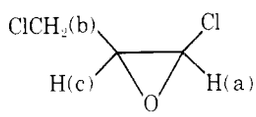
Table I. NMR of Compound 6

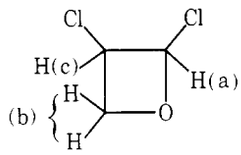
proton(s)	chemical shift, δ (ppm)	no. of protons	peak shape	coupling constant, Hz	slope of lanthanide-induced shift[a]
H(a)	5.28	1	d	3.5	1.56
H(b)	3.81	2	2-d, d	*b*	0.92
H(c)	3.40	1	m		1.96

[a] Slope of a plot of Δδ vs. weight of added Eu(fod). [b] Second-order effects did not allow determination of coupling constant.

complex with epoxide oxygens but not with chlorine.[11] Such a shift, therefore, is consistent with A where the oxygen is proximal to proton H(a) and H(c) and distal to protons H(b). The chemical shift data were inconsistent with structure B



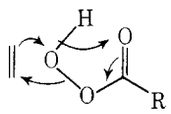
A



B

where the reverse is true. In addition, the NMR pattern of protons H(b) and H(c) in **6** was strikingly similar to that of the corresponding protons in epichlorohydrin (as determined in this laboratory), thus confirming that compound **6** was indeed *cis*-1,3-dichloropropene oxide.

A byproduct from the oxidation of both *cis*- and *trans*-1,3-dichloropropene was an aromatic compound of molecular weight 146 containing two chorine atoms, i.e., dichlorobenzene (substitution pattern not known). In addition, the cis oxide **6** contained some trans oxide (25%) and the trans oxide **7** contained a trace (5%) of the cis oxide after epoxidation of the corresponding alkenes. Dichlorobenzene may be formally thought to arise from bimolecular addition and cyclization of the parent olefin and epoxide followed by loss of 2 mol of HCl and 1 mol of water. However, when *cis*-1,3-dichloropropene was heated with *cis*-1,3-dichloropropene oxide, dichlorobenzene was not formed. The possibility that a reaction between *cis*-1,3-dichloropropene and **6** is acid catalyzed (by the *m*-chloroperbenzoic acid byproduct) or involves free radicals (from *m*-chloroperbenzoic acid) was explored by heating the compounds in the presence of catalytic amounts of either 1,4-dinitrobenzoic acid or benzoyl peroxide or both. In no case was dichlorobenzene a product. This compound, therefore,



probably arises from a reaction involving an intermediate in the synthesis of **6** from the parent olefin. Peracid oxidations, however, are believed to involve a concerted, bimolecular mechanism (i.e., involving no detectable intermediate) between olefin and peracid.[12] The dichlorobenzene must therefore be formed in the course of a second oxidative pathway involving an intermediate such as CH_2Cl–$CHOH$–$CHCl^+$. This would also account for the slight degree of nonstereospecificity during the course of the oxidation resulting in small amounts of trans oxide from the cis olefin and vice versa. The unoxidized olefin remained stereochemically pure so that formation of **7** from *cis*-1,3-dichloropropene, for example, did not involve preliminary isomerization of cis olefin to trans olefin.

Vinyl chloride oxide (**1**) was also synthesized in good yield by *m*-CPBA oxidation of vinyl chloride. It was identified by its NMR spectrum which was identical with the published spectrum.[13] Previously this compound had been synthesized

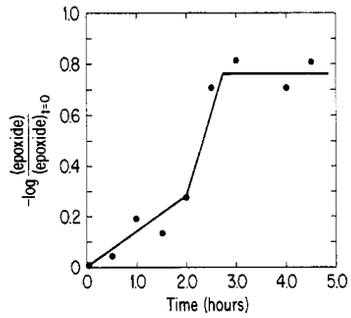


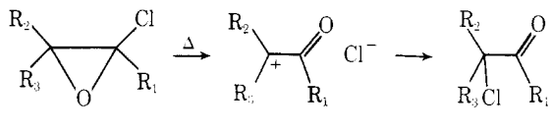
Figure 1. First-order plot for the decomposition of *cis*-1-chloropropene oxide (**4**) in xylene at 200 °C.

by the chlorination of ethylene oxide.[13] However, our procedure was easier to carry out and gave higher yields.

Since epoxides are potential metabolites of haloalkenes,[4,5] it was of interest to determine their stability under physiological conditions. Thus, pseudo-first-order hydrolysis rates were measured at 37 °C in aqueous solution buffered at pH 7.4, data which should be indicative of the epoxide reactivity toward cellular nucleophiles in vivo. All of the compounds tested gave good pseudo-first-order kinetics. As indicated in Table II, the presence of chlorine on the α position greatly increases the hydrolytic reactivity of aliphatic epoxides. Hydrolyses at pH 7.4 of the α-chloroepoxides **1–7** occur with chlorine migration, yielding α-chlorocarbonyl compounds (Table II). Kirrman[10b] reported that other α-chloroepoxides hydrolyzed under neutral conditions to mixtures of α-chloro- and α-hydroxycarbonyl compounds. In the case of **2**, it is clear that hydroxyl attacks at the less hindered monochlorinated carbon. An examination of products formed from hydrolyses of the α-chloroepoxides **1** and **4–7**, which contain only one chlorine, does not indicate the site of hydroxyl attack since addition at either the chlorinated or nonchlorinated carbon can lead to the same products. The rates of hydrolysis of the monochloroepoxides **1** and **4–7** decrease as the substituent at C-2 changes in the order $H > CH_3 \gg CH_2Cl$. Molecular models show that the presence of a large substituent on C-2 will not sterically hinder the approach of OH toward C-1, but the substituent effects indeed indicate that C-2 is the position of attack. Reactions of α-chloroepoxides with secondary amine nucleophiles are also believed to proceed via attack at C-2.[14]

Compounds **1–7** rearrange thermally to α-chlorocarbonyl compounds (Table II), a reaction generally believed to occur with intramolecular chlorine migration.[15] Thermolysis rates of compounds **2, 4, 5,** and **7** were determined in dilute toluene or xylene solutions (Table II). Compounds **2, 5,** and **7** showed good first-order kinetics with respect to epoxide decomposition.[16] The decomposition of **4** is complex (see Figure 1). The early stages of the reaction exhibit roughly first-order kinetics. HCl evolved during the early course of the reaction may catalyze the reaction during its later stages. The rate of thermolysis of **2** in solution was reasonably close to that reported for its thermolysis in the gas phase (1.0×10^{-2} min^{-1} compared with 5×10^{-3} min^{-1} [17] at 130 °C).

There is evidence to suggest that the thermal rearrangement of α-chloroepoxides proceeds through an α-carbonyl carbonium ion intermediate:[15]



I II

The fivefold decrease in the rate of thermolysis of **7** with respect to **5** is consistent with the expected inductive effect ex-

Table II. Hydrolysis and Thermolysis of α-Chloroepoxides

compd	registry no.	hydrolysis rate constant[a] min^{-1}	hydrolysis products	thermolysis rate constant,[b] min^{-1} (temp, °C)	thermolysis product
ethylene oxide		2.1×10^{-5} [c]	ethylene glycol		
epichlorohydrin		6.9×10^{-4} [d]	1,2-dihydroxy-3-chloropropane[d]		
vinyl chloride oxide (1)	7763-77-1	4.6×10^{-1} [e]	chloroacetaldehyde[e]		chloroacetaldehyde[f]
cis-1-chloropropene oxide (*4*)	21947-75-1	6.3×10^{-2}	polymer presumably from 1-chloropropanal	5.8×10^{-3} (200)[g]	1-chloropropanal[h]
trans-1-chloropropene oxide (**5**)	21947-76-2	1.6×10^{-1}	polymer presumably from 1-chloropropanal	3.2×10^{-2} (200)[i]	1-chloropropanal[h]
cis-1,3-dichloropropene oxide (**6**)	66826-72-0	2.4×10^{-3}	α-chloroacrylaldehyde	*j*	
trans-1,3-dichloropropene oxide (**7**)	66826-73-1	2.3×10^{-3}	α-chloroacrylaldehyde	6.1×10^{-3} (200)[i]	2,3-dichloropropanal, α-chloroacrylaldehyde
trichloroethylene oxide (**2**)	16967-79-6	5.3×10^{-1}	dichloroacetic acid[k]	1.0×10^{-2} (130)[l]	dichloroacetyl chloride[m]
tetrachloroethylene oxide (**3**)	16650-10-5	6.0×10^{-2} [c]	trichloroacetic acid[n]	7.2×10^{-3} (100)[n,o]	trichloroacetyl chloride

[a] Pseudo-first-order rate constant determined at 37 °C, pH 7.4. [b] First-order rate constant determined in solution. [c] J. N. Brönsted, M. Kilpatrick, and M. Kilpatrick, *J. Am. Chem. Soc.*, **51**, 428 (1929). Pseudo-first-order rate constant was determined at 20 °C, pH 7.0. [d] W. C. J. Ross, *J. Chem. Soc.*, 2257 (1950). [e] Reference 21. [f] H. Gross and J. Freiberg, *J. Prakt. Chem.*, **311**, 506 (1969). [g] First-order rate constant calculated for initial (linear) portion of reaction. [h] Reference 10b. [i] In xylene. [j] See Experimental Section. [k] Reference 7. [l] In toluene. [m] Reference 17. [n] Reference 9. [o] First-order rate constant determined in neat liquid phase.

erted on a carbonium ion center by a CH_2Cl substituent relative to a CH_3 substituent.[18] The large increase of the rate of thermolysis of **2** with respect to **5** (which was too slow to quantitate at 130 °C) at first sight might appear to argue against such an intermediate carbonium ion since carbonium ions are stabilized by a chlorine to about the same extent as a methyl substituent.[19] However, one must also consider the effects of the formation of new functionalities on $\Delta G^{\ddagger}$. In particular, C-1 is transformed in the transition state (which may be approximated by II) from a saturated carbon to an acyl chloride in the case of **2** or an aldehyde in the case of **5**. One may roughly estimate that the transition state energy for **2** is 15 kcal/mol lower than that for **5**.[20] The increased rate of isomerization of **2** relative to **5** is thus likely controlled by the energetically favorable formation of an acylhalide compared to an aldehyde functionality attached to the cation center.

Finally, it may be noted that epoxides **4** and **5** appear to be thermally more stable than originally reported,[10b] decomposing at an appreciable rate only at temperatures above 180 °C.

Experimental Section

Infrared spectra were determined using a Perkin-Elmer Model 421 spectrophotometer. Proton magnetic resonance spectra were recorded using a Varian Model T-60A spectrometer. Visible absorbances were read from a Gilford Model 240 spectrometer. Gas chromatographic analyses for hydrolysis kinetics of compounds **2** and **3** were performed on a Jarrel-Ash Model 28-710 gas chromatograph. Mass spectra were obtained on a DuPont Model 21-492 double-focusing high-resolution mass spectrometer. Chemical ionization mass spectrometry was performed using isobutane as the ionizing gas. Gas chromatography–mass spectrometry were carried out using a Varian Model 2740 gas chromatograph with a 5 ft × ⅛ in. 3% SE30 column coupled to the mass spectrometer. High performance liquid chromatography (LC) was done on a Waters 6000A chromatograph using a Waters C_{18} μ-Bondapak column. Incubations at 37 °C were done using a Dubnoff Metabolic Shaking Incubator. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

Trichloroethylene Oxide (2). This compound was synthesized by the benzoyl peroxide initiated oxygenation of trichloroethylene as previously described by us.[8]

Tetrachloroethylene Oxide (3). Tetrachloroethylene (100 mL, 0.978 mol) was heated to 90 °C in a photochemical immersion flask under a dry ice condenser. The liquid was irradiated with a Hanovia 250 W medium pressure mercury lamp while oxygen was bubbled through at a rate of 300 mL/min. Infrared spectra taken during the course of the reaction showed absorptions corresponding to tetrachloroethylene, trichloroacetyl chloride, and tetrachloroethylene oxide.[9] No unidentifiable absorptions were observed. The reaction was monitored by IR by observing the disappearance of the tetrachloroethylene absorption at 905 cm^{-1} and the concomitant increase of absorptions at 1753 and 975 cm^{-1} belonging respectively to the acid chloride and the epoxide. During the reaction the ratio of the absorptions at 975 and 1020 cm^{-1} belonging respectively to the epoxide and acid chloride did not change. After 35 h the absorption at 905 cm^{-1} was negligible and the photooxygenation was terminated.

The product mixture (87.2 g, 0.506 mol) was partially esterified by the dropwise addition of 24 mL (0.40 mol) of ethanol at 0 °C. IR showed that the trichloroacetyl chloride was completely converted to the corresponding ethyl ester while **3** remained largely unreacted. This mixture was distilled at 87 mm and material boiling at 39–55 °C was collected. This was redistilled at 70 mm and 11.2 g (12%) of a colorless liquid boiling at 33–35 °C was collected: IR (salt plate) 1320, 1365, 961, 869, 693, and 602 cm^{-1}; mass spectrum (electron impact) *m/e* 180. Anal. Calcd for C_2Cl_4O: C, 13.21; Cl, 78.00. Found: C, 13.24, Cl, 78.08.

***cis*-1-Chloropropene Oxide (4).** A solution of 10.0 mL (0.145 mol) of *cis*-1-chloropropene and 35.0 g (0.172 mol) of 85% *m*-chloroperbenzoic acid in 150 mL of methylene chloride was refluxed for 16 h. An NMR spectrum at this time showed no starting material. The solution was cooled at −20 °C overnight and filtered. The filtrate was washed first with 100 mL of 5% sodium sulfite and then with 100 mL of 10% sodium bicarbonate and the organic layer dried over anhydrous magnesium sulfate. Methylene chloride was removed by distillation at atmospheric pressure. The residue was distilled at 180 mm and the fraction which boiled at 40–55 °C was collected. The heated oil bath was kept below 90 °C. The material was redistilled at 130 mm and 5.0 g (37%) of a colorless liquid boiling at 32–34 °C was collected: IR (CH_2Cl_2) 1478, 1445, 1401, 1380, 1300, 1267, 1220, 1140, 1071, 1012, 964, and 845 cm^{-1}; NMR (neat) δ 5.08 (d, 1 H, H_1, $J_{1,2}$ = 3.5 Hz), 3.08 (d, q, 1 H, H_2, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 5.0 Hz), 1.18 (d, 3 H, H_3, $J_{2,3}$ = 5.0 Hz); mass spectrum (chemical ionization) $(M + H)^+$ *m/e* 93. Anal. Calcd for C_3H_5ClO: C, 38.95; H, 5.45; Cl, 38.31. Found: C, 38.75; H, 5.38; Cl, 38.25.

Compound **4** was stable in 15% methylene chloride solution. When left neat at 4 °C, however, it decomposed to a viscous material after 2 weeks.

***trans*-1-Chloropropene Oxide (5).** This compound was prepared from 10.0 mL (0.145 mol) of *trans*-1-chloropropene using the same procedure that was used to prepare the cis compound. The product

was distilled twice at 190 mm. In the second distillation 4.0 g (32%) of a colorless liquid boiling at 42–44 °C was collected: IR (salt plate) 1450, 1407, 1381, 1288, 1256, 1134, 1065, 1025, 965, and 880 cm^{-1}; NMR (neat) δ 4.82 (d, 1 H, H_1, $J_{1,2}$ = 1.5 Hz), 3.13 (d, q, 1 H, H_2, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 5.0 Hz), 1.22 (d, 3 H, H_3, $J_{2,3}$ = 5.0 Hz); mass spectrum (chemical ionization) $(M + H)^+$ *m/e* 93. Anal. Calcd for C_3H_5ClO: C, 38.95; H, 5.45; Cl, 38.31. Found: C, 38.84; H, 5.37; Cl, 38.29. Compound **5** when stored at 4 °C decomposed to the extent of 20% over 1 month.

***cis*-1,3-Dichloropropene Oxide (6).** A solution of 15.0 mL (0.162 mol) of *cis*-1,3-dichloropropene and 36.8 g (0.181 mol) of 85% *m*-chloroperbenzoic acid in 170 mL of carbon tetrachloride was refluxed for 7 h after which time subsequent NMR spectra showed little change. The mixture was cooled to −20 °C overnight and filtered. The filtrate was washed with 100 mL of 5% sodium bisulfite and 100 mL of 10% sodium bicarbonate and then dried over anhydrous magnesium sulfate. Solvent was removed by distillation at atmospheric pressure. The remainder was distilled in three fractions: Fraction 1 boiled at 34 °C at 163 mm and contained 4.8 g (27%) of *cis*-1,3-dichloropropene. Fraction 2 (**6**) boiled at 78–80 °C at 130 mm and, after a second distillation, yielded 5.0 g (24%) of a colorless liquid: IR (salt plate) 1308, 1270, 1255, 1084, 907, 681, and 645 cm^{-1}; NMR (neat) δ 5.28 (d, 1 H, H_1, $J_{1,2}$ = 3.5 Hz), 3.81 (2-d, d, 2 H, H_3 and H_4), 3.40 (m, 1 H, H_2). Additional absorptions at δ 5.17 (s) and 3.67 (m) were superimposable on a spectrum of **7** and integrated to 25% of **6**; mass spectrum (gas chromatography–MS, chemical ionization) $(M + H)^+$ *m/e* 127 containing 2Cl. Fraction 3 boiled at 48–50 °C at 15 mm and contained 3.0 g (12%) of a colorless liquid: NMR (neat) δ 7.30 (m); mass spectrum (gas chromatography–MS, chemical ionization) $(M + H)^+$ *m/e* 147 containing 2Cl.

NMR Spectra of Compound 6 in the Presence of a Lanthanide Shift Reagent. Eu(fod) was added in 10–20-mg increments to a solution of 20 mg of **6** in 0.5 mL of carbon tetrachloride. NMR spectra were recorded and integrated after each addition.

***trans*-1,3-Dichloropropene Oxide (7).** This compound was prepared from 19.0 mL (0.205 mol) of *trans*-1,3-dichloropropene using a procedure identical to that for *cis*-1,3-dichloropropene oxide. The product mixture was distilled in three fractions: Fraction 1 boiled at 32–34 °C at 150 mm and contained 5.0 g (22%) of *trans*-1,3-dichloropropene. Fraction 2 (**7**) was distilled twice collecting 6.0 g (23%) of a colorless liquid boiling at 95–96 °C at 132 mm: IR (salt plate) 1464, 1413, 1295, 1270, 918, 805, 790, 745, and 694 cm^{-1}; NMR (neat) δ 5.17 (broad s, 1 H), 3.67 (m, 3 H). An additional absorption at δ 5.28 (d, J = 3.5 Hz) integrated to about 5% of **7** was superimposable on a spectrum of **6**; mass spectrum (gas chromatography–MS, chemical ionization) $(M + H)^+$ *m/e* 127 containing 2Cl. Fraction 3 boiled at 60–62 °C at 30 mm and contained 4.0 g (13%) of a colorless liquid whose NMR and gas chromatography–mass spectra were identical to those of the byproduct from the synthesis of *cis*-1,3-dichloropropene oxide.

Formation of Dichlorobenzene during the Synthesis of 6. Six 3-mL glass ampules were sealed containing 50 μL of carbon tetrachloride plus the following compounds: (1) *cis*-1,3-dichloropropene (25 μL) and **6** (25 μL); (2) **6** (50 μL); (3) *cis*-1,3-dichloropropene (25 μL), **6** (25 μL), and 1,4-dinitrobenzoic acid (1 mg); (4) *cis*-1,3-dichloropropene (25 μL), **6** (25 μL), and benzoyl peroxide (1 mg); (5) *cis*-1,3-dichloropropene (50 μL) and benzoyl peroxide (1 mg); and (6) *cis*-1,3-dichloropropene (50 μL), **6** (10 μL), benzoyl peroxide (1 mg), and 1,4-dinitrobenzoic acid (1 mg). These were heated at 85 °C for 40 h after which time NMR spectra were recorded in CCl_4. Spectra for reactions 1–3 and 6 showed no change from starting materials. Reaction 4 showed a new absorbance at δ 7.35 as well as absorbance characteristic of **6**. No *cis*-1,3-dichloropropene remained. Reaction 5 showed a diminished quantity of *cis*-1,3-dichloropropene as well as a new absorbance at δ 7.35. IR's of reactions 4 and 5 showed new absorptions in each case superimposable on a spectrum of chlorobenzene.

***m*-Chloroperbenzoic Acid Oxidation of Vinyl Chloride.** Vinyl chloride (100 mg, 1.62 mmol) and 35.0 mg (1.72 mmol) of 85% *m*-chloroperbenzoic acid were dissolved in 3 mL of chloroform-*d* and sealed in a 5-mL glass ampule. After heating at 55 °C for 3.5 h an NMR revealed, in addition to *m*-chloroperbenzoic acid and *m*-chlorobenzoic acid, vinyl chloride (34%) and two new products A (55%) and B (11%). The major product (A) had an NMR δ 5.00 (d, d, 1 H, H_1, $J_{1,2}$ = 2.5 Hz, $J_{1,3}$ = 1.5 Hz) and 2.96 (m, 2 H, H_2 and H_3), consistent for vinyl chloride oxide (**1**). The minor product B had an NMR δ 9.50 (t, 1 H, J = 1.5 Hz) and 4.02 (d, 2 H, J = 1.5 Hz), consistent for chloroacetaldehyde.

Base-Catalyzed Hydrolysis of Compounds 6 and 7. A solution containing 10 μL of either **6** or **7** and 10 mg of sodium bicarbonate in 0.8 mL of a 1:1 mixture of D_2O and acetone-d_6 was allowed to stand overnight. NMR's of both mixtures after this time were identical, δ 9.53 (s, 1 H), 6.80 (d, 1 H, J = 6.5 Hz), 6.73 (d, 1 H, J = 6.0 Hz); mass spectra (gas chromatography–MS, chemical ionization) $(M + H)^+$ *m/e* 91. These data were consistent for α-chloroacrylaldehyde.

Hydrolysis Kinetics of 2 and 3. A solution of 0.2 mL of acetone in 1.5 mL of 0.5 M sodium phosphate buffer, pH 7.4, was warmed to 37 °C after which 10 μL of either **2** or **3** were added along with an equal volume of a suitable internal standard: chlorobenzene for **2** or ethyl trichloroacetate for **3**. Incubation was continued for 3 half-lives. After incubation for various time intervals, 0.3 mL of ether was added and the phases vigorously mixed for 45 s. An aliquot of the ether layer was immediately analyzed by GLC using a 6 ft × 0.25 in. diameter column packed with 10% Apiezon on Chromosorb W for compound **2** or a 6 ft × 0.25 in. diameter column packed with 10% SE 30 on Chromosorb W for compound **3**. The relative concentration of epoxide was determined from the ratio of its chromatogram peak area relative to that of the respective internal standard. The rates of hydrolysis were calculated from these data.

Hydrolysis Kinetics of Compounds 4–7 at pH 7.4. Following a procedure of Bartsch,[21] 50 mL of a 2:1 solution of 0.2 M tris–HCl buffer, pH 7.4, and acetone were warmed to 37 °C. To this was added 10 μL of epoxide. Incubation was continued for 3 half-lives. At various times 1.5-mL aliquots of this solution were removed and immediately added to a solution containing 30 mg of *p*-nitrobenzylpyridinium chloride in 2.0 mL of ethylene glycol, shaken vigorously for 30 s and warmed at 37 °C for 30 min in the case of **4** and **5** or 1 h in the case of **6** and **7**. After this time 2.5 mL of a 1:1 mixture of triethylamine and acetone were added and the solutions were shaken. After an additional 1 min the absorbance of the solutions at 575 nm was read against a reference containing 1.0 to 0.5 mL tris–HCl (pH 7.4), 0.5 mL of acetone, and 2.0 mL of ethylene glycol. A prior experiment confirmed that the concentration of the epoxide was proportional to the absorbance of the *p*-nitrobenzylpyridine adduct formed in this procedure. Rates of hydrolysis were calculated based on these data. Duplicate experiments show that rate constants were all within ±10%.

Thermal Isomerization of Compound 7. Compound **7** (20 μL) was sealed in a 10-mL ampule and heated in an oil bath to 200 °C for 40 h. An NMR spectrum ($CDCl_3$) showed three components, A, B, and C, in a ratio of 18:23:59. A: NMR δ 5.10 (s, 1 H), 3.63 (m, 3 H); mass spectrum (chemical ionization) $(M + H)^+$ *m/e* 127. B: NMR δ 9.07 (s, 1 H), 6.67 (d, 1 H, J = 2.0 Hz), 6.50 (d, 1 H, J = 2.0 Hz); mass spectrum (gas chromatography–MS, chemical ionization) $(M + H)^+$ 91. C: NMR δ 9.13 (d, 1 H, J = 1.7 Hz), 4.47 (d, t, 1 H, J = 1.7, 6.0 Hz), 3.95 (d, 2 H, J = 6.0 Hz); mass spectrum (chemical ionization) $(M + H)^+$ *m/e* 127. Compounds A and B had NMR and mass spectra identical to *trans*-1,3-dichloropropene oxide and the product from hydrolysis of **7** (α-chloroacrylaldehyde). Compound C had NMR and mass spectrum consistent with 2,3-dichloropropanal.

Thermal Isomerization of Compound 2 in Solution. Into a 3-mL ampule was sealed 0.5 mL of a solution containing 15 mg of **2** in 4.0 mL of xylene (dried and distilled over phosphorus pentoxide). The ampule was heated to 130 °C for 8 h (4 half-lives). Methanol (100 μL) was added to the solution to convert acyl chloride to its corresponding methyl ester. The resultant solution was analyzed using LC on a C_{18} reverse-phase column, eluting with 50% methanol–water. A single peak eluted at a retention time identical to methyl dichloroacetate. No peak corresponding to trichloroacetaldehyde was observed. Comparison of the peak area from isomerized **2** with that from an identical injection sample of a solution of 15 mg of dichloroacetyl chloride and 100 μL of methanol dissolved in 4.0 mL of xylene indicated that **2** isomerized to dichloroacetyl chloride in a yield of 80%. Dichloroacetyl chloride dissolved in xylene was itself unchanged upon heating at 130 °C for 8 h.

Thermal Isomerization of Compounds 2, 4, 5, 6, and 7 in Solution. Into 3-mL ampules were sealed 0.5 mL of a solution containing 10 μL of epoxide in 10 mL of either toluene or xylene (distilled and stored over phosphorus pentoxide). The ampules were heated to the desired temperature in an oil bath and cooled after various times. Samples were heated over a period of at least 3 half-lives. No HCl was detected upon breaking the ampules, although the pH of the solutions was slightly acidic. The contents of the ampules were added to a solution containing 30 mg of *p*-nitrobenzylpyridinium chloride in 2.5 mL of acetone, 1.0 mL of ethylene glycol, and 0.5 mL of 0.2 M tris–HCl buffered at pH 7.4. After these were warmed at 37 °C for either 30 min for **2, 4,** and **5** or 1 h for **6** and **7**, 2.5 mL of a 1:1 mixture of triethylamine and acetone was added. The absorbance was read at 540 nm for compound **2** or at 575 nm for **4–7** against a reference containing acetone, ethylene glycol, and tris–HCl in the above proportions. Rates of thermolyses were calculated from these data. Duplicate experiments show rates were constant to ±10%. A subsequent experiment confirmed that the absorbance of the *p*-nitrobenzylpyridine adduct

formed in this procedure was proportional to the concentration of epoxide for all compounds tested except **6**. The thermolysis rate could therefore not be calculated from **6** from these data. Thermal isomerization kinetics of compounds **2** and **5** were repeated in the presence of 2 mg of solid sodium bicarbonate added to each ampule to absorb any generated HCl. pH at all times remained slightly basic to indicator paper. Rate constants for isomerization were seen to be unaffected by this addition.

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Registry No.—Tetrachloroethylene, 127-18-4; *cis*-1-chloropropene, 16136-84-8; *trans*-1-chloropropene, 16136-85-9; *cis*-1,3-dichloropropene, 10061-01-5; *trans*-1,3-dichloropropene, 10061-02-6; vinyl chloride, 75-01-4.

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(20) $\Delta G_2^{\ddagger} - \Delta G_5^{\ddagger} \approx \Delta H_2^{\ddagger} - \Delta H_5^{\ddagger} \approx (\Delta H_f^{II} - \Delta H_f^{I})_2 - (\Delta H_f^{II} - \Delta H_f^{I})_5 \equiv \Delta_2^5(\Delta H^{\ddagger})$. The substituents at C-2 (R_2 and R_3) as well as the dihedral angle between them remain constant going from I to II. The stabilizing effects of R_2 on the carbonium ion center are similar in **2** and **5** and therefore may be ignored in a discussion of relative transition state energies. Thus, the substituents about C-2 should have a negligible effect on $\Delta_2^5(\Delta H^{\ddagger})$. Therefore, we may roughly estimate $\Delta H_2^{\ddagger} \sim \Delta H_f(CH_3COCl) - \Delta H_f(CH_3CHCl_2)$. $\Delta H_5^{\ddagger} \sim \Delta H_f(CH_3CHO) - \Delta H_f(CH_3CH_2Cl)$. $\Delta H_f^{298K}(CH_3COCl) = -58.7$ kcal/mol (Devore and O'Neal, *J. Phys. Chem.*, **73**, 2644 (1969)). $\Delta H_f^{298K}(CH_3CHCl_2) = -30.7$ kcal/mol (Lacher et al., *Trans. Faraday Soc.*, **63**, 1608 (1967)). $\Delta H_f^{298K}(CH_3CHO) = -39.7$ kcal/mol (Vasil'ev and Vvendenskii, *Zh. Fiz. Khim.*, **39**, 2052 (1965)). $\Delta H_f^{298K}(CH_3CH_2Cl) = -26.7$ kcal/mol (Green and Holder, *J. Chem. Soc.*, 1974 (1962). Therefore $\Delta_2^5(\Delta H^{\ddagger}) \sim -15$ kcal/mol.
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Notes

Zwitterionic Meisenheimer Complex Reactivity. Influence of Cyano and Nitro Groups on Ortho Substituent Attack vs. Meta Bridging

M. J. Strauss* and R. R. Bard

Department of Chemistry, University of Vermont, Burlington, Vermont 05401

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Anionic σ complexes (Meisenheimer complexes) formed from electron deficient aromatic compounds and a variety of organic and inorganic bases have been extensively studied and well characterized.[1-6] We previously reported evidence for zwitterionic σ complexes like **3a** as intermediates in the formation of the bicyclic zwitterion **4a** from reaction of *sym*-trinitrobenzene (**1a**) and α-phenyl-*N,N*-dimethylacetamidine in ethanol[7,8] and Me_2SO. It was of interest to study the effect of diminished electron deficiency of the starting aromatic in this reaction sequence. Surprisingly we have found that an entirely different reaction occurs when the aromatic substrate is 3,5-dinitrobenzonitrile (**1b**). Although related bicyclic ions in which the cyano group is part of the anionic function are well known,[9] the bicyclic zwitterions **4b** or **4c** *were not formed.* Instead, a green solid crystallized from the ethanolic reaction solution which had visible maxima at 469 and 596 nm, characteristic of σ complexes of **1b**.[10] The ^1H NMR and elemental analyses confirm the structure as **2** (see Experimental Section). Compound **2** appears remarkably stable. The diminished electrophilicity of the ring in **3b** relative to **3a** may make the **3b** to **4b** conversion less favorable than that of **3a** to **4a**.

While the ^1H NMR spectrum of **2** is easily recorded in Me_2SO-d_6 at room temperature, heating this solution to 50–60 °C causes absorptions for **2** to diminish as new peaks appear. The latter are identical to those obtained from the reaction product of **1b** and α-phenyl-*N,N*-dimethylacetamidine in Me_2SO. The ^1H NMR spectrum of this product, as well as the elemental analyses, confirm the structure as **5**. A distinction between **5a** and **5b** cannot be made on the basis of the ^1H NMR spectrum.

Although no absoprtions other than those of **2** and **5** appear in the heated Me_2SO solution of **2**, it is unlikely that **2** is a direct precursor to **5**. Cyclization of carbon-bonded σ complexes like **2** does not occur in ethanol or Me_2SO even in the presence of excess amidine.[7,8]

A likely mechanism for the formation of **5** would be dissociation of **2** to amidine and **1b** as the solution is warmed. Attack of amidine on the cyano group or a ring carbon of **1b** can then occur, with eventual cyclization to **5**. It seems clear that amidine attack on **1b** in Me_2SO proceeds differently than in ethanol (i.e., amidine nitrogen attack on the ring or cyano group). In any case, if subsequent cyclization–aromatization is rapid relative to initial complex formation, no intermediates would be observed by NMR. We have no definitive explana-

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