priate bromination product (example *n*-pentane, 25°) showed four peaks. The second, third, and fourth peaks were identified as **1**, **3**, and **4**, respectively, on the basis that the retention time and infrared spectrum[18] of each was identical with that of the appropriate authentic isomer. The second and third peaks were further confirmed as **1** and **3** by heating samples of them at 100° and observing that they rearranged to essentially the same mixtures as reported for authentic **3** and **4**.

The dibromide corresponding to the first peak in the chromatogram and assigned structure **2** was isolated from the dibromide mixture (*n*-pentane, 25°) by low temperature fractional distillation. It was assigned structure **2** on the basis that its infrared spectrum showed the terminal vinyl absorption bands[15] at 930 and 990 cm^{-1}, and that it rearranged[8] on refluxing to **3** and **4**.

The Equilibration Studies.—Solutions of approximately 15% **4** in the solvents listed in Table II were allowed to stand at room temperature (approximately 25°) for about 6 months. Analyses at the end of 3- and 6-month periods were essentially the same. As indicated, the equilibration of **4** without a solvent was studied. The essentially pure **4** used in the equilibration study was prepared by recrystallization of the product obtained from the bromination of isoprene at −45°. The recrystallization was carried out in *n*-pentane at Dry Ice temperatures. Vpc analysis indicated that only traces of the other dibromides remained. The **4** prepared in this manner was used in the equilibration studies without distillation since distillation sometimes resulted in rearrangement. We are unable to account for the fact that distillation of **4**, purified by recrystallization, did not always result in rearrangement. However, equilibration studies in $CHCl_3$ on a sample of **4**, prepared in this way and distilled without rearrangement, gave identical results with that of undistilled **4**.

Registry No.—Isoprene, 78-79-5; **3**, 16526-18-4; **4**, 16526-19-5.

Acknowledgment.—Acknowledgment is made to the Research Corporation and the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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[18] A small sample of each isomer was isolated from the gas chromatograph. These samples were used to make the infrared spectra. The spectra were identical with the spectra of the authentic isomers, except for some very minor impurity peaks in the latter.

The Chlorination of Olefins with Cupric Chloride. A Comparative Study of *trans*-Ethylene-d_2 and *cis*- and *trans*-2-Butene

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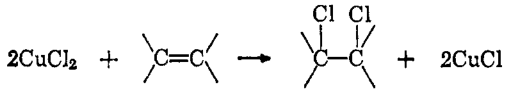
The chlorination of olefins at 320° with cupric chloride does not always proceed with a high degree of *trans* addition. Although both *cis*- and *trans*-2-butene chlorinate by largely *trans* addition, the chlorination of *trans*-ethylene-d_2 is nearly random. The order of stereoselectivity is *cis*-2-butene > *trans*-2-butene ≫ *trans*-ethylene-d_2. The random chlorination of *trans*-ethylene-d_2 occurs during the product-forming step. Neither ethylene-d_2 nor product isomerization is responsible. However, most of the randomly chlorinated product from *cis*- and *trans*-2-butene can be explained by 2-butene isomerization and the interconversion of the 2,3-dichlorobutane diastereomers. The greater stereoselectivity in the chlorination of *cis*- over *trans*-2-butene is mainly due to the isomerization of *meso*- into *dl*-2,3-dichlorobutane. At 320°, this isomerization occurs approximately 1.4 times faster than the isomerization of *dl*- into *meso*-2,3-dichlorobutane. Evidence is also presented which shows that cupric chloride and not chlorine is the chlorinating agent. The mechanism of this reaction is discussed in terms of chloronium ion and radical intermediates.

The literature contains several examples of the use of cupric chloride as a versatile chlorinating agent for a variety of organic molecules.[1-4] Undoubtedly, the most extensive industrial application of this chemistry of cupric chloride is in so-called "oxychlorination" reactions. This is a vapor phase reaction normally carried out at temperatures of 220–330°.[5] In this process, cupric chloride chlorinates the double bond of the olefin and in turn is reduced to cuprous chloride. Cuprous chloride is then reoxidized with hydrogen chloride and oxygen, and the process is repeated many times.



$$2CuCl_2 + {>}C{=}C{<} \longrightarrow {>}\overset{Cl}{C}{-}\overset{Cl}{C}{<} + 2CuCl \quad (1)$$

$$2CuCl + 2HCl + \tfrac{1}{2}O_2 \longrightarrow 2CuCl_2 + H_2O \quad (2)$$

This paper deals with the mechanism of the olefin chlorination step (eq 1). Arganbright and Yates recently reported on the chlorination of *cis*- and *trans*-2-butene with cupric chloride supported on pumice.[1] They found that at 290° this reaction proceeds with a high degree of *trans* addition. In this present work, we have extended the study of olefin chlorination with cupric chloride with the objective of answering the following questions. (1) Do olefin substituents greatly influence the stereochemistry of this reaction? Specifically, is the chlorination of the simplest olefin, ethylene, also highly stereoselective? (2) Why is the chlorination of *cis*-2-butene more stereoselective than *trans*-2-butene? (3) Is elemental chlorine involved in this reaction?

Results

Both *cis*- and *trans*-ethylene-d_2 were required for this study. They are conveniently synthesized by the stereospecific reduction of acetylene-d_2.[6] We confirmed the stereochemistry of these reductions by infrared spectroscopy. The characteristic bands for *cis*- and *trans*-ethylene-d_2 appear at 842 and 987 cm^{-1}, respectively.[7,8]

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[1] R. P. Arganbright and W. F. Yates, *J. Org. Chem.*, **27**, 1205 (1962).

[2] C. E. Castro, E. J. Gaughan, and D. C. Owsley, *ibid.*, **30**, 587 (1965).

[3] J. K. Kochi and D. M. Mog, *J. Amer. Chem. Soc.*, **87**, 522 (1965).

[4] D. C. Nonhebel, *J. Chem. Soc.*, 1216 (1963).

[5] G. W. Hearne, U. S. Patent 2,399,488 (1946); A. J. Johnson and A. J. Cherniavsky, U. S. Patent 2,746,844 (1956).

[6] R. Spector, Ph.D. Thesis, University of Pennsylvania, Philadelphia, Pa., 1965.

[7] R. L. Arnett and B. L. Crawford, *J. Chem. Phys.*, **18**, 118 (1950).

[8] W. M. Schubert, B. S. Rabinovitch, N. R. Larson, and V. A. Sims, *J. Amer. Chem. Soc.*, **74**, 4590 (1952).

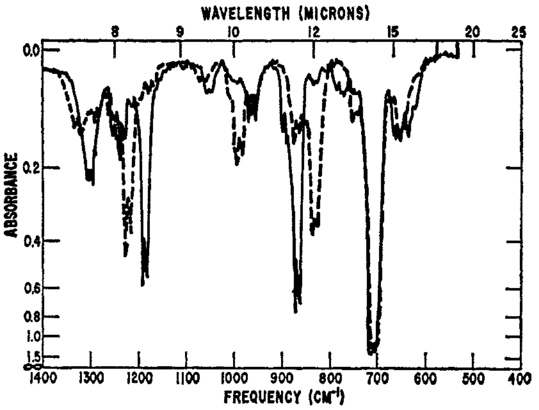
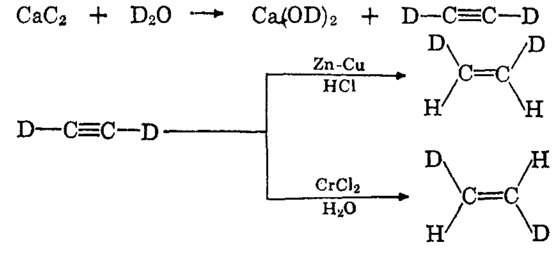
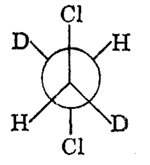


Figure 1.—Gas cell infrared spectrum: ———, 90% *meso*-1,2-dichloroethane-1,2-d_2, 6% $C_2H_3DCl_2$, 4% $C_2H_4Cl_2$; — —, 81% *dl*-1,2-dichloroethane-1,2-d_2, 15% $C_2H_3DCl_2$, 4% $C_2H_4Cl_2$.



The addition chlorination of either ethylene-d_2 can produce two diastereomers, *meso*-1,2-dichloroethane-1,-2-d_2 (**1**) and *dl*-1,2-dichloroethane-1,2-d_2 (**2**). We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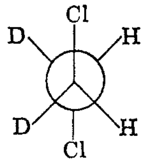

2

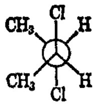
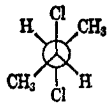
prepared these two reference compounds by the chlorination of *cis*- and *trans*-ethylene-d_2 in acetic acid. Under these conditions, exclusively *trans* addition is expected.[9] The fact that this reaction is indeed stereospecific is evident from the infrared spectra. The spectrum of either compound has intense bands which are absent in the other. The reference bands chosen for calibration are located at 1183 cm^{-1} for the *meso* isomer and 838 cm^{-1} for the *dl* isomer (Figure 1). Mass spectrometry gave the following deuterium distribution: *meso* dichloride **1**, 90% $C_2H_2D_2Cl_2$, 6% $C_2H_3DCl_2$, 4% $C_2H_4Cl_2$; *dl* dichloride **2**, 81% $C_2H_2D_2Cl_2$, 15% $C_2H_3DCl_2$, 4% $C_2H_4Cl_2$. Hydrogen–deuterium exchange likely occurs during the acetylene-d_2 synthesis or the acetylene reduction step or both. A large excess of fresh calcium carbide was used in all acetylene-d_2 syntheses. Small amounts of calcium hydroxide in the carbide could result in exchange with deuterium oxide to give some hydrogen in the acetylene-d_2. Significant amounts of hydrogen in acetylene-d_2 prepared in this way has been reported (3 mol % or as much as 6% C_2HD).[10] However, the infrared spectra clearly show that this exchange, wherever it occurs, is not accompanied by the isomerization of *cis*- and *trans*-ethylene-d_2 or the *meso* and *dl* dichlorides **1** and **2**. For the purposes of this study, 81 and 90% $C_2H_2D_2Cl_2$ is sufficient. It is only important that the isomers are not contaminated with one another.

Now that the dichlorides **1** and **2** have been characterized, the stereochemistry of the chlorination of *trans*-ethylene-d_2 with cupric chloride can be established. This reaction was conducted in an externally heated Vycor tube at 320° with 10% cupric chloride impregnated on a 8–10 mesh pumice support. The infrared spectrum of the purified 1,2-dichloroethane-1,2-d_2 mixture (preparative vpc) indicated that the product comprised 58% *meso*- and 42% *dl*-1,2-dichloroethane-1,2-d_2. The randomly chlorinated product is not due to the isomerization of *trans*-ethylene-d_2 under the reaction conditions. The unreacted ethylene-d_2 contained only 4% of the *cis* isomer. Neither do the products isomerize significantly. Under these conditions, a mixture of 90% of the dichloride **1** and 10% of the dichloride **2** gave a product whose isomer ratio changed only slightly to 84 and 16% of the dichlorides **1** and **2**, respectively. In this later experiment, the copper chloride is first partially reduced with ethylene to make certain that both copper(I) and -(II) are present. Nitrogen is then passed through the mixture of the chlorides **1** and **2**. This nitrogen stream, now containing dichloride vapor is passed through the reactor at the same temperature and contact time used in the chlorination of *trans*-ethylene-d_2.

The chlorination of *cis*- and *trans*-2-butene is much more stereoselective under the conditions used in the chlorination of *trans*-ethylene-d_2 (Table I). Table I also shows that the interconversion of isomeric 2-butenes occurs somewhat more extensively than the isomerization of *trans*-ethylene-d_2, and, as one might expect, *cis*-2-butene isomerizes faster than *trans*-2-butene. The extent of 2-butene isomerization is quite significant compared to the amount of random chlorination.

TABLE I

THE CHLORINATION OF *cis*- AND *trans*-2-BUTENE WITH $CuCl_2$ AT 320°. PRODUCT COMPOSITION

	2,3-Dichlorobutanes, %			
			2-Butenes, %	
Reactants	*dl*	*meso*	*cis*	*trans*
cis-2-Butene	82.5	17.5	90.1	9.9
trans-2-Butene	23.3	76.7	6.3	93.7

The stability of *dl*-2,3-dichlorobutane (**3**) and *meso*-2,3-dichlorobutane (**4**) was also examined under the reaction conditions using partially reduced cupric chloride. The isomerization of these compounds is also significant compared to the amount of random chlorination of the 2-butenes. Moreover, the *meso* dichloride **4** isomerizes about 1.4 times faster than the *dl* isomer **3**. The dichloride **4** gave a product comprising 86.8% of **4** and 13.2% of **3** whereas the dichloride **3** gave 90.9% of **3** and 9.3% of **4**.

The last objective of this study was to determine if elemental chlorine is involved in these reactions. To resolve this question, we chose to measure the rate of chlorine production from our cupric chloride–pumice system at 320°. We then compared this to (1) the rate expected for a rapid equilibrium among cupric

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[9] R. Fahey and C. Shubert, *J. Amer. Chem. Soc.*, **87**, 5172 (1965).

[10] L. C. Leitch and A. T. Morse, *Can. J. Chem.*, **30**, 924 (1952).

chloride, cuprous chloride, and chlorine and (2) the rate of 1,2-dichloroethane production. Chlorine is, indeed, produced when the olefin is replaced by nitrogen and can be conveniently measured iodometrically. Using a nitrogen flow rate of 9.89 mmol/min, the rate of chlorine production is 0.018 ± 0.001 mequiv every 2 hr over three successive 2-hr runs. This is far short of that expected if the following reaction were in rapid equilibrium.

$$2CuCl_2(s) \rightleftharpoons 2CuCl(s) + Cl_2(g)$$

The equilibrium partial pressure of chlorine at 600°K is 4.6×10^{-4} atm.[11] Considering the nitrogen flow through our reactor the expected rate of chlorine production is about 57 times greater than that observed. Replacing part of the nitrogen with ethylene (2.11 mmol/min) but under otherwise identical conditions, 1,2-dichloroethane is produced at 0.45 ± 0.04 mmol/min (three successive measurements) over an 8-min period. This reaction was carried to 24% completion based on cupric chloride. The zero-order dependence on cupric chloride is not surprising. Arganbright and Yates reported that the chlorination of olefins with cupric chloride on pumice appeared to take place at a constant rate.[1]

Discussion

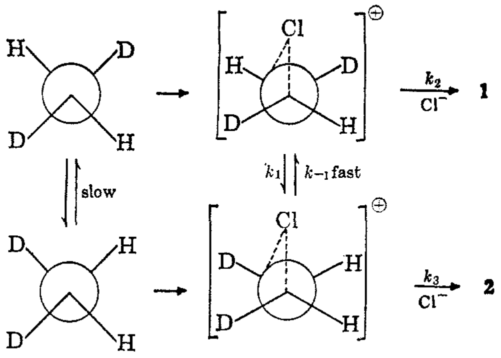
Arganbright and Yates reported that the chlorination of *cis*- and *trans*-2-butene with cupric chloride at 290° proceeds with a high degree of *trans* addition.[1] They proposed a chloronium ion intermediate to account for this. In general, we concur with their observation of the high stereoselectivity with the 2-butenes. But our results also show that the chlorination of olefins with cupric chloride is not always a highly stereoselective reaction. It is strongly influenced by the degree and geometry of olefin substitution.

The chlorination of *trans*-ethylene-d_2 with cupric chloride on pumice occurs with little stereoselectivity. Only 16% of the reaction proceeds by a stereospecific *trans* addition while 84% is random. Our data clearly shows that neither olefin nor product isomerization is responsible. The random chlorination must occur during the product-forming step.

In sharp contrast with *trans*-ethylene-d_2, the chlorination of both *cis*- and *trans*-2-butene is highly stereoselective under the same conditions (Table I). In this system, however, the extent of olefin isomerization and interconversion of the 2,3-dichlorobutane diasteriomers is large compared to the relatively small amount of random chlorination. In fact, the 17.5% of the *meso* dichloride **4** obtained from *cis*-2-butene can be conveniently accounted for in terms of olefin and product isomerization. The unreacted 2-butene contained 9.9% of the *trans* isomer, and under the reaction conditions, the *dl*-dichloride **3** isomerized to 9.1% of the *meso* isomer **4**. The same interpretation can be made to account for the 23.3% of *dl* dichloride **3** obtained from the chlorination of *trans*-2-butene. Although *cis*-2-butene isomerizes faster than *trans*-2-butene it, nevertheless, chlorinates with greater stereoselectivity. The explanation lies in the relative rates for the interconversion of products. The *meso* dichloride isomerizes approximately 1.4 times faster than the dichloride **3**.

The proposal of a chlorinium ion by Arganbright and Yates to account for the stereochemistry of the chlorination of the 2-butenes is a reasonable one. There is strong evidence for the existence of such intermediates. Among the most convincing is a recent report by Fahey on the dramatic stereospecific *trans* addition of chlorine to *cis*-di-*t*-butylethylene.[12] Fahey also observed rearranged products resulting from a stereospecific *trans*-methide shift from the *t*-butyl substituent. If the chloronium ion is the only intermediate in the chlorination of *trans*-ethylene-d_2, then the interconversion of rotamers, steps k_1 and k_{-1}, must be faster than product formation, steps k_2 and k_3 (Scheme I). If one considers the same mechanism for the chlorination of the 2-butenes, then the relative rates for the two steps must be reversed. Product formation must be faster than the interconversion of rotamers.

SCHEME I



However, the interconversion of chloronium ions must go through open-chain transition states. One would then expect the more highly substituted ones to isomerize more rapidly. If this ionic scheme is to be consistent with our observed order of stereoselectivity, the conversion of the chloronium ion into product must be much faster for the 2-butenes than for *trans*-ethylene-d_2. A mechanism which more consistently accounts for our results is one in which the reaction partitions between a radical and bridged ion pathway. Poutsma has observed such a dual mechanism for the dark chlorination of several olefins with chlorine under nitrogen.[13] He has shown that the radical route is much less stereoselective. Competition between the two routes is influenced by olefin substitution, the ionic route being somewhat favored with increasing number of alkyl substituents, particularly at low olefin concentrations.

Since cupric chloride is the chlorinating agent in our system, a cupric chloride–olefin complex must form during the reaction. Partitioning between the radical and ionic pathway might occur by either chlorine atom or (Cl^+) transfer from copper. This is similar to the scheme suggested by Poutsma where the two routes evolved from an olefin–chlorine π complex.[13] Although some chlorine can be produced in our system, it is only 6×10^{-3} times the rate of 1,2-dichloroethane production. Substantial involvement of chlorine through a rapid equilibrium disproportionation of cupric chloride

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(11) J. A. Allen, *J. Appl. Chem.*, **12**, 406 (1962).

(12) R. C. Fahey, *J. Amer. Chem. Soc.*, **88**, 4681 (1966).

(13) M. Poutsma, *ibid.*, **87**, 2172 (1965).

is unreasonable. The rate of chlorine production is kinetically controlled and only 1.8% of that expected for a rapid equilibrium.

Experimental Section

Acetylene-d_2.—A three-necked, 50-ml flask fitted with an addition funnel and a water-cooled condenser was flame dried while being purged with a stream of nitrogen. The nitrogen purge was continued as the apparatus cooled to room temperature. Calcium carbide (25 g) was transferred to the three-necked flask from a freshly opened container. Then 10 ml of deuterium oxide was added to the addition funnel. Another apparatus was now assembled. A 1-gal. glass bottle was filled with water and fitted with a rubber stopper containing two pieces of glass tubing. One piece extended only 1 in. into the bottle and the other extended to the very bottom. Both pieces of tubing contained a two-way stopcock. The nitrogen flow through the three-necked flask was stopped and these two apparatus were connected with Tygon tubing extending from the top of the condenser in the first apparatus to the short piece of tubing in the second. As deuterium oxide was slowly added to the calcium carbide, the water in the 1-gal. bottle was displaced by acetylene-d_2. The addition of deuterium oxide was continued until only 500 ml of water remained. At this point, the stopcocks were closed and the two apparatus disconnected.

***trans*-Ethylene-d_2.**—The following is a modification of the procedure described by Spector.[6] Zinc amalgam was prepared by adding granulated zinc (50 g) to 10 ml of mercury followed by 5 ml of 1 *N* sulfuric acid. The mixture was heated on a steam bath for 20 min. The amalgam was then washed several times with distilled water and placed in a 500-ml, glass-stoppered flask. A solution of 120 g of chromic chloride hexahydrate (0.45 mol) and 75 ml of concentrated hydrochloric acid in 150 ml of water was added. The mixture was stoppered and shaken vigorously until the color turned from green to deep blue, characteristic of the hydrated chromous ion. The stopper was removed periodically to permit small amounts of hydrogen to escape.

The long section of tubing on the 1-gal. bottle containing acetylene-d_2 was connected to an aspirator. The stopcock to the aspirator was opened and the remaining 500 ml of water was removed. The stopcock was then immediately closed. This created a partial vacuum in the bottle. This section of tubing was then inserted into the chromous chloride solution and the stopcock opened. The solution was transferred into the bottle by suction, and the mixture was shaken on a mechanical shaker for 2.5 hr. This reaction was repeated, and the vapor contents of the two bottles were transferred into a steel lecture bottle. The lecture bottle was cooled in liquid nitrogen. Air and hydrogen were then removed with a vacuum pump. The infrared spectrum showed an intense band at 987 cm^{-1}, characteristic of *trans*-ethylene-d_2. There was no band at 843 cm^{-1} for *cis*-ethylene-d_2.[7,8]

***cis*-Ethylene-d_2.**—The following is a modification of the procedure described by Spector.[6] Copper-activated zinc was prepared by adding 150 g of zinc dust to a rapidly stirred solution of 36 g of cupric sulfate pentahydrate in 600 ml of water. Some heat was evolved in this reaction, and the blue solution was decolorized. The mixture was stirred for approximately 15 min and then filtered. The resulting copper-activated zinc was washed several times with water and transferred to a 1-gal. bottle. The bottle was filled with water, and all but 300 ml of water was displaced with acetylene-d_2 according to the procedure described earlier. The final 300 ml of water was removed with an aspirator and replaced with a solution of 24 ml of concentrated hydrochloric acid in 90 ml of water. This mixture was vigorously shaken for 18 hr on a mechanical vibrator. After this time, the copper-activated zinc was coated with zinc chloride and had caked. Gas chromatography also showed that all of the acetylene-d_2 had not yet been reduced. Therefore, the vapor contents were displaced by water into a liquid nitrogen trap where the hydrogen was removed with a vacuum pump. The gas was then transferred into a 1-gal. bottle containing fresh copper-activated zinc and the mixture was shaken for an additional 8 hr. The product, now essentially free of acetylene-d_2, was transferred to a steel lecture bottle. The infrared spectrum had an intense band at 842 cm^{-1} for *cis*-ethylene-d_2 and no band at 987 cm^{-1} for *trans*-ethylene-d_2.[7,8]

***meso*-2,3-Dichloroethane-1,2-d_2 (1).**—A three-necked, 100-ml, round-bottom flask was painted black then fitted with a Dry Ice condenser, magnetic stirring bar, and a sintered-glass, gas-saturating tube. Glacial acetic acid (50 ml) was added followed by 8.6 g (0.121 mol) of chlorine. While the solution was rapidly stirred, 2 l. of *trans*-ethylene-d_2 (0.089 mol) was passed through the gas-saturating tube. It was introduced at such a rate that very little passed through the system unreacted. After the addition was completed, the Dry Ice–acetone mixture was removed from the condenser, and the contents frozen to the base of the condenser were allowed to melt and return to the reaction mixture. The contents were then added to 125 ml of water. The organic phase was removed and washed twice with 10 ml of water. Gas chromatography showed that except for some high boiling products, nearly 100% of this material had the same retention time as 1,2-dichloroethane. The product was further purified by preparative gas chromatography using a 4 ft × 0.25 in. column packed with 20% LB 550X Ucon on Chromosorb R at 90°. A total of 0.34 g (4%) of pure product was obtained. Mass spectroscopy gave the following percentages: 90% $C_2H_2D_2Cl_2$, 6% $C_2H_3DCl_2$, and 4% $C_2H_4Cl_2$. For infrared data, see Figure 1.

***dl*-1,2-Dichloroethane-1,2-d_2 (2).**—This procedure is identical with that used in the synthesis of the *meso* isomer except *cis*- rather than *trans*-ethylene-d_2 was used. A total yield of 0.39 g (4%) of pure product was obtained. Mass spectroscopy gave the following percentages: 81% $C_2H_2D_2Cl_2$, 15% $C_2H_3DCl_2$, and 4% $C_2H_4Cl_2$. For infrared data, see Figure 1.

The Chlorination of *cis*- and *trans*-2-Butene with Cupric Chloride on Pumice.—Cupric Chloride impregnated on pumice was prepared by adding 107 g of 8–10 mesh pumice to a solution of 16.1 g of cupric chloride dihydrate in 60 ml of water. This mixture was constantly stirred over a steam bath to remove the water.

The chlorination of olefins was carried out in a reactor consisting of a vertically mounted (24 × 330 mm) Vycor tube containing a coarse, sintered glass disk at its base. The tube was externally heated, and contained a thermocouple well which extended vertically through the center such that the temperature could be measured at any point along its length. The pumice supported cupric chloride (40 g) was then introduced and gradually heated in a stream of nitrogen fed through the base of the reactor. The temperature along most of the reactor length was adjusted to 320° with a distribution ranging between 300 and 320°. A feed comprising 2.11 mmol of 2-butene/min and 7.18 mmol of nitrogen/min passed through the reactor. The product was collected in a Dry Ice–acetone trap over a 12-min period. An evacuated gas sampling bottle was then connected to the trap, and the unreacted butenes were collected as the product warmed to room temperature. The butenes were then analyzed by gas chromatography at 48° using an 8 ft × 0.25 in. column packed with silver nitrate–benzyl cyanide on 60/80 mesh Chromosorb R. The ratio of *meso*- to *dl*-2,3-dichlorobutanes in the liquid product was also determined by gas chromatography. A 4 ft × 0.25 in. column packed with 20% LB 550X Ucon on Chromasorb R was used with a temperature program from 30 to 200° at 10°/min. Better resolution can be achieved with a 20 ft × 0.25 in. column operated isothermally at 140°. The by-products in this reaction are *cis*- and *trans*-2-chloro-2-butene (5–7%).

Chlorination of *trans*-Ethylene-d_2 with Cupric Chloride on Pumice.—This reaction was identical with that described for the 2-butenes except that the unreacted ethylene-d_2 was collected in a liquid nitrogen trap connected in series with the Dry Ice–acetone trap. A gas-sampling bottle was connected to the liquid nitrogen trap and both were evacuated. The unreacted ethylene-d_2 was then transferred to the gas-sampling bottle as it gradually warmed to room temperature. The unreacted ethylene-d_2 was analyzed by infrared using the calibrated absorption for *cis*- and *trans*-ethylene-d_2 at 842 and 987 cm^{-1}, respectively.[7,8]

The chlorinated product in the Dry Ice–acetone trap was allowed to warm to room temperature, and was washed with 4 ml of water. The organic phase was separated and the 1,2-dichloroethane-1,2-d_2 mixture was isolated pure by preparative gas chromatography using those conditions described earlier. The ratio of *meso*- to *dl*-1,2-dichloroethane-1,2-d_2 was determined by infrared spectroscopy (gas cell) using the calibrated absorption for the *meso* and *dl* isomers at 1183 and 838 cm^{-1}, respectively.

Isomerization of the Dichlorides with Cu(I) and Cu(II) Chlorides on Pumice.—The reactor containing cupric chloride on pumice was assembled as described earlier and heated to 320°. At this temperature, a feed comprising 2.11 mmol of ethylene/min and 7.18 mmol of nitrogen/min was passed through the reactor for 3 min. This reduced part of the cupric chloride so that both Cu(I) and Cu(II) chlorides were present. The system was purged with nitrogen for 30 min. A micro gas scrubbing bottle, containing 120 μl of the appropriate dichloride was connected between the nitrogen line and the reactor. Nitrogen was then passed through the scrubbing bottle at 9.29 mmol/min. The nitrogen, now containing dichloride vapor, passed through the reactor with the same contact time as the olefins described previously. The product was trapped in a Dry Ice–acetone bath and analyzed by gas chromatography or infrared spectroscopy in the usual way.

Rate of 1,2-Dichloroethane Formation from Ethylene and Cupric Chloride.—Ethylene was chlorinated by cupric chloride impregnated on pumice according to the procedures described earlier. Helium was introduced at the end of the reaction zone at 9.29 mmol/min. This diluted the product stream such that 1,2-dichloroethane remained in the vapor phase. The product was collected in gas-sampling bottles over one 2-min and two 3-min time intervals. The product was then analyzed by gas chromatography using calibrated response factors relative to nitrogen. Nitrogen is used as the internal standard because it is metered into the reactor at a known rate which does not change during the reaction. Therefore, the rate of product formation, the rate of ethylene consumption, and the material balance can be determine from the integrated band areas.

Rate of Chlorine Production from Cupric Chloride on Pumice.—The pumice to be used in this experiment was heated in air at 550° for 20 hr to oxidize any organic matter which might be present. It was then impregnated with cupric chloride in the usual way. It was then heated to 320 in the reactor described earlier in a stream of nitrogen (9.89 mmol/min). The effluent was directed into two gas scrubbers containing aqueous potassium iodide solution. This was done for three successive 2-hr runs. After each run, the liberated iodine was titrated with standard sodium thiosulfate solution. The rate of chlorine evolution was nearly constant (0.018 ± 0.001 mequiv/2 hr).

Registry No.—Cupric chloride, 7447-39-4; *trans*-ethylene-d_2, 1517-53-9; *cis*-2-butene, 590-18-1; *trans*-2-butene, 624-64-6; **1**, 16622-55-2; **2**, 16622-56-3.

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Synthesis and Hydrolysis Kinetics of Lincomycin Acetals

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A series of *para*-substituted O-benzylidene acetals at the 3,4 position of the antibiotic lincomycin was synthesized in search of an easily cleaved acetal. The hydrolysis reactions of these acetals follow pseudo-first-order kinetics and appear to follow the generally accepted mechanism for simple acetal hydrolysis. The pH-rate profile for the acetal containing a *p*-phenolic substituent indicates that the hydronium ion catalysis of the phenolate ion form as well as the phenol form of the derivative has to be considered. The second-order rate constants of hydrolysis for the series of arylidene derivatives at 70° gave a correlation coefficient of 0.996 in a modified Hammett σ^+ plot with a ρ value of -1.85. From this correlation a σ^+ value of -3 is estimated for the *p*-phenolic oxy anion. The use of arylidene derivatives as protective groups is discussed.

Benzylidene acetals of polyfunctional molecules are commonly used as protective groups.[1] In search of an easily cleaved acetal of lincomycin, the effect of substituents on the rate of hydrolysis of arylidene acetals was studied since Kreevoy and Taft[2] only quantitated the substituent effect for numerous aliphatic acetals and ketals. While the study was being completed, an article by Fife and Jao[3] was published in which the effect of substituents on the rates of hydrolysis of cyclic and acyclic arylidene acetals were found to give plots of log *k vs.* σ or σ^+ with curvature for *para*-substituted compounds. In the present study with *para*-substituted 3,4-O-benzylidene acetals of lincomycin, a correlation coefficient of 0.996 was obtained in a modified Hammett σ^+ plot. This type of correlation is useful in the selection of acetals to use as protective groups.

The antibiotic lincomycin proved to be an ideal molecule in which to study the effect of substituents on the rates of acetal hydrolysis, since acetals are easily formed with the *cis* hydroxyls on C_3 and C_4 of lincomycin (see Figure 1). In addition, the analytical problem was simplified by the lack of an intense uv chromophore in lincomycin. A range of hydrolysis rates is provided by the following substituents in the *para* position of 3,4-O-benzylidenelincomycin: chloro, hydrogen, methyl, methoxy, and hydroxyl.

Results

Synthesis and Structure Determination of the Lincomycin Acetals.—Acetals are commonly prepared by catalysis with strong acids, dehydrating agents ($ZnCl_2$, etc.), and in some cases with neutral amine salts of strong acids (NH_4Cl, etc.). Since lincomycin is somewhat unstable in strong acid media, acetal formation was attempted using lincomycin–HCl with excess aldehyde without any additional acid. Acetal formation was found to occur readily under these conditions in virtually quantitative yield when benzene was used to remove the water azeotropically.

The lincomycin acetals were initially isolated as the hydrochloride salts, but only the *p*-chloro-, -hydrogen-, and -methyl-substituted 3,4-O-benzylidene derivatives could be recrystallized as the hydrochloride salts. The less stable acetals, such as the 3,4-O-(*p*-hydroxybenzylidene) and the 3,4-O-anisylidene derivatives, decomposed rapidly on attempted recrystallization from hydroxylic solvents, yielding lincomycin–HCl. Recrystallization of the hydrochloride salts from nonhydroxylic solvents was difficult since the lincomycin acetals are very insoluble in most of these solvents. Consequently, the 3,4-O-anisylidene and 3,4-O-(*p*-

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