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Kinetics and Mechanism of the Epoxidation of Unsaturated Fatty Acids

A study was made of the epoxidation of octadecenoic acids with peroxybenzoic acid in benzene. Activation energies, frequency factors, enthalpies of activation, entropies of activation, and free energies of activation were obtained for the following fatty acids: *cis*-9-octadecenoic acid (oleic), *trans*-9-octadecenoic acid (elaidic), 12-hydroxy-*cis*-9-octadecenoic acid (ricinoleic), 12-hydroxy-*trans*-9-octadecenoic acid (ricinelaidic), *cis*-11-octadecenoic acid (vaccenic), and *cis*-6-octadecenoic acid (petroselinic). It was observed that the reaction rate was adversely affected by the proximity of the carboxyl group, that is, the closer the carboxyl to the reaction site the lower the rate. A shift from a *trans* to a *cis* configuration results in an approximate 50% increase in reaction rate with a corresponding decrease in free energy of activation of 260 cal/mol. The effects of isomerism and the replacement of substituent groups on the reaction rate were generally additive. A mechanism for the peroxydation of octadecenoic acids is proposed.

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SCOPE

Epoxidation is a controlled reaction of an unsaturated compound with a relatively mild oxidizing agent to give an epoxy (oxirane) compound. At the present time, the peracid most used commercially in epoxidation is peracetic acid. It is readily prepared from hydrogen peroxide and glacial acetic acid in the presence of a strong acid catalyst such as sulfuric acid.

While peracetic acid is the compound of choice commercially, it is difficult to use in making the type of fundamental studies reported here because it is unstable in its pure form. Its tendency to decompose makes analysis difficult. One cannot be sure whether the disappearance of the peracid in the course of the study is due to epoxidation or simple decomposition. As a result, due to its greater stability perbenzoic acid was chosen for this study. Perbenzoic acid has the additional advantages that it can be obtained as a pure compound with a minimum of hazard and tends to react more completely. Consequently, kinetic data and experiments undertaken to develop mechanistic information are much more accurate.

The empirical observations of numerous workers concerned with the epoxidation reaction since its discovery at the turn of the century have pointed out that under similar experimental conditions the rate of reaction of olefins with organic peracids is a function of the structure of the unsaturated compounds. Over the years many attempts were made to explain this behavior. D. Swern in 1947, 1948, and 1953 proposed several theories. In 1953 he suggested a mechanism in which the transition state would be similar to the so-called "pi complexes." In 1951 Badger proposed a molecular addition to one of the carbons adjacent to the double bond. In 1955 Lynch and Pausacker said the olefinic bond itself was attacked. Edward and Cohen in 1960 suggested an ionic or free radical mechanism for the decomposition of perbenzoic acid depending on media; while in 1962 and 1963 Tokumaru et al., proposed a free radical mechanism. Thus, the

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possibility that the free radical fragments of peracid present could attack the seat of unsaturation of the fatty acid must be considered.

An experimental program was undertaken to gain some insight into the mechanism of the epoxidation of unsaturated fatty acids and to develop kinetic data which would contribute to the primary goal. Specifically, C_{18} monounsaturated straight chain acids were epoxidized at temperatures from 11° through 39°C utilizing perbenzoic acid. In this temperature range, the reactants were fairly stable and the reaction proceeded at reasonable rates, thus permitting development of meaningful data for thermodynamic and kinetic equations. As a result rate constants, reaction orders, enthalpies and entropies of activation, free energies, etc. could be determined. These data can be expected to contribute to reactor and process equipment design.

The effect on reaction rate of structure of the unsaturated fatty acids, as well as of the reaction conditions such as temperature, acidity, polarity of solvent and ionic concentration was investigated, and a probable mechanism of the reaction is presented based on the results obtained.

CONCLUSIONS AND SIGNIFICANCE

In the epoxidation of octadecenoic acids, the following conclusions were reached in the study of the thermodynamic and kinetic data:

1. The reaction rate is adversely affected by the proximity of the carboxyl group.

2. The effect of the carboxyl group on the reaction site is negligible (within experimental error) past carbons nine and ten.

3. The shift from a *trans* to a *cis* configuration results in an approximate 50% increase in reaction rate in the temperature range studied.

4. The replacement of a substituent hydroxyl group with hydrogen results in an approximate 20% increase in rate in the temperature range studied.

5. The effects of isomerism and the removal of the substituent group on reaction rate were generally additive.

6. Entropy of activation increased by 0.8 entropy units in going from a *cis* to a *trans* configuration and by 0.3 entropy units when hydrogen was replaced by a hydroxyl group.

7. The free energy of activation increased by 260 cal/mol in going from the *cis* to the *trans* configuration and by 85 to 90 cal/mol with the replacement of a hydrogen with a hydroxyl group.

8. The free energies of activation for the reactions studied were approximately 10 to 12 k cal and the entropies of activation were approximately −20 e.u.

The order of reaction was studied in some detail to determine whether it was second order. The results at three separate temperatures indicate that within experimental error the reaction was precisely second order. It was considered to be first order in respect to each component. The mechanism proposed, which appears to meet and satisfy all the test conditions imposed on the reaction, is a concerted or molecular addition. In this proposal the reaction proceeds with the formation of an internally bonded nonionic complex as the transition state. The complex would not be affected by acidity, ionic concentrations, or free radical traps. On the other hand, any change in electron density caused by electron-withdrawing groups such as the carboxylic group would affect the reaction rate.

EXPERIMENTAL TECHNIQUES

Apparatus

The apparatus used for the measurements was a bath controlled to ± 0.03°C. The bath itself consisted of a glass vessel containing low viscosity (50 SUS) mineral oil in which the heaters, cooling coil, and the reaction flask were immersed. An auxiliary source of coolant was required for studies below room temperature.

The temperature controls were set using calibrated ASTM thermometers which were checked against a master thermometer each day.

Kinetic Measurements

The fatty acid olefin (ca 0.002 mole) was weighed into a 25 ml wide neck, screw capped volumetric flask. The flask was made up with purified, fractionated benzene (procedure described below) to within 0.5 in. of the calibration mark and capped. Five ml of a perbenzoic acid-benzene stock solution (0.0400 M) was pipetted into a second 25 ml wide neck, screw capped volumetric flask. It was similarly made up with the treated fractionated benzene to about 0.5 in. from the calibration mark and capped. These flasks, the reaction vessel, and a third flask containing an additional quantity of purified benzene, were placed in the thermostatic bath and allowed to equilibrate. When the reactants had reached the bath temperature the flasks were brought up to mark using the purified benzene from the third flask, which was also at the bath temperature. The reactants were then added to the equilibrated reaction vessel and a timer started. The reaction mixture was shaken vigorously to effect intimate mixing.

Five ml aliquots were then withdrawn at designated intervals by means of a volumetric pipette (held at approximately bath temperature) and rapidly transferred into a flask containing an agitated solution of potassium iodide and sulfuric acid. After continuously agitating with a magnetic stirrer for approximately 100 sec., the evolved iodine was titrated with 0.05 N potassium thiosulfate to measure the unreacted peracid. As a rule, six to seven samples were taken in the course of each experiment.

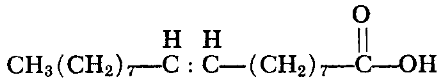
The fatty acids obtained from commercial sources were analyzed by vapor phase and thin film chromatography. The purity of each acid was determined to be better than 99.0%.

The benzene was purified by the method described by Vogel in his text published in 1962. The midcut of 500 ml, b.p. 80.2°C, was stored over sodium strips and used as required for the kinetic study.

DISCUSSION OF RESULTS

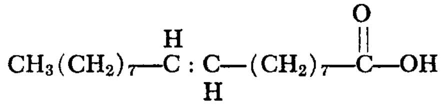
The temperatures chosen for this study represent a range that permitted reasonable reaction rates for all the compounds studied. The exact temperatures used were 11.3°, 23.4°, 30.8°, and 37.8°C, with the bath temperature capable of control within ± 0.03°C. The fatty acids studied in the course of this research were *cis*-9-octadecenoic acid, *trans*-9-octadecenoic acid, 12-hydroxy-*cis*-9-octadecenoic acid, 12-hydroxy-*trans*-9-octadecenoic acid, *cis*-11-octadecenoic acid, and *cis*-6-octadecenoic, which are commonly known as oleic, elaidic, ricinoleic, ricinelaidic, vaccenic, and petroselinic acids, respectively.

The formula for oleic acid (*cis* form) is



$$CH_3(CH_2)_7\overset{H}{C} : \overset{H}{C}(CH_2)_7\overset{O}{\overset{\|}{C}}OH$$

The formula for elaidic acid (*trans* form) is



$$CH_3(CH_2)_7\overset{H}{C} : \underset{H}{C}(CH_2)_7\overset{O}{\overset{\|}{C}}OH$$

Reaction Rates

The rate data obtained were plotted as $1/a$ versus time, with a being the concentration of reactant A at a given time t. A straight line resulted which indicated that the reaction was of second order, first order in each reactant. The slope of the straight line obtained is the reaction rate constant. The rate equation used for this study is derived from the integrated form developed by Arbuzow and Michailov in 1930.

$$\frac{1}{b-a}\ln\frac{a(b-x)}{b(a-x)} = kt \qquad (1)$$

Since we used equal initial concentrations, the left side of Equation (1) becomes indeterminate. However, this condition of equal initial concentration is equivalent mathematically to a second-order reaction of one reactant with a simplified equation, that is,

$$1/C - 1/C_0 = kt \qquad (2)$$

Generally, under experimental conditions, equal initial concentrations are not easily attained and under these circumstances Equation (1) would be determinate. As a result it is possible to develop the following relationship

$$1/(d-x) - 1/d + \frac{s^2}{3}\left(1/(d-x)^3 - 1/d^3\right) + \ldots\ldots = kt \qquad (3)$$

where s = 1/2 the difference in concentration of the reactants $= 1/2(a-b)$

d = average concentration of the reactants $= \dfrac{a+b}{2}$

x = decrease in concentration of one reactant

Comparing Equations (2) and (3), we see that the quantity

$$\frac{s^2}{3}\left(1/(d-x)^3 - 1/d^3\right)$$

represents an error term which was used to establish the permissible divergence in initial concentrations of the reactants. In the experiment with the widest divergence in initial concentrations, that is, oleic acid = 0.0391 and peracid = 0.0369 meq/ml, the error introduced was approximately 0.1%. In the ordinary course of this study, the error term was far less, being of the order of 0.01 to 0.05%. Figure 1 is a graph of kinetic data for the epoxidation of oleic acid at 11.3°, 23.4°, 30.8°, and 37.8°C, and is representative of the rate data obtained.

Table 1 summarizes typical rate constants obtained.

Effect of Isomerism and Substitution on Reaction Rate

A 2 × 2 statistical experiment comparing the effect of *cis* versus *trans* isomerism and the effect of the replacement of a hydrogen on the carbon in the 12-position with a hydroxyl group was conducted. Of the two factors considered isomerism had by far the greatest effect. For example, in moving from a *trans* to a *cis* configuration an approximate 50% increase in reaction rate was obtained. The replacement of the hydroxyl group with hydrogen resulted in an approximate 10 to 20% increase in rate. The effect of the isomerism and the hydroxyl group was generally additive as the rate increased by 75 to 80% in the case of oleic as compared to ricinelaidic acid.

The data on the *cis-trans* relationship would permit a projection of reaction rates for other octadecenoic acids where either the *cis* or *trans* rate data is known and some estimate of the others is required.

Effect of Proximity of Carboxyl Group to Double Bond on Reaction Rate

Some effort was made to gain an insight into the contribution of the substituent effect of the carboxyl group on the reactivity of the double bond. The carboxyl group has a tendency to withdraw electrons from the neighboring atoms, reducing the activity of the double bond and, as a consequence, reducing the rate of epoxidation of the olefinic structure. The overall effect would be enhanced as the distance between the carboxyl group and the double bond was reduced. These previously developed deductions were, in fact, confirmed in our experimental work. Table 3 shows the effect on reaction rates as the spacing between the carboxyl group and the bond is varied. The spacing is assumed proportional to the number of carbon atoms between the groups.

The increasing reactivity with increase in distance be-

TABLE 1. SUMMARY OF REPRESENTATIVE EMPIRICAL RATE CONSTANTS* FOR THE EPOXIDATION OF OCTADECENOIC ACIDS BY PERBENZOIC ACID AS DETERMINED BY THE EQUATION $1/C - 1/C_0 = kt$

	Temperature, °C			
Fatty acid	11.3	23.4	30.8	37.8
Oleic	0.542	1.28	2.06	3.30
Elaidic	0.352	0.830	1.34	2.14
Ricinoleic	0.441	1.18	1.81	—
Ricinelaidic	0.312	0.739	1.10	1.74
Petroselinic	0.457	0.969	1.56	—
Vaccenic	0.617	1.34	2.01	3.13
70/30 Oleiclinoleic	0.533	1.27	1.70	—

* liters/mol-min.

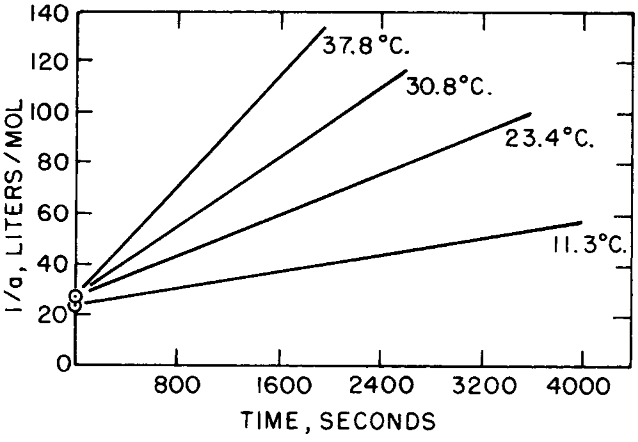


Fig. 1. Graph of kinetic data for the epoxidation of oleic acid with perbenzoic acid in benzene.

TABLE 2. EMPIRICAL REACTION RATE CONSTANTS* COMPARING CIS VERSUS TRANS ISOMERISM AND REPLACEMENT OF HYDROGEN WITH A HYDROXYL GROUP AT 23.4°C

	cis	trans
R—H	1.28	0.830
R—OH	1.18	0.74

* l/mol-min.

TABLE 3. EFFECT OF PROXIMITY OF CARBOXYL GROUP TO DOUBLE BOND ON EPOXIDATION REACTION RATE

Distance from carboxyl group	*Reaction rate, 30.8 °C
One carbon (Δ α oleic)	0.01
Six carbon (Petroselinic)	1.56
Nine carbon (Oleic)	2.06

* k = l/mol-min.

tween the carboxyl group and the double bond is obvious. Additional data were obtained with vaccenic acid which has the double bond 11 carbons from the carboxyl group. Although theoretically the reaction rate should have increased over that of oleic, the differences were so slight as to be within experimental error. We may conclude that the effect of the carboxyl group on the reactivity of the double bond is not significant beyond a distance of nine carbons.

Effect of Acid on the Reaction Rate

In order to determine the effect of acid on the reaction rate, an equimolar concentration 0.002 M of benzoic acid was added to the reaction mixture. The presence of this acid, chosen because it did not interact with either reactants or products, did not change the rate constants significantly. This conclusion is consistent with the general adherence to the second-order law observed in all cases and indicates that the corresponding benzoic acid formed as a reaction product does not affect the rate.

Effects of Polar Solvent and/or Salts on the Reaction Rate

If the reaction under study was ionic and the ionization of the perbenzoic acid was the rate determining step, the addition of a polar solvent such as ethyl ether and/or a salt such as magnesium perchlorate would enhance the reaction. To evaluate this premise the reactants were added to ethyl ether at 30.8°C. Subsequently, the reaction in ethyl ether was run with the addition of magnesium perchlorate. The presence of the polar solvent alone or with the salt did not increase the reaction rate.

Variation of Rate Constants With Temperature

The rate constants were correlated with temperature using the Arrhenius equation

$$k = Ae^{-E/RT}$$

Empirical constants for the Arrhenius equation obtained from the data using standard statistical regression techniques, are summarized in Table 4.

Thermodynamic Properties for the Epoxidation of Unsaturated Fatty Acid by Perbenzoic Acid

The thermodynamic properties were obtained from the variation of ln k with $1/T$. Activation energy and frequency factors were obtained directly. The enthalpy of activation was calculated from the relationship

$$\Delta H^* = E_c - RT$$

while the enthropy of activation was calculated from the frequency factor A by means of the equation

$$A = e(k_B T/h)e^{\Delta S/R}$$

The free energy of activation could then be obtained by

$$\Delta F^* = \Delta H^* - T\Delta S^*$$

Thermodynamic properties obtained in this study are summarized in Table 5.

In general, the entropy of activation increased by 0.8 entropy units in going from the *cis* to the *trans* configuration and by 0.3 entropy units when hydrogen was replaced by an hydroxyl group.

The free energy of activation increased in a consistent manner as the reaction encountered more difficulty in proceeding. Oleic and vaccenic acids had the lowest free energy. This is consistent as the double bond in these compounds compared to the other acids is more remote from the carboxylic group. Consequently, the latter had little effect on the reaction. Theoretically, one would expect that the free energy of vaccenic acid be lower than oleic acid. The difference, however, appears to be small enough to be obscured by the experimental error.

The free energy of activation increased by 260 cal/mol in going from the *cis* to the *trans* configuration and by 85-90 cal/mol with the replacement of a hydrogen by a hydroxyl group on the twelfth carbon.

Proposed Mechanism—Concerted or Molecular Addition

Results of the experiments designed to test the validity of a free radical mechanism on one hand or an ionic one on the other hand tended to discount each one. A free radical mechanism was discounted because the reaction under study was stereospecific. The ionic reaction was suspect since the reaction did not demonstrate an increase in rate as the ionic strength of the reaction medium was increased.

Being unable to confirm either a homolytic or heterolytic mechanism in this study, it was necessary to investigate other possibilities. In the peracid oxidation of phenyl hydrazones (Pausacker and Lynch in 1954), stilbenes (Lynch and Pausacker in 1955), and alkyl sulfides (Overberger

TABLE 4. EMPIRICAL ARRHENIUS EQUATIONS FOR THE EPOXIDATION OF FATTY ACIDS WITH PERBENZOIC ACID IN BENZENE

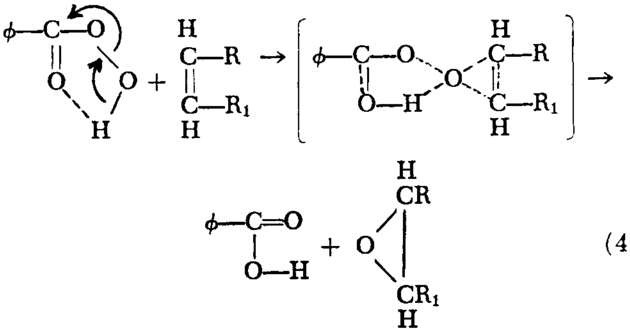
Oleic acid	$\ln k = 20.561 - 6013/T$
Vaccenic acid	$\ln k = 19.799 - 5786/T$
Ricinoleic acid	$\ln k = 20.420 - 6013/T$
Petroselinic acid	$\ln k = 20.377 - 6032/T$
Elaidic acid	$\ln k = 20.136 - 6013/T$
Ricinelaidic acid	$\ln k = 19.981 - 6013/T$

TABLE 5. SUMMARY OF THERMODYNAMIC PROPERTIES

Acid	ln A	$-\Delta S$ cal/mol-deg, 30.8°	E_c, k cal/mol	ΔH^*, k cal/mol	ΔF^*, k cal/mol
Oleic	20.561	19.713	11947.8	11344.0	17334.8
Vaccenic	17.799	21.227	11497.3	10893.5	17344.4
Ricinoleic	20.420	19.993	11947.8	11344.0	17419.9
Petroselinic	20.337	20.079	11985.7	11381.9	17483.9
Elaidic	20.136	20.558	11947.8	11344.0	17591.6
Ricinelaidic	19.981	20.865	11947.8	11344.0	17684.9

and Cummins in 1953), the authors in each case suggested some sort of a molecular mechanism. This mechanism, adapted to the reaction under study, can be represented by scheme (4):

Concerted or Molecular Addition

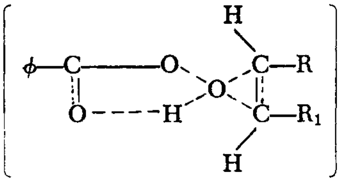

(4)

The reaction represented by (4) proceeds with the formation of a type of pi-complex as a transition state.

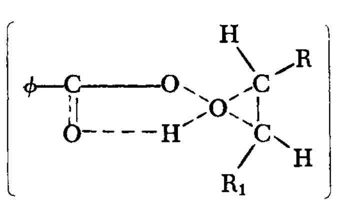
Now if this is true and if the transition state in the perbenzoic acid epoxidation of olefinic fatty acids consists of an internally bonded nonionic structure, an increase in the ionic strength of the reaction medium by the addition of salt, that is, magnesium perchlorate, should not affect the reaction rate and, in fact, did not.

Behavior of this reaction with respect to solvent polarity as well as the presence of the salt is similar to that observed in peracid oxidation of phenylhydrazones, stilbenes, and alkyl sulfides mentioned earlier.

Additional information was obtained by comparison of the reaction rates of *cis* and *trans* isomers. It can be used as a supporting evidence for the character of the transition state in (4). The rates of epoxidation of the *cis* isomers, oleic and ricinoleic acids, were found to be approximately 50% larger than those of their respective *trans* isomers, elaidic and ricinelaidic acids, for example, Table 1. For steric reasons, the transition complex in (4)



would be formed much more readily in case of the *cis* isomers and with comparatively little interference on the part of small H atoms than in the case of *trans* isomers



where a bulky R_1 (or R) group may inhibit or render difficult the approach of the peracid to the double bond of the olefin.

It should be pointed out that the adoption of scheme (4) as a true representation of the process does not interfere with Swern's original idea that perbenzoic acid's oxygen is of essentially electrophilic character and therefore attracted to the center of high electron density—in this case, the double bond. This has been previously substantiated by the effect of the proximity of the carboxylic acid group to the double bond. It can be further evidenced by the substitution of hydrogen in the beta position to the double bond by the electronegative (electron-attracting) hydroxyl group (Pauling in 1940) which decreases the electron density of that double bond by means of the induction process. The nucleophilic character of the reaction center being diminished is reflected in lowered reaction rates with hydroxylated acids, that is, ricinoleic and ricinelaidic acids.

From all of the above, we may conclude that the scheme illustrated confronts and satisfies the test conditions imposed on the reaction. Consequently, we propose that the mechanism is a concerted or molecular addition which proceeds with the formation of an internally bonded, nonionic complex as the transition state.

NOTATION

A = frequency factor, Arrhenius equation
a = concentration of reactant a, meq/ml
b = concentration of reactant b, meq/ml
C = concentration of single reactant, meq/ml
d = average concentration of the reactants = $a + b/2$, meq/ml
E = energy of activation, cal/gmol
F = free energy, cal/gmol
H = enthalpy, cal/gmol
h = Planck's constant, 6.624×10^{-27} erg-sec.
k_B = Boltzmann's constant = 1.380×10^{-16} erg/°T
k = rate constant, 1/mol-min
R = universal gas constant, 82.06 ml-atm/gmol-°K
S = entropy, cal/mol-deg
s = one half the difference in concentration of the reactants = $\frac{1}{2}(a - b)$ meq/ml
T = temperature, °K
t = time, min
X = decrease in concentration of one reactant, meq/ml
$_0$ = initial condition
$_c$ = concentration units
* = activation condition

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