THE PEROXIDE EFFECT IN THE ADDITION OF REAGENTS TO UNSATURATED COMPOUNDS AND IN REARRANGEMENT REACTIONS

FRANK R. MAYO AND CHEVES WALLING[1]

George Herbert Jones Laboratory, University of Chicago, Chicago, Illinois

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I. INTRODUCTION

The fact that oxygen and peroxides affect the direction of addition of hydrogen bromide to allyl bromide was discovered in 1931 (53). Subse-

[1] Present address: E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

quent work has demonstrated that the same agents also determine the direction of addition of various addenda to a large number of other ethylene derivatives. Because of the many papers concerned with such phenomena and the variety of interpretations offered, a critical review of the experimental work and theoretical conclusions seems desirable. Recently, J. C. Smith (139, 140, 141) has reviewed the field fully, but from a different viewpoint.

This review is based on the premise that several types of substitution and addition can proceed in solution by at least two mechanisms: a chain reaction involving free radicals and occasionally atoms, and an ionic (or molecular) reaction. The chain hypothesis has shown that several apparently different types of reaction are actually closely related, and has led to the discovery of new syntheses. Although, in most instances, details of the ionic or molecular mechanism are not yet clear, the data available permit prediction of the products of many reactions.

This review will be concerned with the addition of hydrogen bromide, mercaptans, and bisulfites to unsaturated compounds, and with certain rearrangements. The discussion will refer almost entirely to liquid-phase reactions. The important effects of oxygen and peroxides on the bromination and chlorination of hydrocarbons, acids, acid halides, and ketones, on chlorinations with sulfuryl chloride, and on carboxylation reactions will be omitted because rapid development of these fields has just begun.

II. The Addition of Halogen Acids to Unsaturated Compounds

A. NORMAL AND ABNORMAL ADDITIONS OF HALOGEN ACIDS

1. Status of the subject in 1930

Previous to 1930, many hypotheses were current regarding the factors which controlled the direction of addition of unsymmetrical reagents to ethylene derivatives. Particular confusion existed with respect to some addition reactions which could be used to help in deciding between conflicting hypotheses. It was with the hope of reconciling some of the discordant data that an intensive investigation of the addition of halogen acids to unsymmetrically substituted ethylenes was undertaken in this laboratory.

The addition of hydrogen bromide to allyl bromide seemed of particular interest, as various workers had reported addition products ranging from nearly pure 1,2-dibromopropane to nearly pure 1,3-dibromopropane, even under supposedly identical experimental conditions. These investigators ascribed the discrepancies to variations in the temperature, the reaction time, or the concentration of hydrogen bromide, and to the presence of water or light (for references, see 53). Other factors which have been

thought to direct the addition of a halogen acid to an alkene are solvents (46, 114, 117), their dielectric constants or internal pressures (44), magnetic fields (17), and previous treatment of the alkene (for references on the electromer controversy, see 77). In the vapor-phase reaction, surfaces and metal halides (15, 163, 164), oxidizing atmospheres (11), and light (10) have also been supposed to play a rôle.

It is noteworthy that most of the work on the addition of halogen acids has been carried out with hydrogen bromide, since hydrogen chloride often adds too slowly and hydrogen iodide frequently gives unstable addition products. This choice is unfortunate, because hydrogen bromide is the only halogen acid whose direction of addition to alkenes is affected by air and peroxides, and therefore the only one which can give results of doubtful significance. The following discussion will show the extent of this peroxide effect with hydrogen bromide and the absence of this effect with hydrogen chloride and hydrogen iodide.

2. The peroxide effect

The peroxide effect was discovered during an investigation of the addition of hydrogen bromide to allyl bromide (53). When these substances are allowed to react at room temperature in the dark, the reaction may take either one of two courses:

$$\mathrm{CH_2{=}CHCH_2Br} + \mathrm{HBr} \begin{cases} \nearrow \mathrm{CH_3CHBrCH_2Br} & (1) \\ \searrow \mathrm{CH_2BrCH_2CH_2Br} & (2) \end{cases}$$

If the reactants are pure and freshly prepared, and if oxygen is excluded from the reaction vessel, reaction 1 takes place exclusively[2] and several days are required for substantially complete reaction. If the reaction occurs in the presence of small quantities of oxygen or if peroxides are introduced either deliberately or by use of old allyl bromide, then reaction 2 takes place almost quantitatively in a few hours. As reaction 1 is that which takes place with pure reagents in the absence of catalysts, it has been termed the *normal reaction;* reaction 2 is *abnormal.* Such a reversal of addition has been called a "peroxide effect", and it has been observed in additions of hydrogen bromide to many ethylene derivatives. In order to show that the normal and abnormal reactions take place by different mechanisms, the characteristics of the normal addition reaction will be discussed before the abnormal reaction is taken up in detail.

[2] Slight corrections (87) to the original work (53) justify this statement.

3. The normal addition of halogen acids

The normal product of the addition of hydrogen bromide to an alkene is uniquely and conveniently defined in terms of the addition of hydrogen chloride and hydrogen iodide, since these halogen acids are not susceptible to a peroxide effect and never add abnormally in the liquid phase. The addition of hydrogen chloride or hydrogen iodide and the normal addition of hydrogen bromide to an alkene or a halogenated alkene usually give a single product, the one which would be predicted from Markovnikov's rule (109). That is to say, the halogen of the halogen acid always becomes attached to the least hydrogenated of the two doubly bound carbon atoms. The product thus obtained is apparently the thermodynamically more stable one of the two possibilities (20).[3] The hydrogen chloride and hydrogen iodide additions in tables 1 and 2 have been carried out since the discovery of the peroxide effect. In many instances antioxidants or peroxides have been employed, or else the reaction has been carried out in a solvent with the object of altering the composition of the addition product. The addition of hydrogen chloride to propene has also been carried out in quartz apparatus in the presence of ultraviolet light (94). With three exceptions, each of these additions yields only one addition product. One exception is 1-bromopropene, which with both hydrogen chloride and hydrogen iodide gives a mixture made up of one-third 1,1-dihalide and two-thirds 1,2-dihalide, thus supplying convincing evidence that (within the limits of experimental error) these two halogen acids always add in the same way. Another mixture is that obtained by the action of hydrogen chloride on 2-pentene. As will be shown in table 4, hydrogen bromide behaves similarly to 1,2-dialkylethylenes. The third example of a mixture is the addition of hydrogen chloride to 1,3-butadiene, resulting in 75 to 80 per cent of the 1,2-addition product and 20 to 25 per cent of the 1,4-addition product. This proportion is not affected by temperature over the range $-78°$ to 25°C. or by the presence of acetic acid. An earlier compilation (52) showed that in general the addition of hydrogen chloride or hydrogen iodide to alkenes has been reported to give only one addition product. Michael and Leighton (115) claim to have obtained a small proportion of *n*-propyl iodide by the addition of hydrogen iodide to

[3] These statements do not hold for temperatures above 200°C. Isopropyl and propyl bromides isomerize in the liquid phase at 250–275°C. to equilibrium mixtures containing about 30 per cent of primary halide (15); isobutyl and tertiary butyl bromides are known to behave similarly. The vapor-phase addition of hydrogen chloride to isobutene (2-methylpropene) at 270°C. gives an addition product containing mostly *tert*-butyl chloride but also about 8 per cent of isobutyl chloride (112). Thus a portion of the product obtained by the addition of a halogen acid at high temperature disagrees with Markovnikov's rule. The nature of such reactions is now under investigation in this laboratory.

propene, and Ingold and Ramsden (44) claim to have obtained up to 24 per cent of primary iodide by carrying out this reaction in certain solvents. In this laboratory, repeated attempts (84) to confirm these claims have failed. It has been found that peroxides accelerate the rate of addition of hydrogen iodide (62, 84), but this effect is explained by the fact that

TABLE 1

The addition of hydrogen chloride to unsaturated compounds

UNSATURATED COMPOUND	FORMULA	ADDITION PRODUCT	REFERENCES
Vinyl chloride	$CH_2=CHCl$	CH_3CHCl_2	(57, 83)
Trichloroethylene	$CCl_2=CHCl$	CCl_3CH_2Cl	(74)
Propene	$CH_3CH=CH_2$	$CH_3CHClCH_3$	(15, 83, 94)
1-Bromopropene	$CH_3CH=CHBr$	$CH_3CH_2CHBrCl$ (35%) $CH_3CHClCH_2Br$ (65%)	(70, 83)
2-Bromopropene	$CH_3CBr=CH_2$	$CH_3CBrClCH_3$	(83)
1-Chloropropene	$CH_3CH=CHCl$	$CH_3CH_2CHCl_2$	(70, 83)
2-Chloropropene	$CH_3CCl=CH_2$	$CH_3CCl_2CH_3$	(83)
Allyl chloride	$CH_2ClCH=CH_2$	$CH_2ClCHClCH_3$	(83)
Isobutylene	$(CH_3)_2C=CH_2$	$(CH_3)_3CCl$	(83, 129)
2-Pentene	$CH_3CH_2CH=CHCH_3$	$CH_3CH_2CHClCH_2CH_3$ (50%) $CH_3CH_2CH_2CHClCH_3$ (50%)	(77)
Trimethylethylene	$(CH_3)_2C=CHCH_3$	$(CH_3)_2CClCH_2CH_3$	(117)
Δ^2-Pentenoic acid	$CH_3CH_2CH=CHCOOH$	$CH_3CH_2CHClCH_2COOH$	(131)
Δ^3-Pentenoic acid	$CH_3CH=CHCH_2COOH$	$CH_3CHClCH_2CH_2COOH$	(131)
Δ^4-Pentenoic acid	$CH_2=CHCH_2CH_2COOH$	$CH_3CHClCH_2CH_2COOH$	(131)
Δ^{10}-Undecenoic acid	$CH_2=CH(CH_2)_8COOH$	$CH_3CHCl(CH_2)_8COOH$	(1)
1,3-Butadiene	$CH_2=CHCH=CH_2$	$CH_3CHClCH=CH_2$ (75–80%) $CH_3CH=CHCH_2Cl$ (20–25%)	(71)
1-Hexyne	$CH\equiv C(CH_2)_3CH_3$	$CH_2=CCl(CH_2)_3CH_3$	(36)
2-Chloro-1-hexene	$CH_2=CCl(CH_2)_3CH_3$	$CH_3CCl_2(CH_2)_3CH_3$	(36)

peroxides liberate iodine from hydrogen iodide and that iodine is a catalyst for the normal addition of hydrogen iodide.

Because it has sometimes been difficult to eliminate completely the abnormal addition of hydrogen bromide, the use of hydrogen chloride or hydrogen iodide as standards for the normal addition has been found convenient and reliable in doubtful cases (83). The normal addition products of many alkenes are listed in table 3.

Present indications are that the addition of hydrogen fluoride to alkenes

also follows Markovnikov's rule (32, 102, 143). It will be indicated later that a peroxide effect with this reagent is very unlikely.

The available data justify only the following general statements as to the relation between the rate of the normal addition and the structure of the alkene. In the case of any one alkene, hydrogen chloride adds more slowly than hydrogen bromide, and the latter usually adds more slowly than hydrogen iodide. In the normal addition of hydrogen bromide (on which the most information is available), substitution of the ethylene hydrogens by alkyl or phenyl groups increases the rate of addition, whereas substitution by halogen retards the addition. Even substitution of hydrogen on an adjacent carbon atom by halogen retards addition. Some data to illustrate these statements appear in table 5.

TABLE 2

The addition of hydrogen iodide to unsaturated compounds

UNSATURATED COMPOUND	FORMULA	ADDITION PRODUCT	REFERENCES
Vinyl chloride	$CH_2{=}CHCl$	CH_3CHICl	(57)
Propene	$CH_3CH{=}CH_2$	CH_3CHICH_3	(62, 84)
1-Bromopropene	$CH_3CH{=}CHBr$	CH_3CHICH_2Br (64%) CH_3CH_2CHIBr (36%)	(84)
Allyl bromide	$CH_2{=}CHCH_2Br$	CH_3CHICH_2Br	(62, 84)
Allyl chloride	$CH_2{=}CHCH_2Cl$	CH_3CHICH_2Cl	(84)
1-Butene	$CH_2{=}CHCH_2CH_3$	$CH_3CHICH_2CH_3$	(62)
Trimethylethylene	$(CH_3)_2C{=}CHCH_3$	$(CH_3)_2CICH_2CH_3$	(117)
4,4-Dimethyl-1-pentene	$(CH_3)_3CCH_2CH{=}CH_2$	$(CH_3)_3CCH_2CHICH_3$	(62)
Undecenoic acid	$CH_2{=}CH(CH_2)_8COOH$	$CH_3CHI(CH_2)_8COOH$	(1)
β-Iodocrotonic acid	$CH_3CI{=}CHCOOH$	$CH_3CI_2CH_2COOH$	(110)
Tetrolic acid	$CH_3C{\equiv}CCOOH$	$CH_3CI{=}CHCOOH$	(110)

Since a large portion of this review will be concerned with the mechanism of the abnormal addition of hydrogen bromide, it seems appropriate to discuss first the mechanism of normal addition. Maass and his associates have investigated the reaction of hydrogen bromide with propene and of hydrogen chloride with propene and the butenes in the absence of solvents. They find that those alkenes which (as indicated by the melting-point curves of mixtures) form 1:1 complexes with halogen acids at low temperatures react around room temperature to give addition products more easily than those which do not form complexes, that the addition is complicated by a dimerization reaction so that rate equations could not be established, and that excess halogen acid is more effective than excess alkene in accelerating the addition (19, 106, 107). No electrical conductance could be ob-

served in these mixtures, and it was found that hydrogen chloride accelerated the addition of hydrogen bromide (106). The rate of addition of hydrogen chloride to propene increases with temperature from about −80° to +45°C. Between 45°C. and the critical temperature of the mixture (70°C.), the reaction has a negative temperature coefficient which Holder and Maass (39) have ascribed to loss of orientation or "structure" in the liquid. These liquid-phase reactions, as well as the normal addition of hydrogen bromide to allyl bromide (53), are mostly or entirely homogeneous. Above the critical temperature, at high pressure, the hydrogen chloride–propene reaction is very slow, and has a positive temperature coefficient (39). The vapor-phase additions of halogen acids to alkenes are heterogeneous, bimolecular reactions (19, 39, 99), accelerated by metal halides (15, 163). Equilibria and activation energies have been reported in a few instances (48, 99).

Kinetic investigations of the addition of halogen acids to alkenes (113, 122) in inert solvents indicate that the reaction is largely, if not entirely, of an order higher than the second. Consequently, inert solvents greatly reduce the rate of addition. That the rates are lower in ether and in dioxane than in hydrocarbon solvents is apparently a consequence of combination of the halogen acid with the solvent (122). Among oxygen-free solvents, the rate of addition increases in approximately the same order as the dielectric constants of the solvents, but in the presence of water or carboxylic acids, the reaction may be faster than in the absence of a diluent (53).

The existing data, inadequate as they are, nevertheless indicate that the conventional mechanism of normal addition, as described by Robinson (128) and Ingold (43), is an oversimplification. According to this mechanism, the proton of the halogen acid (with or without ionization) becomes attached to one of the doubly bound carbon atoms, leaving the other as a positive carbonium ion which subsequently reacts with the halide ion. Ogg (123) has pointed out that such a positive ion would be configurationally unstable and therefore inconsistent with known *trans* additions of halogen acids to some ethylene bonds. He suggests that the negative halide ion adds first to give a configurationally stable negative carbonium ion which later adds a proton. Neither mechanism is satisfactory under conditions where the reaction is of higher than the second order. Sherman, Quimby, and Sutherland (134) have discussed both a non-ionic bimolecular mechanism and a chain mechanism for the normal addition in the vapor-phase or in inert solvents. The chain mechanism is that to be described in section II, B, 5 for the abnormal reaction; reasons for rejecting it as a normal mechanism will subsequently become clear. No homogeneous bimolecular addition has yet been observed in the vapor phase,

but the possibility of such a reaction cannot yet be wholly excluded for the liquid phase.

Urushibara and Sinamura (151) have suggested a different chain mechanism for the normal addition of hydrogen bromide:

$$RCH{=}CH_2 + H^\bullet \rightarrow R\dot{C}HCH_3 \quad (3)$$

$$R\dot{C}HCH_3 + HBr \rightarrow RCHBrCH_3 + H^\bullet \quad (4)$$

Aside from the fact that this chain lacks any experimental support, it must be discarded on thermodynamic grounds. As has been mentioned elsewhere (87), reaction 4 is endothermic by about 35 kg-cal., an impossible condition for a step in a rapid chain reaction.

An explanation which seems to eliminate all of the above difficulties is that the reaction occurs, not simply between halogen acid and alkene, but between halogen acid and a halogen acid–alkene complex[4] which may contain a hydrogen bond. Such a mechanism explains why the rate depends more upon the halogen acid than upon the alkene concentration (19, 39, 106). Because the complex would be expected to be less stable at higher temperatures, the negative temperature coefficients observed in some instances (39, 111) can be accounted for. The increased reaction velocity in hydroxylic and carboxylic solvents may be due to the fact that reaction is easier when either the complex or the halogen acid is ionized.

The effects of catalysts are consistent with this idea of the mechanism of normal addition. Anhydrous ferric and aluminum chlorides are the most powerful known accelerators for the addition of hydrogen chloride and hydrogen bromide, and are particularly useful with those alkenes which otherwise react very slowly. Tests have shown that these catalysts affect only the rate and not the product of addition; in their presence only the normal addition product is obtained (83).[5] Zinc, thallous, cobaltous, and ferrous halides are moderate accelerators of the addition of hydrogen bromide to allyl bromide; cadmium, lead, stannous, cuprous, and nickelous

[4] Coffin, Sutherland, and Maass (18a) have previously considered this and other possibilities, but have rejected them in favor of the hypothesis that reaction takes place between two molecules of complex. They consider that the latter explanation best interprets the retardation of some additions by excess alkene. This possibility must still be admitted, but in view of the fact that the authors mentioned used no solvents and could obtain no rate constants, the simpler mechanism seems preferable for the present, since it has some support from additions in solvents (113).

[5] An anomalous case is reported by Schjånberg (131), who considers that ferric chloride is a negative catalyst for the addition of hydrogen chloride to the three isomeric straight-chain pentenoic acids. That this is not a general rule for acids is shown by the fact that normal addition to Δ^{10}-undecenoic acid is accelerated by ferric chloride (139). Further work may clarify this question.

bromides (87) and platinum black (152) are weak accelerators of the same reaction. There has been little need to accelerate the addition of hydrogen iodide to alkenes, but mercuric iodide and free iodine have been found effective (84). *tert*-Butyl isocyanide accelerates the addition of hydrogen bromide to allyl bromide (53), vinyl bromide (54), and vinyl chloride (57). This effect is probably due to the formation of some kind of an ammonium salt by the reaction of the isocyanide with hydrogen bromide, since dimethylammonium bromide and tetraethylammonium bromide have been found to accelerate the addition of hydrogen bromide to allyl bromide (112). These various catalysts may alter the uncatalyzed mechanism in several ways. The metal halide (or iodine) may replace one molecule of halogen acid in the halogen acid–alkene complex; or by combining with the halogen acid, it may activate the proton so that the latter more easily forms complexes with alkenes. Whatever complex is formed, the activity of substituted ammonium halides suggests that the alkene complex may react with the halide ion of a salt more easily than with a halogen acid.

B. THE PEROXIDE EFFECT IN THE ADDITION OF HYDROGEN BROMIDE

1. Products of addition

Table 3 lists those ethylene and acetylene derivatives for which the direction of addition of hydrogen bromide is known to be affected by oxygen or peroxides. In many instances, both products indicated have been obtained in a pure condition. In the others, more or less difficulty has been encountered in completely suppressing one of the competing additions, and mixtures have been obtained, their composition depending on the experimental conditions. In the whole of table 3, there is only one instance where it is well established that the normal addition product is a mixture: 1-bromopropene gives about one-third 1,1-dihalide and two-thirds 1,2-dihalide, a result already indicated for the additions of hydrogen chloride and hydrogen iodide. In the presence of peroxides, hydrogen bromide adds to give 1,2-dibromopropane exclusively.

Table 3 shows that peroxides alter the direction of addition of hydrogen bromide to unsaturated hydrocarbons, halides, acids, and esters. Five examples indicate that the effect apparently applies to acetylene as well as to ethylene derivatives. In most of the compounds cited, the double bond is at the end of the carbon chain, but recent work with trimethylethylene, 2-bromo-2-butene, and 2-methyl-2-nonadecene shows that the effect is not confined to terminal double bonds.

Table 4 lists alkenes for which it has not yet been possible to reverse the addition of hydrogen bromide. This table refers only to studies carried out since the discovery of the peroxide effect, where attempts have been made to obtain more than one product. There is some uncertainty about

TABLE 3

The peroxide effect in the direction of addition of hydrogen bromide

UNSATURATED COMPOUND	NORMAL PRODUCT	ABNORMAL PRODUCT	REFERENCES
Vinyl bromide, CH_2=$CHBr$	CH_3CHBr_2	CH_2BrCH_2Br	(54)
Vinyl chloride, CH_2=$CHCl$	$CH_3CHClBr$	CH_2BrCH_2Cl	(57)
Trichloroethylene, CCl_2=$CHCl$	CCl_2BrCH_2Cl	$CHCl_2CHClBr$	(74)
Propene, CH_2=$CHCH_3$	$CH_3CHBrCH_3$	$CH_2BrCH_2CH_3$	(15, 55, 60)
1-Chloropropene, $CHCl$=$CHCH_3$	$CHClBrCH_2CH_3$	$CH_2ClCHBrCH_3$	(70, 83)
2-Chloropropene, CH_2=$CClCH_3$	$CH_3CClBrCH_3$	$CH_2BrCHClCH_3$	(70)
Allyl chloride, CH_2=$CHCH_2Cl$	$CH_3CHBrCH_2Cl$	$CH_2BrCH_2CH_2Cl$	(133)
1-Bromopropene, $CHBr$=$CHCH_3$	$CH_2BrCHBrCH_3$ (65%) $CHBr_2CH_2CH_3$ (35%)	$CH_2BrCHBrCH_3$	(70, 83)
2-Bromopropene, CH_2=$CBrCH_3$	$CH_3CBr_2CH_3$	$CH_2BrCHBrCH_3$	(70, 83)
Allyl bromide, CH_2=$CHCH_2Br$	$CH_3CHBrCH_2Br$	$CH_2BrCH_2CH_2Br$	(53, 87, 151, 152, 154, 155)
1-Butene, CH_2=$CHCH_2CH_3$	$CH_3CHBrCH_2CH_3$	$CH_2BrCH_2CH_2CH_3$	(58)
3-Bromo-1-butene, CH_2=$CHCHBrCH_3$	$CH_3CHBrCHBrCH_3$	$CH_2BrCH_2CHBrCH_3$	(66)
2-Bromo-2-butene, CH_3CBr=$CHCH_3$	$CH_3CBr_2CH_2CH_3$	$CH_3CHBrCHBrCH_3$	(161)
Isobutylene, $(CH_3)_2C$=CH_2	$(CH_3)_3CBr$	$(CH_3)_2CHCH_2Br$	(59, 65)
1-Pentene, CH_2=$CH(CH_2)_2CH_3$	$CH_3CHBr(CH_2)_2CH_3$	$CH_2Br(CH_2)_3CH_3$	(61)
Trimethylethylene, $(CH_3)_2C$=$CHCH_3$	$(CH_3)_2CBrC_2H_5$	$(CH_3)_2CHCHBrCH_3$	(117, 162)
2-Bromo-1-hexene, CH_2=$CBr(CH_2)_3CH_3$	$CH_3CBr_2(CH_2)_3CH_3$	$CH_2BrCHBr(CH_2)_3CH_3$	(168)
4,4-Dimethyl-1-pentene, CH_2=$CHCH_2C(CH_3)_3$	$CH_3CHBrCH_2C(CH_3)_3$	$CH_2Br(CH_2)_2C(CH_3)_3$	(56)
1-Nonene, CH_2=$CH(CH_2)_6CH_3$	$CH_3CHBr(CH_2)_6CH_3$	$CH_2Br(CH_2)_7CH_3$	(69, 101)
1-Undecene, CH_2=$CH(CH_2)_8CH_3$	$CH_3CHBr(CH_2)_8CH_3$	$CH_2Br(CH_2)_9CH_3$	(69, 101)
1-Tridecene, CH_2=$CH(CH_2)_{10}CH_3$	$CH_3CHBr(CH_2)_{10}CH_3$	$CH_2Br(CH_2)_{11}CH_3$	(69, 101)
1-Pentadecene, CH_2=$CH(CH_2)_{12}CH_3$	$CH_3CHBr(CH_2)_{12}CH_3$	$CH_2Br(CH_2)_{13}CH_3$	(69, 101)
2-Methyl-2-nonadecene, $(CH_3)_2C$=$CH(CH_2)_{15}CH_3$	$(CH_3)_2CBr(CH_2)_{16}CH_3$	$(CH_3)_2CHCHBr(CH_2)_{15}CH_3$	(30)

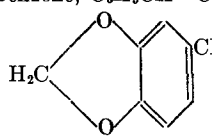
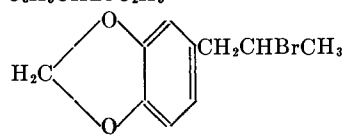
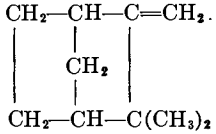
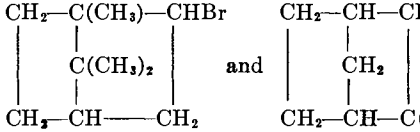
Styrene, $C_6H_5CH{=}CH_2$	$C_6H_5CHBrCH_3$	$C_6H_5CH_2CH_2Br$	(142, 162)
Vinylacetic acid, $CH_2{=}CHCH_2COOH$	$CH_3CHBrCH_2COOH$	$CH_2BrCH_2CH_2COOH$	(104)
Allylacetic acid, $CH_2{=}CH(CH_2)_2COOH$	$CH_3CHBr(CH_2)_2COOH$	$CH_2Br(CH_2)_3COOH$	(25, 64, 104)
Δ^6-Heptenoic acid, $CH_2{=}CH(CH_2)_4COOH$	$CH_3CHBr(CH_2)_4COOH$	$CH_2Br(CH_2)_5COOH$	(25)
Δ^8-Nonenoic acid, $CH_2{=}CH(CH_2)_6COOH$	$CH_3CHBr(CH_2)_6COOH$	$CH_2Br(CH_2)_7COOH$	(25)
Δ^{10}-Undecenoic acid, $CH_2{=}CH(CH_2)_8COOH$	$CH_3CHBr(CH_2)_8COOH$	$CH_2Br(CH_2)_9COOH$	(4, 35, 156)
Ethyl Δ^{10}-undecenoate, $CH_2{=}CH(CH_2)_8COOC_2H_5$	$CH_3CHBr(CH_2)_8COOC_2H_5$	$CH_2Br(CH_2)_9COOC_2H_5$	(5)
Δ^{10}-Undecenyl acetate, $CH_3COO(CH_2)_9CH{=}CH_2$	$CH_3COO(CH_2)_9CHBrCH_3$	$CH_3COO(CH_2)_{10}CH_2Br$	(5)
Δ^3-Pentenoic acid,* $CH_3CH{=}CHCH_2COOH$	$CH_3CHBr(CH_2)_2COOH$	$CH_3CH_2CHBrCH_2COOH$	(12, 131)
Propyne, $CH{\equiv}CCH_3$	$CH_3CBr_2CH_3$	$CH_2BrCHBrCH_3$	(63)
1-Hexyne, $CH{\equiv}C(CH_2)_3CH_3$	$CH_2{=}CBr(CH_2)_3CH_3$	$CHBr{=}CH(CH_2)_3CH_3$	(168)
Δ^{10}-Undecynoic acid, $CH{\equiv}C(CH_2)_8COOH$	$CH_2{=}CBr(CH_2)_8COOH$	$CHBr{=}CH(CH_2)_8COOH$	(35)
Tetrolic acid,† $CH_3C{\equiv}CCOOH$	(*trans*)$Br(H_3C)C{=}C(H)COOH$	(*trans*)$H(H_3C)C{=}C(Br)COOH$	(116)
Phenylpropiolic acid,† $C_6H_5C{\equiv}CCOOH$	(*cis*)$C_6H_5(Br)C{=}C(H)COOH$	(*trans*)$C_6H_5(H)C{=}C(Br)COOH$	(116)

* The composition of the normal addition product is based on work with hydrogen chloride. The addition of hydrogen bromide (without special precaution to exclude oxygen) gave 8 per cent of the product listed as abnormal and 92 per cent of the normal product. The proportion of β-bromovaleric acid might be increased above 8 per cent under proper conditions.

† These acids are included here on the basis of analogies to be discussed in the section on the effects of solvents. The reference cited does not mention the addition of peroxides or antioxidants, or exclusion of air, but reports differences in the addition products which depend on the solvent employed. Grigorieff (29) investigated the addition of hydrogen bromide to tetrolic acid in the absence of solvents. In the presence of antioxidants, the primary product was a β-bromocrotonic acid of melting point 54°C.; in the presence of peroxides, a β-bromocrotonic acid of melting point 94°C. Both isomers on further reaction with hydrogen bromide gave only β,β-dibromobutyric acid. These reactions require further investigation.

TABLE 4

Unsaturated compounds which do not exhibit a peroxide effect with hydrogen bromide

UNSATURATED COMPOUND	ADDITION PRODUCT	REFERENCES
Section A:		
2-Pentene, $CH_3CH{=}CHC_2H_5$	Approximately 50 per cent of each of the two possible addition products	(77)
Δ^9-Undecenoic acid, $CH_3CH{=}CH(CH_2)_7COOH$		(2)
Δ^9-Undecenamide, $CH_3CH{=}CH(CH_2)_7CONH_2$		(2)
9-Undecene-1-ol, $CH_3CH{=}CH(CH_2)_8OH$		(2)
Section B:		
Δ^{10}-Undecenol, $CH_2{=}CH(CH_2)_9OH$	$CH_3CHBr(CH_2)_9OH$	(5)
Section C:		
Propenylbenzene, $C_6H_5CH{=}CHCH_3$	$C_6H_5CHBrC_2H_5$	(98)
Safrole, 		(103)
1-Bromo-2-butene,* $CH_2BrCH{=}CHCH_3$	$CH_3CHBrCHBrCH_3$ (22%) $CH_2BrCH_2CHBrCH_3$ (78%)	(66)
1-Bromo-1-hexene, $CHBr{=}CH(CH_2)_3CH_3$	$CH_2BrCHBr(CH_2)_3CH_3$	(168)
Camphene, 		(38)
Section D:		
Crotonic acid, $CH_3CH{=}CHCOOH$	$CH_3CHBrCH_2COOH$	(30, 116, 162)
Ethyl crotonate, $CH_3CH{=}CHCOOC_2H_5$	$CH_3CHBrCH_2COOC_2H_5$	(162)
Acrylic acid, $CH_2{=}CHCOOH$	CH_2BrCH_2COOH	(95)
Methyl methacrylate, $CH_2{=}C(CH_3)COOCH_3$	$CH_2BrCH(CH_3)COOCH_3$	(126)

β-Bromocrotonic acid, $CH_3CBr{=}CHCOOH$	$CH_3CBr_2CH_2COOH$	(29)
Cinnamic acid, $C_6H_5CH{=}CHCOOH$	$C_6H_5CHBrCH_2COOH$	(116)
Bromomaleic acid, $HOOC{-}\overset{Br}{\overset{\vert}{C}}{=}\overset{H}{\overset{\vert}{C}}{-}COOH$	meso and racemic $HOOCCHBrCHBrCOOH$	(95, 93)
Bromofumaric acid, $HOOC{-}\overset{Br}{\overset{\vert}{C}}{=}\underset{H}{\underset{\vert}{C}}{-}COOH$		

* This unsaturated compound rearranges under the influence of hydrogen bromide; *cf.* V, A.

placing compounds in this table, because a past failure to obtain a second addition product does not prove that future attempts will likewise be failures. For example, early attempts to reverse the addition of hydrogen bromide to styrene failed, but improved technique gave up to 80 per cent of the abnormal product (162).

It seems well established that peroxides do not affect the direction of addition of hydrogen bromide to the ethylene derivatives in section A of table 4. Here the normal addition products are 50–50 mixtures, and complete reversal of the addition gives the same result. Note that, as far as directing tendency is concerned, methyl has the same effect as ethyl or a long-chain alkyl with a substituent on the end.[6] Thus there are few examples of a peroxide effect upon non-terminal double bonds. It should be pointed out here that symmetrically substituted ethylenes, e.g., 2-butene, can give only one structurally distinct addition product, but this fact does not preclude the possibility that the product in question can be formed by two mechanisms.

Alkenes containing a group which inhibits abnormal addition may fail to give an abnormal product. The only known example of such a compound is Δ^{10}-undecenol (in section B of table 4); primary alcohol groups are weak inhibitors of abnormal addition. Until more data on such compounds are available, it should be concluded that the presence of an inhibiting group in an alkene makes abnormal addition less likely but not impossible.

In section C are listed some doubtful cases in which attempts to obtain two addition products have been made. It is probably because the best experimental procedures have not yet been employed that the second products have not been detected. In the opinion of the reviewers, propenylbenzene, safrole, and (if isomerization[7] can be retarded) 1-bromo-2-butene should give two addition products. Because of the behavior of 1-bromopropene, no comment is made on additions to 1-bromohexene. Camphene is a special case, because its predicted abnormal addition product is unknown and because acids rearrange its carbon skeleton.

Section D (table 4) consists of α, β-unsaturated acids and esters. Even when an improved technique was used, crotonic acid and crotonic ester gave only β-bromobutyric acid or ester, with no indication of α-brominated derivatives. Attempts to obtain a second addition product from the other acids listed have failed, but the improved technique has not yet been

[6] The case of Δ^3-pentenoic acid, listed in table 3, is not an exception to this statement, since the carboxyl group is separated from the double bond by only one methylene group. Normal addition gives one product.

[7] This rearrangement, together with the addition of hydrogen bromide to butadiene, will be considered in the section on rearrangements (V, A).

employed. Explanations will be considered in the section on the mechanism of the abnormal addition. A fact pertinent to bromomaleic and bromofumaric acids is that 1,1-dibromosuccinic acid is unknown and may be incapable of existence. Although no instance is known of a peroxide effect on an acid containing an α,β-double bond, there are indications of such an effect on the α,β-triple bonds of tetrolic and phenylpropiolic acids (table 3).

The present section has thus far dealt only with the effects of oxygen and peroxides on the direction of addition of hydrogen bromide in liquid-phase reactions. The data on vapor-phase reactions are contradictory but of interest because, about ten years before the peroxide effect was reported in the scientific literature, suggestions of such an effect in the vapor phase appeared in Bauer's patents. He claimed that the addition of hydrogen chloride, bromide, or iodide to acetylene and vinyl bromide, in the presence of an oxidizing atmosphere containing oxygen, ozone, chlorine, or nitrogen oxides (11), or in the presence of light (10), gives ethylene halides rather than ethylidene halides. Kharasch and Walker (97) have found that oxygen accelerates the addition of hydrogen bromide to propene, 2-pentene, and butadiene, and Kistiakowsky and Stauffer (99) mention a similar effect in the addition of "halogen acids" to "isobutene." Brouwer and Wibaut (15) state that oxygen does not affect the direction of addition of either hydrogen bromide or hydrogen chloride to propene. Vapor-phase reactions need further investigation.

2. Rates of addition

A consideration of the rates of some normal and abnormal addition reactions will be of assistance in showing that the two reactions are independent and competing, and that the susceptibility of an alkene to the peroxide effect is directly related to the rate of its normal addition reaction. No quantitative data are available, but table 5 has been compiled from experiments which have been carried out in the same laboratory under comparable conditions: that is, at room temperature, with about 1.5 moles of hydrogen bromide per mole of alkene, and (except as noted) in the absence of solvents.

The alkenes are listed approximately in order of increasing rate of normal reaction with hydrogen bromide and of decreasing susceptibility to the peroxide effect. When the normal addition is extremely slow (section A), traces of oxygen and peroxides can exert a maximum effect; unless the normal addition is specifically catalyzed, abnormal addition predominates, even in the presence of an antioxidant. When the normal addition is somewhat faster (section B), it can outrun the abnormal addition only when the latter is inhibited by an antioxidant. With allyl bromide (sec-

tion C), exclusion of air and ordinary purification of materials permit the normal to exclude the abnormal addition, although the latter occurs in the presence of air. With the alkenes in section D, air alone is ordinarily insufficient to influence the course of the reaction and definite admixture of peroxides is required to prevent fairly rapid formation of the normal addition product. In section E, the normal addition is so fast that it must

TABLE 5

Rate of addition of hydrogen bromide to unsaturated compounds

UNSATURATED COMPOUND	NORMAL ADDITION			ABNORMAL ADDITION			REFERENCES
	Yield*	Time	Conditions†	Yield*	Time	Conditions†	
	per cent	*hours*		*per cent*	*hours*		
Section A:							
Trichloroethylene	0	1440	(1)	27	24	(3)	(74)
1-Bromopropene	Very little		(1)	84	3	(3)	(70)
1-Chloropropene	25	850	(1)	21	1	(3)	(70)
Section B:							
Vinyl bromide	79	1632	(1)	70	31	(2)	(54)
Vinyl chloride	59	336	(1)	76	48	(2)	(57)
Section C:							
Allyl bromide	95	240	(1)	100	<16	(2)	(53)
Section D:							
2-Bromopropene	92	27	(1)	80	5	(2)	(70)
2-Chloropropene	70	40	(1)	>86	7	(2)	(70)
Propylene	70	3	(1)	41	0.25	(3)	(55)
Isobutylene	100	1	(2)	‡		(3)	(59)
Section E:							
2-Bromo-2-butene	55	2	(1)	Faster		(4)	(161)
Trimethylethylene	‡		(1)	‡		(4)	(162)
Styrene	‡		(2)	‡		(4)	(162)

* When a 90 to 100 per cent yield was obtained, the time given represents only an upper limit to the period required for substantially complete reaction.

† Conditions: (1) air absent, antioxidant present; (2) air present; (3) peroxide present; (4) dilute pentane solution with a peroxide present (otherwise no solvent was employed). All reactions were carried out near room temperature, usually in sealed tubes.

‡ Reaction appeared to occur as rapidly as hydrogen bromide was added.

be retarded by the use of a solvent in order to obtain the abnormal product. Even so, about 20 per cent normal addition occurs.

These observations are all consistent with the view that the two types of addition are independent but competing; the structure of the alkene and the conditions of addition determine the product which predominates. This view is supported by the fact that each alkene in sections B and C

has yielded many different mixtures of the two possible products at rates intermediate between those of the independent reactions. Similar examples will be indicated in the section on the influence of experimental conditions.[8]

Evidence showing how the rate of abnormal addition varies with the structure of the alkene is unsatisfactory, but indications are that the alkenes in section A, particularly trichloroethylene, are also distinguished by slow abnormal additions.

3. Catalysts of abnormal addition

Of the materials which catalyze the abnormal addition, the first ones to be detected, and the most important on account of their wide prevalence, are oxygen and peroxides. Most alkenes, on standing, react with air to form materials which give the familiar test for peroxides; that is, they give an intense red color when shaken with an aqueous solution containing ferrous and thiocyanate ions.[9] The ability of these natural peroxides to cause abnormal addition depends on the extent of their formation and on the rate of the normal addition. For allyl bromide, where the most data are available and where the rate of the normal addition is moderate, the quantities of oxygen or peroxide required are small. Urushibara and Takebayashi (154) state that 1.5 cc. of oxygen per 24.2 g. of allyl bromide (0.03 mole per cent) is sufficient to give a product containing 96 per cent of 1,3-dibromopropane (abnormal). Because about three times as much

[8] Such observations disagree with the opinion of Urushibara and Takebayashi (151) that the normal and abnormal additions so cancel each other that only one can proceed at a time. This view is based on a chain mechanism for normal addition which the reviewers have questioned in section II, A, 3. Assumptions about the effect of one mechanism on the other seem unnecessary, because any rate of reaction or any addition product thus far recorded may be accounted for on the following basis: The abnormal addition may have an induction period (140), proceed very rapidly for a time through the action of peroxides, and then more slowly through the effect of oxygen.

[9] Urushibara and Takebayashi (153) state that when oxygen was passed through allyl bromide in the dark, no peroxides were formed in one month, whereas a strong test could be obtained after the bromide was kept for a few hours in diffused light. However, Urushibara and Sinamura (151) record that when oxygen and hydrogen bromide together were passed through allyl bromide in the dark, considerable oxidation took place, as indicated by formation of water, the liberation of heat, the temporary formation of bromine, and the development of a peroxide test. A good yield of 1,3-dibromopropane was obtained. Such experiments have never been carried out in this laboratory, but it has been repeatedly observed that, when allyl bromide is stored in the dark in a bottle containing air, and only intermittently exposed to light for the purpose of withdrawing samples, a weak peroxide test can be obtained after a few days and a very strong test after a few weeks. The 1- and 2-chloro- and bromo-propenes, as well as styrene, form peroxides more rapidly.

peroxide (formed spontaneously and determined by its ability to oxidize iodide ion) was required to produce a similar effect, they suggest that molecular oxygen, rather than organic peroxides, is responsible for the peroxide effect, and that peroxides function by liberating this gas. The reviewers know of no observations that alkene peroxides liberate oxygen.

Added peroxides are quite as effective as those formed spontaneously in the alkene. Among those which have been successfully used are benzoyl peroxide, lauroyl peroxide, perbenzoic acid, and ascaridole (natural menthene peroxide). The quantities employed have usually been of the order of 1 mole per cent.

Smith has observed the rate of addition of hydrogen bromide to undecenoic acid in various solvents and under various atmospheres. He found that there is an induction period in the abnormal addition when air or benzoyl peroxide is the catalyst, but not when perbenzoic acid, which liberates bromine immediately, is used. In experiments with purified materials in fairly concentrated solution, air, but not perbenzoic acid, gave an abnormal addition reaction. Smith concludes that oxygen is essential for the abnormal reaction and that peroxides serve as subsidiary catalysts (35, 140). Observations in this laboratory (53, 55, 61, 63, 70) show that both benzoyl peroxide and ascaridole can serve as catalysts for the abnormal reaction in the absence of air, but that the rate and extent of abnormal addition are often more unpredictable with peroxides[10], particularly perbenzoic acid, than with oxygen.

A simple explanation of these results, as well as those of Urushibara, Takebayashi, and Smith, is as follows: Either oxygen or peroxides can serve as catalyst for the abnormal addition reaction by reacting with hydrogen bromide. If the peroxide reacts rapidly, as do ascaridole and perbenzoic acid, the catalyst is quickly destroyed before much abnormal addition has taken place. On the other hand, benzoyl peroxide[11] and oxygen react very slowly with hydrogen bromide under the usual experimental conditions, and thus exert a catalytic effect over a comparatively long period. The observations of other workers that peroxides may be less effective than oxygen in catalyzing abnormal addition are not questioned; nevertheless their conclusion that molecular oxygen is necessary seems to the reviewers to be unjustified.

Other gases than oxygen, and other oxidizing agents than peroxides, have been investigated for a possible effect on the abnormal addition. Nitrogen, hydrogen, nitric oxide, and nitrogen dioxide were tried with

[10] With trichloroethylene (74) benzoyl peroxide caused abnormal addition when air did not.

[11] This statement applies particularly to experiments without solvents, when the benzoyl peroxide dissolves slowly.

allyl bromide and found to be without effect (53). Neither lead dioxide nor bromine (in the dark and in the absence of air) had any effect on the addition to allyl bromide (53), nor did *N*-bromobenzamide and iodine affect addition to propene (111). Smith, however, working with diffused light and in a hydrogen atmosphere, found that intermittent additions of bromine caused an abnormal addition to undecenoic acid in carbon tetrachloride solution (140). Harris and Smith (35) report that α-heptenylheptaldehyde and 10,11-epoxyundecanoic acid are catalysts for the abnormal addition of hydrogen bromide to undecenoic acid in the presence of air, but have only a small effect in its absence. In the faster addition of hydrogen bromide to propene (without a solvent), both propylene oxide and propionaldehyde, when peroxide-free, were ineffective even in the presence of air (111). Therefore such catalysts probably function because they, or impurities which they contain, are oxidized by air to peroxides.[12]

Finely divided iron, cobalt, and nickel are strong catalysts for the abnormal addition of hydrogen bromide to allyl bromide and undecenoic acid; these reactions will be considered later.

4. Inhibitors of abnormal addition

It has been found that small proportions, usually 1 to 5 mole per cent, of certain substances prevent abnormal addition when this reaction would otherwise predominate. These inhibitors are commonly called antioxidants because they overcome the effect of oxygen, but many of them are not inhibitors of autoöxidation reactions. Table 6 summarizes some of the available information on inhibitors of abnormal addition, and permits rough evaluation of their effectiveness. The alkenes in section A are those which put antioxidants to the most severe test. For these compounds no antioxidant has been found which completely prevents abnormal addition, except in the presence of a catalyst for the normal reaction. In section B, the inhibitors are effective for propene only when this compound is carefully and freshly purified and when a clean vacuum line is used. The other sections bring out further differences in the effectiveness of antioxidants, and it can be concluded that compounds with sulfhydryl groups are the best inhibitors; some phenols and aromatic amines are less effective. It should be noted that the effectiveness of the inhibiting substances is related to their solubility. This fact may account for the moderate efficacy of diphenylamine (the hydrobromide of which is rather soluble

[12] Note added August 8, 1940: This conclusion is supported by the paper of M. Takebayashi (Bull. Chem. Soc. Japan **15**, 116 (1940)). He found that the effect of aldehydes on the addition of hydrogen bromide to undecenoic acid depended on the peroxide content of the aldehydes.

TABLE 6

Inhibitors of abnormal additions

REAGENTS AND CONDITIONS	EFFECTIVE	PARTIALLY EFFECTIVE	INEFFECTIVE
Section A:			
1-Halopropenes; air absent (70)		Thiophenol Ethyl mercaptan	Diphenylamine Catechol
Section B:			
Various alkenes in hydrocarbon solvents; air absent			
(a) CH_2=$CH(CH_2)_nCOOH$ (25)		Diphenylamine	
(b) Butylacetylene, 2-bromo-1-hexene (168)		Hydroquinone + ferrous bromide*	
(c) Propene (113)		*p*-Thiocresol Thiophenol 4-*tert*-Amylphenol	
Section C:			
Trimethylethylene in ether solution at 0°C.; air present (117)	Hydroquinone	Diphenylamine	
Section D:			
Allyl bromide and undecenoic acid in the presence of finely divided metals; air absent			
(a) Undecenoic acid in toluene solution (158), or allyl bromide (157); nickel	Catechol Hydroquinone	Diphenylamine	
(b) Allyl bromide; iron (87)	Thiophenol Catechol Cuprous bromide, stannous bromide	Resorcinol Phenol Diphenylamine Ferrous bromide,* nickelous bromide, cobaltous bromide*	

Section E:			
Vinyl halides; air absent (54, 57)	Thiocresol (freshly distilled) Thiophenol Diphenylamine Phenyl-β-naphthylamine Dimethylaniline Nitric oxide	Thiocresol (partially oxidized) *tert*-Butyl isocyanide*†	Manganous chloride Ammonium bromide Diphenyl ether Potassium cyanide
Section F:			
Allyl bromide; air present (53, 87)	Diphenylamine Hydroquinone Phenyl-β-naphthylamine Dimethylaniline Resorcinol		Diphenyl ether Ammonium bromide Potassium cyanide

* A part of the inhibitory effect of these substances on abnormal addition may be due to their ability to catalyze the normal addition.

† Effectiveness depends on peroxide content of vinyl halide.

in the reaction mixtures), for the fact that catechol is often better than hydroquinone, and for the differences between some of the metal halides.

Ethanol has been found to inhibit abnormal addition to Δ^{10}-undecenoic acid (35) and to trimethylethylene (162). In a later section it will be shown that this inhibiting effect decreases at lower temperatures.

5. The bromine-atom mechanism of abnormal addition

At this point it seems desirable to correlate the data so far presented by means of a mechanism for the abnormal addition. Since this reaction can be caused by relatively small quantities of oxygen and peroxides and inhibited by equally small quantities of antioxidants, it is established that the abnormal addition is a chain reaction. In choosing a mechanism for the reaction, it must be explained how oxygen and peroxides start reaction chains, how the chains give the abnormal addition product, and why hydrogen bromide is the only halogen acid capable of reacting through such a chain. In order to meet the last requirement, it seems necessary that the oxygen or peroxides function through the hydrogen bromide rather than through the alkene; otherwise it would be difficult to explain why the addition of other unsymmetrical reagents is not also reversed by these reagents. If oxygen or peroxides attack hydrogen bromide, bromine should result; but molecular bromine has no effect on the reaction in the dark. It has therefore been suggested that the slow oxidation of hydrogen bromide in dilute solution gives bromine atoms. In adding to a double bond, these atoms need not attack the same doubly bound carbon atom which would be attacked by the proton in the normal addition. Although oxidation of hydrogen bromide might conceivably give positive bromine ions, and although these ions should add abnormally to double bonds, formulation of the mechanism of the abnormal addition in terms of bromine atoms (70)[13] is preferred, because more energy would be required to separate charged particles in non-polar solvents. According to this mechanism, the reaction should proceed as follows:

$$HBr + O_2 \xrightarrow{\text{(alkene)}} H{-}O{-}O^{\bullet} + Br^{\bullet} \qquad (5)$$

$$RCH{=}CH_2 + Br^{\bullet} \rightarrow R\underset{\bullet}{C}HCH_2Br \qquad (6)$$

$$R\underset{\bullet}{C}HCH_2Br + HBr \rightarrow RCH_2CH_2Br + Br^{\bullet} \qquad (7)$$

The individual steps suggested will next be discussed.

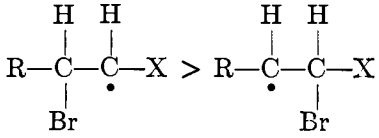
[13] The suggestion that the abnormal addition is a chain mechanism involving bromine atoms was made simultaneously and independently, but without details, by Hey and Waters (37). Previously, Burkhardt (16) had suggested that free radicals might account for the abnormal addition of thiophenol to styrene; *cf.* section III, B.

The oxidation of hydrogen bromide by oxygen is ordinarily slow, but Urushibara and Sinamura have shown that in the presence of an alkene such as allyl bromide, peroxides are very rapidly formed (151). These organic peroxides react slowly with hydrogen bromide. The same authors also showed that the interaction of hydrogen bromide, oxygen, and stilbene gives stilbene dibromide, thus proving the oxidation of hydrogen bromide. Similarly, the abnormal addition of hydrogen bromide to allyl bromide is accompanied by the formation of small amounts of a high-boiling liquid which is apparently 1,2,3-tribromopropane (94, 151). The essential feature of reaction 5 is that at least a small portion of the bromine formed must be liberated in the atomic state. This requirement is consistent with the fact that those peroxides which react more slowly with hydrogen bromide are usually more effective; it also agrees with the observation of Smith (140) that bromine is a catalyst for the addition of hydrogen bromide in diffused light. The fate of the $HO_2\bullet$ radical is unimportant. It may react with hydrogen bromide to give another bromine atom and hydrogen peroxide, or it may combine with alkene.

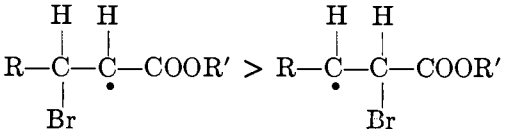
If reaction 5 is assumed, reaction 6 can follow very easily. In the normal addition to the type of alkene chosen as an example, the proton becomes attached to the terminal carbon atom, showing that this atom is the relatively negative carbon atom of the double bond. In abnormal addition the bromine atom becomes attached to this terminal carbon atom. It has already been suggested (70) that the oxidizing properties of the bromine atom cause it to attack the carbon atom with the higher electron density. This explanation is simple and plausible, but the following one has additional advantages: The point of attack by the bromine atom is little affected by the polarity of the double bond, but depends upon the relative stability of the two bromoalkyl radicals which may be formed. If the directions of all additions by the chain mechanism are to be explained on this basis, the following orders of decreasing stabilities of free radicals (each formed by the addition of a bromine atom to a double bond) are required:

Radicals from hydrocarbons: tertiary > secondary > primary

Radicals from vinyl-type halides:

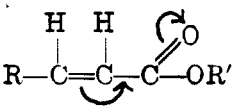


Radicals from acids, esters:



Radical stability in this discussion is intended in the sense of higher heat of formation; no reference to the mean life of the radical is implied. If these relative stabilities can be proved correct, then the hypothesis of radical stability explains why addition of hydrogen bromide by the abnormal rather than the normal mechanism gives complete reversal of addition with hydrocarbons, only partial reversal with 1-bromopropene (to give exclusively 1,2-dibromopropane), and no change when the ethylene bond is conjugated with the carboxyl group.

This hypothesis suggests that the addition of hydrogen bromide to such conjugated double bonds may take place through two mechanisms to give only one product. Addition by the normal mechanism must be fast as compared with addition by the chain mechanism, in order to agree with the following qualitative rate indications. The rate of addition of hydrogen bromide to crotonic acid and its ethyl ester is unaffected by peroxides, even when the normal addition is retarded by the use of an inert solvent (162). These conclusions as to the relative rates of addition by the two mechanisms are in agreement with experiments (to be described in section V, C) on the relative rates of isomerization of maleic acid to fumaric acid by corresponding mechanisms. Smith (141) has suggested that since ethylene bonds conjugated with carboxyl groups should be represented by the formula



and that since there is no "accumulation" of electrons on the α-carbon atom, there is no tendency for the bromine atom to attack this position or for abnormal addition to occur. This explanation is in good agreement with the qualitative observations on the rate of addition of hydrogen bromide, but not with the isomerization studies mentioned. In the opinion of the writers, no explanation yet proposed for the absence of abnormal addition to conjugated systems is wholly satisfactory.

In order to obtain the addition product from the free radical formed in reaction 6, reaction 7 is necessary. This latter step regenerates a bromine atom, so that the chain reactions (6 and 7) can continue indefinitely. The inhibition of the abnormal reaction by small quantities of antioxidants is excellent evidence that this reaction is of the chain type. The small amounts of antioxidants usually needed to inhibit and the small amounts of peroxides necessary to cause abnormal addition indicate that the chains must be very long. If 0.03 mole per cent of oxygen causes nearly complete abnormal addition to allyl bromide (154), and if each molecule of

oxygen generates four bromine atoms by oxidizing hydrogen bromide, then the average chain length is at least 1000. If the efficiency in generating bromine atoms is low, as seems likely, then the chains must be much longer. These chain lengths, together with the observed high velocity of the abnormal addition and the known instability of aliphatic free radicals, indicate that both steps in the chain reaction must take place very rapidly and with little or no activation energy. The inhibition of the reaction by antioxidants suggests that these function by reacting with bromine atoms. It is also possible, as originally suggested (53), that antioxidants to some extent destroy organic peroxides. Other observations on the abnormal addition are consistent with the chain mechanism suggested. The abnormal reaction is retarded by glass wool (139), although apparently not by coarser packing (155). When non-polar solvents are used, the absence

TABLE 7

*Heats of addition of halogen acids to double bonds**

STEP IN CHAIN REACTION	ΔH (IN KILOGRAM-CALORIES PER MOLE)			
	X = F	X = Cl	X = Br	X = I
(6) $RCH{=}CH_2 + X^{\bullet} \rightarrow R\dot{C}HCH_2X$	64; 66	27; 25	13	−1; +4
(7) $R\dot{C}HCH_2X + HX \rightarrow RCH_2CH_2X + X^{\bullet}$	−60	−15	0	16

* When two values are given for ΔH, the first is based on the bond-energy estimates of Sherman and Ewell (31), the second on the estimates of Pauling (124). One value for ΔH indicates that both sources give the same result.

of a large dilution effect (113) shows that the abnormal reaction cannot be of second or third order.

It will now be indicated why hydrogen bromide is the only halogen acid capable of giving an abnormal addition. The exposition assumes that a rapid chain reaction is impossible when any step is appreciably endothermic. Table 7 gives estimates of the heats evolved in reactions 6 and 7 for various halogen acids; it is assumed that ΔH for each reaction is simply the difference between the energies of the bonds formed and the energies of the bonds broken. The heats indicated are only approximate, for the bond energies are none too well established for the molecules to which they are meant to apply and are still less reliable when applied to free radicals.[14] Table 7 shows that reaction 6 for hydrogen bromide is definitely exothermic and that the heat of reaction 7 is very close to zero. However, the addition

[14] Actually, the activation energy rather than the ΔH will determine the probability of reaction. Because long chains occur in some additions, it is assumed here that the activation energy is small when ΔH is positive or zero.

of hydrogen chloride by the same mechanism encounters difficulty in two places, reactions 5 and 7. Since the oxidation of hydrogen bromide is ordinarily slow (reaction 5), the oxidation of hydrogen chloride is probably slower, possibly negligible. In reaction 7 the carbon–chlorine bond formed is weaker than the hydrogen–chlorine bond broken; the reaction is endothermic by about 15 kg-cal. per mole, and unlikely to occur rapidly enough to support long chains at ordinary temperatures. Both of these difficulties apply also to hydrogen fluoride and to most other acids. Attempts to reverse the direction of addition of sulfuric acid to propene, 1-pentene, and 2-pentene have failed (14).

In the addition of hydrogen iodide, reactions 5 and 7 should proceed easily, but reaction 6 may not. Another difficulty with the addition of hydrogen iodide is that the normal addition is ordinarily rapid and is further catalyzed by molecular iodine. Any reagent which generates iodine atoms must necessarily generate also the catalyst for the normal addition. Still another possibility is that iodine, since it does not add readily to alkenes, may accumulate in the reaction mixture and inhibit any possible abnormal addition of hydrogen iodide by an iodine-atom mechanism. According to the chain mechanism proposed, the unsymmetrical reagents, HX, which can add by a chain mechanism are restricted to narrow limits. The requisites are as follows: the radical (or atom) X must be able to break a carbon–carbon double bond and add to one carbon atom; the free radical formed must be able to take a hydrogen atom away from HX to regenerate another X radical. It will be shown later that this mechanism can also be applied to additions of mercaptans and bisulfites.

The next abnormal additions to be considered are those occurring when air and peroxides have been excluded from reaction mixtures (135, 136) and when antioxidants have been added (25, 70, 117). The discussion of antioxidants showed that these substances exert effects ranging from complete to barely perceptible repression of the abnormal addition. Since different antioxidants have variable effects under the same experimental conditions, the occasional failure of the best antioxidants and the more frequent failure of inferior inhibitors indicate only that the proportions used or the inhibiting qualities of the compounds were inadequate; they do not indicate a difference in the nature of the abnormal reaction. It is thus proved for the weaker antioxidants, and inferred for the rest, that only a small proportion of the collisions of a bromine atom with an antioxidant molecule are effective in terminating chains. The smaller this proportion, the greater must be the chain lengths and the fewer the number of bromine atoms necessary to cause abnormal addition. Since there is no basis for estimating an upper limit on chain lengths, it can be argued that traces of peroxides and oxygen which would defy elimination or detection by any known method

may be wholly responsible for all abnormal addition reactions. On the other hand, infinitesimal quantities of atoms or radicals may appear spontaneously in the solution with the result that chains are initiated. The dissociation of hydrogen bromide into atoms would require 87 kg-cal. per mole (31, 124), but the dissociation of a carbon–bromine bond in an alkyl halide requires on the average only 50 to 60 kg-cal. Such a dissociation might initiate two chains if the free radical reacted with hydrogen bromide to give an alkene and a bromine atom. Sherman, Quimby, and Sutherland (134)[15] have utilized such a chain-initiating step in calculating the activation energy of the addition of hydrogen bromide to vinyl bromide by the chain mechanism just described, and have arrived at a value of 29 kg-cal., one-half the estimated strength of the carbon–bromine bond. If this value is approximately correct, the abnormal addition can be initiated without the assistance of oxygen or peroxides. Such an activation energy, however, is probably higher than that for most normal addition reactions; hence appreciable abnormal addition of spontaneous origin could be expected only when the normal addition is very slow. Although oxygen and peroxides are usually responsible for the abnormal addition of hydrogen bromide to alkenes, it is futile at present either to assert or to deny that they are always entirely responsible. The significant aspects of the peroxide effect in additions of halogen acids are that abnormal addition takes place only with hydrogen bromide, and then by a chain mechanism, and that oxygen and peroxides are largely, if not entirely, responsible for this reaction.

6. Other mechanisms proposed for abnormal addition

The first mechanism to be proposed for abnormal addition was that of Urushibara and Takebayashi (155). Because iron and certain other metals also caused abnormal addition, they suggested that the effect of oxygen was due to its paramagnetic properties. The oxygen or metal was supposed to exert a physical influence on the surrounding alkene molecules such that the polarity of the double bond was affected. The shortcomings of this hypothesis have been mentioned elsewhere (87), and are admitted by at least one of the above workers (151), who now favors the bromine-atom chain mechanism.

Winstein and Lucas (165) have proposed an explanation for abnormal addition to a double bond the polarity of which (as indicated by the normal addition) is $\overset{+}{\text{C}}\text{—}\overset{-}{\text{C}}$. They suggested that oxygen forms with

[15] These workers proposed the chain mechanism for both the normal and the abnormal additions of all halogen acids to alkenes a year before investigators in this laboratory suggested it only for the abnormal addition of hydrogen bromide.

double bonds of this type a complex represented by the following resonance forms:

If the second form makes the larger contribution to the complex, the proton of the attacking halogen acid attaches itself to the carbon atom which would have been relatively positive in the pure alkene. The oxygen is then displaced by a bromide ion, and abnormal addition results. Conn, Kistiakowsky, and Smith (20) concur essentially in this suggestion. However, such behavior of an oxygen molecule in forming successive loose complexes with several hundred molecules of alkene is not wholly consistent with the rapid irreversible reaction of oxygen on alkenes in the presence of hydrogen bromide (151).

Michael (114, 117) has recently attacked all previous mechanisms for abnormal addition and has suggested one of his own. On the basis that oxygen in the atmosphere or in the molecules of the solvents is negative, he proposes that oxygen from either source may become associated with the more positive of the doubly bound carbon atoms, thus making this atom relatively negative. If the effect of oxygen (or oxygen compound) is sufficient to reverse the polarity of the double bond, then the addition of halogen acid is also reversed.

All of these hypotheses may be said to account for an abnormal addition of hydrogen bromide, but all fail to indicate why hydrogen chloride and hydrogen iodide do not give a similar reaction. Further, all of them except that of Urushibara and Takebayashi fail to explain why some finely divided metals cause abnormal addition. This latter effect will soon be considered in the light of the chain mechanism.

7. The influence of experimental conditions on additions of hydrogen bromide

The following discussion of the effects of solvents, temperature, light, and metals on the liquid-phase addition of hydrogen bromide to alkenes will assume that all of the abnormal product results from addition of hydrogen bromide by the bromine-atom chain mechanism, whereas all of the normal product results from addition by other mechanisms. The reaction product obtained is the result of competition between the two mechanisms; hence its composition may vary from one extreme to the other. Experimental conditions may favor one mechanism and hinder the other, but the fact that the direction of addition of hydrogen chloride and hydrogen iodide has not yet been certainly (44, 84) altered by any agent indicates

that these conditions affect the halogen acid or its mechanism of addition, and not the unsaturated compound.

Solvents principally affect the rate of the normal addition reaction. Because of the high order of this reaction, its rate is greatly decreased by dilution with inert solvents, and the abnormal addition may then outrun the normal reaction. This effect is strikingly demonstrated in the addition of hydrogen bromide to propene. When no solvent is used, the normal addition requires only a few minutes and abnormal addition is difficult to obtain, except in the presence of added peroxides (54). But when the reaction mixture is diluted with about ten volumes of pentane, abnormal addition is substantially complete[16] within half an hour at 0°C., even when the reaction mixture is prepared from purified materials in the absence of air (113). However, the addition of an antioxidant prevents abnormal addition; then several weeks are required for the normal reaction. Smith has shown that, at high dilution, the addition to undecenoic acid is highly sensitive to the presence of air (140). Both observations show clearly how dilution affects the competition between the two mechanisms, why past claims that a direct solvent effect is responsible for abnormal addition are open to serious doubt, and how a peroxide effect may be obtained with alkenes to which normal addition is rapid.

Small amounts of polar solvents such as water and acetic acid may increase the rate of the normal addition, probably because of dielectric effects and the change from a molecular to an ionic mechanism. This acceleration is partly responsible for the small amount of abnormal addition in polar solvents. Some solvents may, however, be weak inhibitors of abnormal addition, as will be indicated in the discussions of the temperature and light effects.

Table 8 summarizes work on the addition of hydrogen bromide to alkenes in solvents. All the experiments listed fulfill the following conditions: (*a*) they have been carried out since the discovery of the peroxide effect; (*b*) both products have been obtained in the same solvent by the same workers; (*c*) either addition product can be made to predominate by the suitable use of oxygen, peroxides, or antioxidants. The facts that a large variety of alkenes and solvents have been employed, and that many different workers have participated in obtaining these results, are convincing evidence that the mechanism of addition is the factor which determines the composition of the addition product.

[16] Such a velocity would lead one to expect considerable abnormal addition in the absence of a solvent and of air, but no such reaction has actually been observed. If some association product of hydrogen bromide or propene or both is a weak inhibitor of abnormal addition, then this reaction, in agreement with qualitative indications, would be accelerated by dilution.

Some workers in the field disagree with the above conclusion, and maintain that solvents immediately affect the direction of addition, presumably through their effect on the polarity of the double bond. Gaubert, Linstead, and Rydon base their contention on the inability of diphenylamine to prevent formation of primary bromides from terminally unsaturated acids in hexane solution (25). Sherrill and coworkers (135, 136) insist that their 1-alkenes were peroxide-free and that the formation of primary

TABLE 8

Solvents in which hydrogen bromide yields either of two addition products

ALKENE	SOLVENTS EMPLOYED	REFERENCES
Allyl bromide	Water, 90% acetic acid, propionic acid, ligroin, carbon disulfide, chloroform, carbon tetrachloride, 1,2-dibromopropane, 1,3-dibromopropane, acetyl bromide*	(53)
Vinyl bromide	Acetic acid, nitrobenzene	(54)
Vinyl chloride	Acetic acid, nitrobenzene, mesitylene	(57)
Propene	Pentane, acetic acid	(60, 113)
1-Butene	Ligroin	(58)
1-Pentene	Pentane, propionic acid	(61)
Isobutylene	Pentane, carbon disulfide, propionic acid, ethyl bromide, benzonitrile, nitrobenzene, water	(65)
Trimethylethylene	Pentane, ethyl bromide, ether, methanol, ethanol, acetic acid*	(117, 162)
Styrene	Pentane	(162)
2-Bromo-2-butene	Acetic acid	(161)
2-Bromo-1-hexene	Benzene	(168)
Allylacetic acid	Hexane	(64)
Δ^{10}-Undecenoic acid	Ligroin, hexane, toluene, benzene, carbon disulfide, carbon tetrachloride, chloroform	(4, 35)
Ethyl Δ^{10}-undecenoate	Benzene, ligroin	(5)
Undecenyl acetate	Benzene, ligroin	(5)
Undecynoic acid	Benzene	(35)

* In the experiments indicated in these two solvents, less than 50 per cent abnormal addition in the presence of air or peroxides was observed.

bromides in solvents must therefore be a solvent effect. They used no antioxidants. Michael and coworkers claim to have demonstrated a solvent effect in the addition of hydrogen bromide to tetrolic and phenylpropiolic acids (table 3) and to trimethylethylene (table 8). In the first instance, they employed no antioxidants; in the second, the "solvent effect" was diminished by antioxidants and vanished in experiments with hydrogen chloride (table 1) or hydrogen iodide (table 2). The reviewers question not the experimental results of these workers, but their conclusions.

An effect of the solvent on the polarity of the double bond, and thus on the direction of normal addition, would be most likely in instances where the normal addition product is a mixture, and where the directing effects of the substituents on the doubly bound carbon atoms are nearly balanced. No such effect has yet been reported with this type of ethylene derivative. The addition of hydrogen bromide to 2-pentene has been carried out without a solvent and in acetic acid solution (77). With Δ^9-undecenoic acid the reaction has been run in ligroin, hexane, benzene, and acetic acid (2, 34). In all cases, the addition product consisted, within experimental error, of equal proportions of the two possible halides. The fact that no solvent effect on the direction of normal addition has yet been established does not prove that none will ever be found, but the existence of such an effect should be demonstrated, not with hydrogen bromide (which is the only halogen acid capable of addition by an abnormal mechanism) but with hydrogen chloride or hydrogen iodide.

Increasing the reaction temperature generally increases the difficulty of eliminating abnormal addition. Air does not cause much abnormal addition to pure allyl bromide at 0°C., but it does at room temperature (53). Removal of air prevents abnormal addition at room temperature, but this procedure becomes ineffective at 76°C. However, the addition of an antioxidant reduces the proportion of abnormal addition product to about 10 per cent, even at 100°C., indicating that the effect of temperature is on the relative rates of the normal and abnormal addition reactions, and not on the allyl bromide (see footnote 3). Vinyl bromide (54) and vinyl chloride (57), to which the normal additions are slower, present similar difficulties beginning at lower temperatures, for antioxidants are always required to eliminate abnormal addition to these substances at room temperature, and partial failure of antioxidants has been observed at 46° and 76°C., respectively.

Abnormal addition to allyl bromide (53) and trimethylethylene (117) has been observed at −78°C. with small quantities of peroxides, showing that long chains are formed and that their propagation requires a negligible activation energy. Differences in the effectiveness of different antioxidants indicate that at least some, and probably all of them, require at least a small activation energy for reaction with bromine atoms. It follows that the proportion of effective collisions between a bromine atom and an antioxidant must increase as the temperature rises.[17] Therefore, the increasing predominance of abnormal addition at high temperatures in the presence of antioxidants cannot be ascribed to increased chain lengths, but must be due to the origin of many more chains. Although the

[17] This phenomenon has been observed when alcohols, acetic acid, or acetyl bromide have been used as solvents; it will be described shortly.

decomposition of peroxides or their reaction with hydrogen bromide may have a high temperature coefficient, either reaction should lead to rapid exhaustion of traces of peroxides in experiments from which air has been excluded. Here the spontaneous origin of chains (i.e., without the influence of oxygen and peroxides), a reaction of high activation energy and high temperature coefficient, may become significant. The normal addition of hydrogen bromide to allyl bromide and vinyl bromide has a temperature coefficient of about 2 for 10°C. That of the abnormal addition is much larger, at least over certain ranges of temperature.

The temperature effect in solvents fits into the scheme already outlined. If the solvent (ligroin, chloroform, carbon tetrachloride with allyl bromide (53), ether with trimethylethylene (117)) decreases the rate of normal reaction, then the abnormal addition becomes more prominent and appears at a lower temperature. If the solvent (acetic acid, water, acetyl bromide with allyl bromide) increases the rate of the normal reaction, then abnormal addition becomes less prominent.

The fact that abnormal addition is easily obtained in many solvents indicates that their inhibiting properties are usually negligible. Nevertheless, almost any of the aliphatic solvents in table 8 can react with bromine atoms, as shown by the mechanism of aliphatic substitution. In the solvents which inhibit, the effect increases with increasing temperature. In the presence of peroxides, no abnormal addition to trimethylethylene takes place in ethanol solution at 20°C. or in methanol at 0°C., but the proportion of abnormal addition increases at lower temperatures (117). Acetic acid and acetyl bromide seem to have definite inhibiting properties in additions to allyl bromide at 76°C.; moreover, in the light, acetic acid seems to be a better inhibitor of abnormal addition at 25°C. than at 10°C. Ordinarily, little difficulty is encountered in obtaining abnormal addition in glacial acetic acid (*cf.* table 8), but experiments with allyl bromide in this solvent show that small amounts of admixed water favor abnormal addition.

Light accelerates both the normal and the abnormal additions of hydrogen bromide to allyl bromide (53) and vinyl bromide (54), but the effect on the abnormal addition is usually far greater than on the normal reaction. The rate of addition to allyl bromide in the light is greatest in the presence of air, slower in the absence of air, and still slower in the presence of added antioxidants. In the first two instances, the abnormal addition product is formed exclusively; in the last, predominantly. These observations are corroborated by others made on vinyl chloride (57) and trichloroethylene (74).

In additions to allyl bromide in the light, the effects of various spectral regions and of solvents have been investigated. In the absence of air

and antioxidants, abnormal addition was substantially complete in 1 to 4 hr., regardless of whether the light supplied was near ultraviolet, red and infrared together, or a combination of either with visible light.[18] In the presence of 1.4 mole per cent of diphenylamine, a combination of red and infrared light was clearly shown to accelerate the normal addition by a factor of 5 to 10 without causing much abnormal addition. Visible and near ultraviolet radiation gave increasing proportions (up to 74 per cent) of abnormal addition product at about the same total reaction rate. Thus the shorter wave lengths make repression of abnormal addition more difficult. In the absence of air and antioxidants, abnormal addition occurs exclusively when heptane, carbon disulfide, acetyl bromide, or benzoyl chloride are used as solvents. In acetic acid solution, only very small proportions of abnormal addition product are obtained; none of this product is formed in the presence of hydroquinone. Comparison of these experiments with those carried out in the absence of a solvent indicates that acetic acid has some inhibiting properties for the abnormal addition, and that the effect of light on the competition between the normal and abnormal reactions is much like that of increased temperature.

Inasmuch as the individual effects of light and temperature on the rates of the normal and abnormal additions are known only qualitatively, and since the effects of temperature on the inhibiting properties of solvents and antioxidants have not been isolated, the combined effects of light and temperature cannot yet be completely resolved. The effect of lowering the reaction temperature in the photochemical addition of hydrogen bromide to vinyl bromide (54) is impressive. Although no normal addition occurs at room temperature in the presence of antioxidants, a 50 to 60 per cent yield of an 80 per cent normal product was obtained in 16 hr. at 5°C. Thus not only was the proportion of abnormal addition greatly reduced by lowering the temperature, but the normal addition product was formed at the rate of about 3 per cent per hour, as against 1 per cent per day in the dark at room temperature,—an increase by a factor of about 70 in spite of a 20°C. temperature decrease. The case of allyl bromide is less clear-cut. The effect of light in accelerating the normal addition is smaller, and lowering the reaction temperature in the presence of antioxidants does not significantly increase the proportion of normal addition product.[19] The available data do not permit estimation of the

[18] Comparisons of rates are not possible, because the amount of light transmitted by the filters is not known.

[19] Kharasch and Mayo (53), using thiocresol as an antioxidant, observed 71 per cent and 30 per cent normal addition at 5°C. and at room temperature, respectively, but in view of the fact that the combined yields of both addition products were 54 per cent and 91 per cent, respectively, and that normal addition is fastest during

effect of light on the rates of the two possible additions in glacial acetic acid solution, but they show conclusively that in the light more abnormal addition takes place at 5°C. than at room temperature. This fact can be explained by the assumption that acetic acid is less effective as an inhibitor at lower temperatures. Such a conclusion is consistent with observations made at higher temperatures or in the presence of alcohols. It may be noted that at 5°C. a reaction mixture containing diphenylamine reacted more slowly than one containing oxygen and gave slightly less abnormal addition product,—a fact which may be taken to indicate that the effect of light in accelerating the abnormal addition is large compared with that of oxygen.

The acceleration of both the normal and abnormal addition by light, the increased light effect in the presence of oxygen, some relations between the combined effects of light and temperature, and the partial and variable effects of antioxidants in repressing abnormal addition in the light all show the close analogy between the effect of light and that of increased temperature. These observations are consistent with the concept that all abnormal addition products result from a reaction by the chain mechanism. Since the effect of light is greatest in the presence of oxygen, illumination apparently accelerates peroxide formation and oxidation of hydrogen bromide, but it apparently also serves to initiate chains without the assistance of oxygen. The fact that light accelerates the normal (as well as the abnormal) addition, and that the effect is much greater with vinyl bromide than with allyl bromide, shows that either the alkene, its complex with hydrogen bromide, or some impurity absorbs visible radiation. The greater effectiveness of the shorter wave lengths in accelerating abnormal addition to allyl bromide is consistent with the greater activation energy of this reaction. Although in the absence of air and peroxides, reaction mixtures usually remain colorless in the dark, the presence of oxygen, peroxides, or light usually leads to the development of variable quantities of dark-colored materials. These may assist in the transference of energy to substances which otherwise absorb only weakly.

It was found by Urushibara and Takebayashi that, if the addition of hydrogen bromide to allyl bromide takes place in the presence of finely divided and freshly reduced iron, nickel, or cobalt, varying quantities of abnormal product are formed, even in the presence of some antioxidants.

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the first part of the reaction when the concentrations of reactants are highest, the conclusion that temperature lowering increases the yield of normal addition product is not justified. A recent experiment with catechol at 5–10°C. (112) gave in 65 hr. a 92 per cent yield of a mixture containing only 26 per cent of the normal addition product, again indicating that temperature lowering may have no marked effect.

They observed similar phenomena when hydrogen bromide was added to undecenoic acid in toluene solution. Their work has been reviewed elsewhere (151) and that portion of it concerned with the effect of reduced iron on allyl bromide has been confirmed, extended, and explained in a paper from this laboratory (87). The complete inhibition of the iron-promoted abnormal addition by some antioxidants, and its partial inhibition by others (*cf.* table 6), are strong indications that abnormal addition is the result of the bromine-atom chain mechanism. The fact that some hydrogen and metal bromide are formed suggests that interaction of the metal with hydrogen bromide or allyl bromide yields some hydrogen atoms or free radicals. Reaction of hydrogen atoms with hydrogen bromide or allyl bromide would yield free radicals or bromine atoms, either of which might initiate chains for the abnormal addition.

$$Fe + HBr \rightarrow FeBr\bullet + H\bullet \quad (8)$$

$$RCH{=}CH_2 + H\bullet \rightarrow R\dot{C}HCH_3 \quad (9)$$

$$H\bullet + HBr \rightarrow H_2 + Br\bullet \quad (10)$$

$$Fe + R'Br \rightarrow FeBr\bullet + R'\bullet \quad (11)$$

Thus far, iron-promoted abnormal addition has not been found with any alkene which gives a rapid normal addition with hydrogen bromide, but it has been observed with allyl chloride and possibly with vinyl bromide. Other metals have failed to cause abnormal addition to allyl bromide, because they do not react with anhydrous hydrogen bromide, because the bromides formed are strong catalysts for the normal addition (section I, A, 3), or because their bromides are strong inhibitors for the abnormal reaction (table 6).

The success of the bromine-atom chain mechanism in correlating the metal effect with the peroxide effect, an advantage not possessed by any other mechanism yet proposed for either reaction, is a strong point in favor of this interpretation. However, the value of a hypothesis lies in its ability to predict new reactions as well as to explain known ones. At the end of this paper, it will be shown how many new applications of this concept have been developed since it was first formulated.

In concluding this section dealing with the influence of experimental conditions on the direction of addition, the conditions which should be chosen to promote either normal or abnormal addition of hydrogen bromide are summarized. To favor normal addition, this reaction may be accelerated by the use of high concentrations of reactants, particularly hydrogen bromide, or by the use of fairly small proportions of polar solvents (acetic acid), or of catalysts (ferric and aluminum bromides); and the abnormal addition can be inhibited by the use of antioxidants. To favor

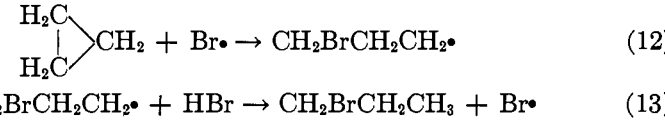
abnormal addition, this reaction may be accelerated by the use of oxygen, peroxides, certain metals (iron, nickel), light, or elevated temperatures; the normal addition (unless it is naturally slow) should be retarded by dilution with inert, non-polar solvents. It should be added that any atom or free radical which can react with the hydrogen atom or the bromine atom of hydrogen bromide or with an alkene may be capable of starting a reaction chain.

8. The addition of hydrogen bromide to cyclopropane

Cyclopropane is closely related to propene, in that both react with some acids and oxidizing agents to give propane derivatives. They differ in that cyclopropane gives 1,3-derivatives of propane, whereas propene gives 1,2-derivatives. In an investigation of the addition of hydrogen bromide to cyclopropane (78), although the product was always *n*-propyl bromide, striking analogies with addition to alkenes were found in rates of reaction.

When equimolecular mixtures of cyclopropane and hydrogen bromide were allowed to react in sealed tubes at room temperature in the absence of air and light, 50 to 60 per cent reaction took place in 4 hr. If 3 mole per cent of water or acetic acid was added to the mixture, about 90 per cent reaction took place in the same period, indicating that addition occurred largely through a polar molecular or ionic mechanism like that for the normal addition of halogen acids to alkenes. Similar proportions of catechol or thiocresol acted like water or acetic acid, but oxygen or visible light had only a small accelerating effect on the reaction. However, if the reaction mixture was made up of 10 moles of cyclopropane to 1 mole of hydrogen bromide, thus in effect diluting the previous reaction mixtures with 9 moles of hydrocarbon, then characteristics of the abnormal addition of hydrogen bromide to alkenes appeared. In the absence of oxygen and light, only 8 per cent reaction took place in 2 hr. Light alone increased this yield to 11 to 12 per cent; oxygen alone, to 81 per cent; oxygen and light together, to 99 per cent; peroxides and light, to 74 per cent. Catechol and diphenylamine had small to moderate inhibiting effects on the accelerated reaction. That the effects were not larger is due to the fact that the antioxidants (and also water) accelerated addition by favoring the competing normal mechanism, as in concentrated solution.

These phenomena suggest that oxygen and peroxides react with hydrogen bromide to give bromine atoms, or with cyclopropane to give free radicals, and that addition of hydrogen bromide may then take place through the following chain mechanism:



(12)

$$CH_2BrCH_2CH_2\bullet + HBr \rightarrow CH_2BrCH_2CH_3 + Br\bullet \qquad (13)$$

In additions of hydrogen bromide to pure alkenes, light is more powerful than oxygen in promoting abnormal addition, but the reverse is true for cyclopropane. Hence the analogy between alkenes and this compound is not complete. Possibly the chain may require modification to include oxygen (78).

III. The Addition of Mercaptans and Thio Acids to Unsaturated Compounds

A. INTRODUCTION

A mercaptan, like a halogen acid, when it is added to an unsymmetrically substituted ethylene bond, can yield either of two products:

$$RCH{=}CH_2 + R'SH \rightarrow RCH_2CH_2SR' \text{ (abnormal addition)} \quad (14)$$

$$RCH{=}CH_2 + R'SH \rightarrow RCH(CH_3)SR' \text{ (normal addition)} \quad (15)$$

These two possible reactions are here designated "normal" and "abnormal" additions on the assumption that mercaptans should add like halogen acids. Actually, both additions have been recorded, but when the absorbing compound is a hydrocarbon, the abnormal addition reaction is the one commonly observed when no catalysts for the normal addition are employed. This fact accounts for the acceptance of the rule prematurely proposed by Posner (125) for the addition of mercaptans to alkenes: namely, that the sulfur becomes attached to the carbon atom holding the most hydrogen atoms. The products and mechanism of the abnormal addition of mercaptans to alkenes will be first discussed; then those of the normal addition reaction. It will be shown that both have much in common with the additions of hydrogen bromide. Finally, the range of applicability of both reactions will be indicated.

Although mercaptans usually add abnormally, there is no evidence of such an addition for hydrogen sulfide, which adds only at fairly high temperatures. Under pressure and below 200°C., all the mercaptans and sulfides obtained are normal addition products, and their formation is catalyzed by sulfur (45, 49). The vapor-phase reaction at atmospheric pressure has been studied at 200-300°C. over a nickel-kieselguhr catalyst (9) and at 300°C. over silica gel (108). In the first instance, 5 to 25 per cent of a mixture containing about 65 per cent of isopropyl mercaptan and 35 per cent of *n*-propyl mercaptan was obtained from propene. This reaction product was considered to be an equilibrium mixture of the two possible addition products (*cf.* footnote 3). In the second instance, mercaptans, sulfides, and thiophene derivatives of unknown structure were obtained.

B. THE ABNORMAL ADDITION OF MERCAPTANS AND THIO ACIDS

It has been clearly shown (6, 16, 49, 76) that the abnormal addition of mercaptans to alkenes is catalyzed by oxygen and peroxides, that it is inhibited by hydroquinone and piperidine, and that it is accelerated by light. The peroxides formed when an alkene is exposed to air are sufficient to catalyze the abnormal addition; careful purification of the reactants and exclusion of air prevents, or greatly retards, any addition. Table 9 summarizes the evidence that the abnormal addition of mercaptans to alkenes can be inhibited by antioxidants, and initiated by oxygen or peroxides, particularly in the presence of light. It is therefore a chain reaction. The structures of the products formed also supply excellent evidence that the addition does not proceed through a polar or ionic mechanism. Table 10 lists other reactions which show that abnormal addition products are commonly formed when air is not excluded. Table 9 records two instances in which both normal and abnormal addition products are formed, although the latter predominate. In every other addition listed in either table, the abnormal addition product is formed exclusively. The known examples include both aliphatic and aromatic mercaptans, mercaptoacetic acid, and thioacetic acid; the alkenes contain aromatic and aliphatic substituents, but all except trimethylethylene have terminal double bonds.

In 1934, Burkhardt (16) mentioned that the abnormal addition of thiophenol to styrene might be due to the presence of "sulfur in a positive ion or in an oxidizing form," possibly as a free radical, and possibly through a chain reaction. A more definite proposal that the abnormal addition takes place through a chain reaction involving free radicals was subsequently made from this laboratory (76):

$$\mathrm{RSH} + \mathrm{O_2\ (or\ peroxide)} \xrightarrow{\text{(alkene)}} \mathrm{RS\bullet} + \mathrm{HO_2\bullet} \qquad (16)$$

$$\mathrm{RS\bullet} + \mathrm{R'CH{=}CH_2} \rightarrow \mathrm{R'\underset{\bullet}{C}HCH_2SR}\ (\Delta H = 13\ \text{kg-cal. per mole}) \qquad (17)$$

$$\mathrm{R'\underset{\bullet}{C}HCH_2SR} + \mathrm{RSH} \rightarrow \mathrm{R'CH_2CH_2SR} + \mathrm{RS\bullet}\ (\Delta H = 0) \qquad (18)$$

The effects of oxygen, peroxides, light, and antioxidants and the nature of the addition product so resemble those observed in the abnormal addition of hydrogen bromide that little further comment on these points is necessary. In both instances, the heats of reaction of the corresponding steps, as calculated from estimated bond energies (124), are almost identical (*cf.* table 7). The well-known easy oxidation of mercaptans to disulfides and the suggested dissociation of disulfides into free radicals (132) further support the mechanism suggested.

Substantial addition of mercaptoacetic acid to styrene in the absence

TABLE 9

Evidence of abnormal addition of mercaptans to alkenes

ALKENE	MERCAPTAN	EXPERIMENTAL CONDITIONS*	ADDITION PRODUCT	EVIDENCE OF MECHANISM	REFERENCES
$C_6H_5CH{=}CH_2$	C_6H_5SH	a	$C_6H_5CH_2CH_2SC_6H_5$ (<2% isomer)	Accelerated by light and air; inhibited by piperidine	(6)
$C_6H_5CH{=}CH_2$	CH_3SH	a	$C_6H_5CH_2CH_2SCH_3$	Accelerated by light and oxygen	(51)
$CH_3CH{=}CH_2$	C_2H_5SH	b	n-$C_3H_7SC_2H_5$ (50%) i-$C_3H_7SC_2H_5$ (14%)	Ascaridole as catalyst†	(49)
1-Octene	C_2H_5SH	b	n-$C_8H_{17}SC_2H_5$ (28%) $C_6H_{13}CHSC_2H_5$ (4%) $\vert$ CH_3	Alkene peroxide or ascaridole as catalyst†; only 4 to 5% total sulfides in presence of hydroquinone	(49)
$RCH{=}CH_2$ (R equals $CH_3(CH_2)_n$, where n = 8, 10, 12, 14, 16)	R′SH (R′ equals n-$C_{12}H_{25}$-, phenyl, p-tolyl, or β-naphthyl	b	RCH_2CH_2SR' (nearly quantitatively)	Alkene peroxide as catalyst. Lauryl mercaptan gave < 10% sulfides in presence of hydroquinone.† Thiocresol and peroxide-free tridecene alone gave very small yield; with ascaridole, a good yield	(49)
$CH_3(CH_2)_{10}CH{=}CH_2$	$HS(CH_2)_nSH$ (n = 2 to 12, 18)	b	$CH_3(CH_2)_{12}S(CH_2)_nS(CH_2)_{12}$-$CH_3$ (nearly quantitatively except when n = 18)	Alkene peroxide as catalyst	(49)
n-$C_{12}H_{25}SCH_2CH{=}CH_2$	n-$C_{12}H_{25}SH$	b	n-$C_{12}H_{25}S(CH_2)_3SC_{12}H_{25}(n)$	Ascaridole as catalyst	(49)
$C_6H_5CH{=}CH_2$	$HSCH_2COOH$	a	$C_6H_5CH_2CH_2SCH_2COOH$	Rapid reaction in presence of ascaridole as catalyst. No reaction in absence of air and presence of hydroquinone	(76)
$(CH_3)_2C{=}CH_2$	$HSCH_2COOH$	a	i-$C_4H_9SCH_2COOH$		(76)
$CH_2OHCH{=}CH_2$	CH_3SH	a	$HO(CH_2)_3SCH_3$	Accelerated by oxygen and light; inhibited by piperidine, sulfuric acid; mercury salts had various effects	(50)

* a = reaction in absence of solvent at or near room temperature; b = reaction for 10 hr. in sealed vessel at 180°C. in absence of a solvent.

† Different product obtained without this catalyst; *cf.* table 11.

TABLE 10

Abnormal additions of mercaptans and thio acids to alkenes

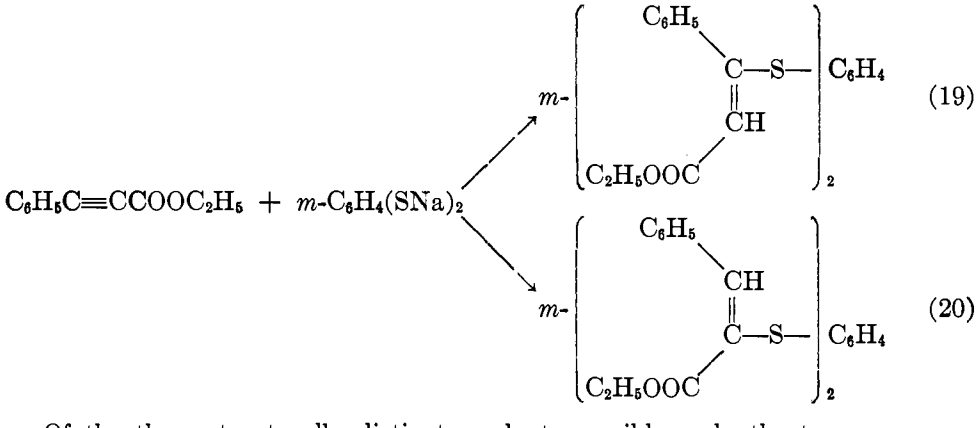
ALKENE	MERCAPTAN OR THIO ACID	TEMPERATURE	ADDITION PRODUCT	REFERENCES
		°C.		
$CH_3CH{=}CH_2$	C_6H_5SH	120	n-$C_3H_7SC_6H_5$ (60%)	(47)
$C_2H_5CH{=}CH_2$	C_6H_5SH	100	n-$C_4H_9SC_6H_5$ (73%)	(47)
$(CH_3)_2C{=}CH_2$	C_6H_5SH	20	i-$C_4H_9SC_6H_5$ (90%)	(47)
n-$C_3H_7CH{=}CH_2$	C_6H_5SH	50	n-$C_5H_{11}SC_6H_5$ (25%)	(47)
i-$C_3H_7CH{=}CH_2$	C_6H_5SH	55	i-$C_3H_7CH_2CH_2SC_6H_5$ (80%)	(47)
$(CH_3)_2C{=}CHCH_3$	C_6H_5SH	Room temperature	$(CH_3)_2CHCH(CH_3)SC_6H_5$* (60%)	(47)
$CH_3CH{=}CH_2$	C_2H_5SH	100	n-$C_3H_7SC_2H_5$ (64%)	(45)
$(CH_3)_2C{=}CH_2$	C_2H_5SH	100	i-$C_4H_9SC_2H_5$ (94%)	(45)
i-$C_3H_7CH{=}CH_2$	C_2H_5SH	Room temperature	i-$C_3H_7CH_2CH_2SC_2H_5$ (5%)	(45)
$(CH_3)_2C{=}CHCH_3$	C_2H_5SH	Room temperature	i-$C_3H_7CH(CH_3)SC_2H_5$ (90%)	(45)
$(CH_3)_2C{=}CH_2$	n-C_4H_9SH	100	i-$C_4H_9SC_4H_9(n)$ (66%)	(45)
$(CH_3)_2C{=}CH_2$	CH_3COSH	100	i-$C_4H_9SCOCH_3$ (60%)	(45)
i-$C_3H_7CH{=}CH_2$	CH_3COSH	100	i-$C_3H_7CH_2CH_2SCOCH_3$ (86%)	(45)
$(CH_3)_2C{=}CHCH_3$	CH_3COSH	70	i-$C_3H_7CH(CH_3)SCOCH_3$ (87%)	(45)
$C_6H_5CH{=}CH_2$	CH_3COSH	Room temperature	$C_6H_5CH_2CH_2SCOCH_3$ (85%)	(41)

* Different addition product obtained under other conditions; *cf.* table 11.

of solvents requires a few minutes (76) or a few hours (40) at room temperature, the rate apparently depending upon the purity of the materials and the presence of light. The addition is said to be about as fast in glacial acetic acid solution as in the absence of a solvent, but it is much slower in benzene (40). There is accordingly a difference between hydrogen bromide and mercaptans with respect to the effect exerted by inert solvents on the rates of the respective abnormal additions of these substances.

C. THE NORMAL ADDITION OF MERCAPTANS

Until recently, the only examples of normal addition of mercaptans to double bonds involved alkenes in which these bonds were conjugated with carbonyl groups, and there only the normal addition was observed. The hydrogen of the mercaptan becomes attached to the α-carbon atom and the sulfur to the β-carbon atom of the unsaturated acid or ketone (121, 145). Such additions are catalyzed by both acids (hydrogen chloride in acetic acid) and bases (piperidine or sodium ethylate). The unilateral addition of mercaptans to such double bonds agrees closely with the behavior of hydrogen bromide; so also does the formation of two products in the one known instance of addition to a triple bond conjugated with a carbonyl group. The following reaction is reported to occur in toluene solution at room temperature (22):



Of the three structurally distinct products possible, only the two symmetrical ones are reported.

Table 11 summarizes normal additions of mercaptans to hydrocarbons, a catalyst being required in every case. Jones and Reid (49) found that sulfur catalyzes the normal addition; Ipatieff, Pines, and Friedman state that sulfuric acid is also effective. The use of sulfuric acid was introduced by Posner (125), who, however, thought that it accelerated the abnormal addition. The mechanism of normal addition of mercaptans is unknown,

TABLE 11

Normal additions of mercaptans to alkenes and alkynes

ALKENE OR ALKYNE	MERCAPTAN	EXPERIMENTAL CONDITIONS*	ADDITION PRODUCT	EVIDENCE OF MECHANISM	REFERENCES
$CH_3CH{=}CH_2$	C_2H_5SH	b	*i*-$C_3H_7SC_2H_5$ (82%) *n*-$C_3H_7SC_2H_5$ (8%)	Sulfur as catalyst†; no reaction in absence of sulfur	(49)
1-Octene	C_2H_5SH	b	$C_6H_{13}CHSC_2H_5$ (59%) $\vert$ CH_3	Sulfur as catalyst†	(49)
$CH_3CH{=}CH_2$	C_6H_5SH	b	*i*-$C_3H_7SC_6H_5$ (*ca.* 35%)	Sulfur as catalyst	(49)
$RCH{=}CH_2$	$C_{12}H_{25}SH$	b	Mixture	Sulfur as catalyst†	(49)
$(CH_3)_2C{=}CH_2$	*t*-C_4H_9SH	c	$(t\text{-}C_4H_9)_2S$	Nickel, cobalt, or iron sulfide as catalyst	(3)
$(CH_3)_2C{=}CH_2$	C_6H_5SH	a	*t*-$C_4H_9SC_6H_5$ (70%)	75% sulfuric acid as solvent and catalyst†	(47)
$(CH_3)_2C{=}CHCH_3$	C_6H_5SH	a	*t*-$C_5H_{11}SC_6H_5$ (60%)	20% sulfuric acid in acetic acid as solvent and catalyst†	(47)
$C_6H_5C{\equiv}CH$	*m*-$C_6H_4(SH)_2$	a	*m*-$C_6H_4(SCC_6H_5)_2$ $\Vert$ CH_2	Sodium salt of mercaptan used	(22)
n-$C_4H_9C{\equiv}CH$	C_2H_5SH	b	*n*-$C_4H_9CSC_2H_5$ $\Vert$ CH_2 and *n*-$C_4H_9C(SC_2H_5)_2$ $\vert$ CH_3	Sulfur as catalyst; structures not proved	(49)

* a = reaction at room temperature; b = reaction for 10 hr. in sealed vessel at 180°C. in absence of solvent; c = reaction under pressure at 35–200°C. (patent claim).

† Different product obtained without this catalyst; *cf.* table 9 or 10.

but several analogies to the normal additions of halogen acids can be pointed out: (*a*) The catalysis of mercaptan addition by sulfuric acid resembles the participation of two molecules of halogen acid in the addition of one such molecule, and suggests that the alkene–acid complex reacts with mercaptan. (*b*) The catalysis of mercaptan addition by bases recalls the accelerating effect of ammonium salts on halogen acid additions, and suggests that mercaptide ion may sometimes participate in the reaction. (*c*) Catalysis by sulfur resembles the catalysis of hydrogen iodide addition by iodine. (*d*) Catalysis by metal sulfides is somewhat analogous to catalysis of halogen acid additions by metal halides.

The fact that an alkene is symmetrically substituted does not prevent the addition of a mercaptan from taking place through two distinct mechanisms. The addition of ethyl mercaptan to cyclohexene is catalyzed by either peroxides or sulfur, although cyclohexyl ethyl sulfide is the only possible product. Peroxide catalysis is prevented by hydroquinone, with the result that no addition takes place (49).

D. SCOPE OF THE MERCAPTAN–ALKENE REACTION

The following work is cited to indicate the applicability of the mercaptan–alkene reaction, but, except in additions to ethylene, the structures of the addition products have not been established. Posner (125) found that thiophenol or benzyl mercaptan would add to a large number of solid and liquid hydrocarbons, the only exceptions noted being stilbene and 1,4-diphenylbutadiene. He obtained no significant addition to ethylene or propene at ordinary temperatures, but Jones and Reid (49) added ethyl mercaptan and trimethylene dimercaptan to ethylene at high temperatures and pressures in the presence of sulfur. Von Braun and Plate (13) explained the ready polymerization of allyl, crotyl, furfuryl, and cinnamyl mercaptans by the interaction of sulfhydryl groups with double bonds. Holmberg (40) found that mercaptoacetic acid added readily to cinnamyl alcohol, its acetate, and its benzoate. The ready addition of mercaptoacetic acid to many unsaturated compounds and the easy estimation of the sulfhydryl group have led to the use of this reaction in the determination of the degree of unsaturation in oils, fats (7), and gasoline (42). It is stated that peroxides in the latter instance retard the reaction of 2-octene, a claim not in accord with any other available information.

Morgan and Friedman (118) have studied the rate and extent of addition of mercaptoacetic acid, cysteine, and glutathione to maleic acid. They used evacuated reaction tubes and buffered aqueous solutions of sodium salts at a pH of 7.4 and a temperature of 37°C. Part of the maleic acid which did not react was isomerized to fumaric acid, a point to be

considered in a later section. However, none of these mercaptan derivatives was found to add to fumaric, citraconic, mesaconic, or α-phenyl-β-styrylmaleic acids or to *cis*- and *trans*-cinnamic acids.

IV. The Reaction of Bisulfites with Unsaturated Compounds

A. INTRODUCTION

It has long been known that ammonium and alkali-metal bisulfites in aqueous solution add to carbon double bonds, thus forming alkyl sulfonates:

$$R_1R_2C{=}CR_3R_4 + NaHSO_3 \rightarrow R_1R_2CHCR_3R_4(SO_3Na) \qquad (21)$$

Until recently, the best-known of these additions were those to aldehydes, ketones, and acids unsaturated in the α,β-positions (144). Here the products were exclusively those which correspond to the ones obtained by normal addition of halogen acids,—the proton going to the α-carbon atom, the sulfonate group to the β-carbon atom. It has also been shown that bisulfites sometimes add to double bonds in alcohols, in aldehydes, and in liquid and gaseous hydrocarbons where these bonds are not conjugated with carbonyl groups (for references see 75, 144), but the structures of most of the products are unknown. Ethylene and cyclohexene give only one addition product; allyl alcohol was concluded to yield 3-hydroxypropyl-1-sulfonate; the structure assigned to the styrene addition product (6) was in error (75).

Kolker and Lapworth (100) shook their reaction mixtures with kieselguhr in order to maintain contact between hydrocarbon and water solution, and thus obtained addition products from several hydrocarbons. They noted that dilution of the bisulfite solution favored reaction. Other workers found that refluxing the reactants was sometimes successful; still others reported that reaction often failed to take place in sealed tubes, even at higher temperatures. Some of these observations suggested that the addition of bisulfite to unconjugated double bonds may take place through a radical-chain mechanism, and subsequent work agrees with this hypothesis. Since the reaction with aliphatic double bonds seems to consist mostly, if not entirely, of simple addition, it will be discussed first. The more complicated reaction with styrene will be considered later.

B. THE ADDITION OF BISULFITES TO ALIPHATIC UNSATURATED COMPOUNDS

The work dealing with the effect of oxidizing agents on the addition of bisulfites to alkenes has been carried out largely in this laboratory; the three different techniques employed will be indicated. Except with allyl alcohol, all the additions of bisulfites were carried out at room temperature.

Bisulfites were added to ethylene, propene, and isobutylene (75, 29) by shaking an aqueous solution of the salts with the gas under pressures

of 15 to 40 pounds per square inch. Under these conditions the gases in question did not react with bisulfites in the absence of oxygen. Admission of a little air permitted reaction to proceed only temporarily, and repeated intermittent admissions were required to obtain substantially complete reaction of the bisulfite. Based on the amount of bisulfite consumed, propene and isobutylene gave as much as 55 per cent and 62 per cent, respectively, of organic sulfonates, the remainder of the salt being oxidized to bisulfate. Ethylene gave lower yields. The products isolated were exclusively the primary sulfonates, corresponding to an abnormal addition of hydrogen bromide or mercaptan. No normal addition of bisulfite is known where the double bond is not conjugated with a carbonyl group. When such conjugation occurs, there is no peroxide effect; experiments with crotonic acid (96) show that, just as in hydrogen bromide additions, oxygen here has no effect either on the rate or the direction of addition.

Liquid cyclohexene, 2-pentene, trimethylethylene, 2,4,4-trimethyl-2-pentene, isoprene, and pinene were shaken with bisulfite solutions under constant oxygen pressures (130). Oxygen was consumed slowly during the course of the reaction, and, if the supply was interrupted, interaction of the hydrocarbon with bisulfite also stopped. The first three of the substances named gave as much as 90 per cent or more of sulfonates, the yields being greatest at 30 mm. of oxygen and decreasing progressively at 152 or 760 mm. The last three alkenes reacted less easily and gave yields of only 15 to 20 per cent. Cyclohexene gave a cyclohexylsulfonate; no other addition products were identified. The product from isoprene still contained one double bond; that from pinene was unstable. Trimethylethylene and 2-pentene seemed to give mixtures of sulfonates.

Additions to allyl alcohol were carried out in sealed tubes at 100°C. (75). Evacuation of these tubes did not prevent addition, but when 10 mole per cent of hydroquinone was added to the reaction mixture before evacuation, no reaction occurred. In the presence of oxygen, up to 65 per cent of sodium 3-hydroxypropane-1-sulfonate was obtained, as demonstrated by conversion of the product to 3-chloropropane-1-sulfonamide. On the assumption that unsymmetrical reagents add to allyl alcohol in the same way that they add to the allyl halides, the above addition to allyl alcohol is abnormal.

In additions to both propene (75) and the liquid alkenes (130), sodium or ammonium nitrites, which are also capable of oxidizing bisulfites, have been found to exert an effect like that of oxygen. In experiments with cychlohexene, 0.06 mole of nitrite per mole of bisulfite, introduced slowly over a long period, gave 84 per cent sulfonate, whereas a larger proportion of nitrite (0.1 mole), introduced all at once, gave only 55 per cent yield. In an experiment with trimethylethylene, 0.005 mole of sodium nitrite

per mole of bisulfite gave 90 per cent yield of addition product, indicating that about 180 molecules of organic sulfonate were formed per molecule of nitrite reduced.

It has already been shown by Franck and Haber (23) and by Bäckström (8) that the oxidation of sulfite and bisulfite are chain reactions involving the $\cdot SO_3^-$ ion radical and the $\cdot HSO_3$ radical. The necessity for using oxygen or other oxidizing agents in the addition reaction, the small proportion of agent required, and the advantage of introducing this agent gradually, as well as the inhibition of the reaction by hydroquinone, and the fact that the product corresponds to an abnormal addition, all suggest a chain reaction involving free radicals (75):

$$SO_3^{--} + \text{oxidant} \rightarrow \cdot SO_3^- + \text{oxidant}^- \quad (22)$$

$$\cdot SO_3^- + RCH{=}CH_2 \rightarrow R\dot{C}HCH_2SO_3^- \quad (23)$$

$$R\dot{C}HCH_2SO_3^- + HSO_3^- \rightarrow RCH_2CH_2SO_3^- + \cdot SO_3^- \quad (24)$$

The extent to which the sulfite-ion radical and the sulfonate-ion radical may be associated with a proton is not known. The range of pH over which addition can take place suggests that either or both charged and uncharged radicals may participate.

The oxidation of bisulfite to bisulfate during oxygen-catalyzed additions causes an increase in the acidity of the solution and a retardation of the addition. The increase in acidity can be overcome by substituting sulfite for that part of the bisulfite oxidized, so that normal sulfate rather than bisulfate is formed. If too large a proportion of sulfite is used, some of this substance adds to the alkene, thus liberating an equivalent of alkali which also retards the addition reaction. If the ratio of sulfite to bisulfite in the initial solution is the same as the ratio of sulfate to sulfonate in the reaction products, then the pH of the sulfite–bisulfite buffer remains practically constant and the addition of bisulfite proceeds at a maximum rate and to a maximum extent. This optimum proportion of sulfite to bisulfite varies with both the rate of oxidation and of addition, and therefore depends upon the concentration of sulfite, the alkene used, and the other experimental conditions. The pH of the sulfite–bisulfite buffer depends upon the sulfite–bisulfite ratio and on the cation.

Although the pH of such buffers is thus of little theoretical significance, some representative data are cited here. In the addition to cyclohexene, using oxygen at 1 atm. pressure, the optimum pH of a sodium salt buffer was about 6.4 and that of a similar ammonium salt buffer about 6.0 (130). In additions to propene, oxygen was supplied intermittently; the optimum pH of a sodium salt buffer was 5.8 (76.5 per cent bisulfite, 23.5 per cent sulfite), and that of an ammonium salt buffer was 6.0 (55 per cent bisulfite, 45 per cent sulfite). With propene, the pH of these solutions remained

constant while 95 per cent of the available sulfite was consumed, and the proportions of sulfonate and sulfate formed corresponded closely to the bisulfite–sulfite ratio (29). It follows that if an alkene reacts sluggishly with bisulfite, the proportion of oxidation increases and a higher proportion of sulfite should be used.

Although the only products isolated from the reaction of bisulfites with simple alkenes are the addition products, there is evidence that some by-products are formed. Kolker and Lapworth (100) observed the formation of variable, but usually very small, proportions of what they thought to be sulfite esters. These by-products were easily oxidized by bromine and permanganate. When hydrolyzed with acid, they yielded sulfur dioxide. By hydrolysis with acid, the formation of small amounts of sulfur dioxide has in some cases been confirmed qualitatively in this laboratory, but since most crude addition products do not reduce iodine (29), the ability of these products to reduce bromine and permanganate is more likely due to unsaturation rather than to the presence of sulfite esters. Attempts have been made, by bromide–bromate titration (105) and by permanganate assay (81), to estimate the degree of unsaturation in the crude sulfonic acids. Since the two methods do not agree and since the existence and proportions of unsaturated sulfonate, hydroxysulfonate, and sulfite esters in the addition products have not yet been demonstrated, the results cannot be considered reliable. In additions to propene (29), about 15 per cent unsaturation in the products is claimed when the buffers are of nearly ideal composition. With more acid or more basic buffers, the yields of sulfonic acids are much lower, but the proportion of unsaturation increases with the acid concentration. In additions to liquid alkenes using oxygen at 1 atm. pressure, 1.5 per cent to 18 per cent unsaturation has been reported in the product. With nitrite instead of oxygen, it was shown conclusively that unsaturation was absent (130). The significance of unsaturation will be considered in the case of styrene, where various reaction products have been isolated and analytical methods have been tested.

The yields of addition products from the less reactive alkenes are decreased by the use of either alcohol or hydrocarbon solvents and slightly increased by the use of ethylenediamine. Since ethylenediamine has little effect in nitrite-promoted additions, it probably serves mostly to inhibit the oxidation of bisulfite (29, 130).

Attempts to add bisulfites to acetylene yielded only traces of unidentified sulfonic acids (29).

C. THE REACTION OF BISULFITES WITH STYRENE

Since the reaction of styrene with bisulfites is fully described in a recent paper (81), the work need be only briefly summarized here. The reactions

were carried out under constant oxygen pressure. At 1 atm. of oxygen, sodium and ammonium sulfite–bisulfite mixtures gave 30 per cent or less of organic sulfonates (the remainder of the sulfite being oxidized to sulfate), but yields up to 68 per cent were obtained at lower oxygen pressures. The reaction of styrene was about as sensitive to excess acid and base as the reactions of those aliphatic olefins which are liquids at room temperature.

In the presence of oxygen, the organic sulfonates always consisted of three types of salts. Where sodium salts were used, the final mixture contained about 25 per cent of addition product (I) corresponding to an abnormal addition reaction, 10 per cent of substitution product (II), and 65 per cent of hydroxysulfonate (III):

$C_6H_5CH_2CH_2SO_3Na$	$C_6H_5CH{=}CHSO_3Na$	$C_6H_5CHOHCH_2SO_3Na$
I	II	III

The proportions of these products varied slightly. Ammonium salts (from ammonia or the methylamines) gave somewhat more substitution product (II) and correspondingly less addition product (I) than sodium salts; ethylene diammonium sulfite gave a higher proportion (82 per cent) of hydroxysulfonate (III). Additions of aqueous sulfurous acid to styrene in the presence of a large excess of dimethylaniline or pyridine gave about 60 per cent yields of total sulfonates. This increase is probably due to the fact that these bases increase the miscibility of bisulfite and hydrocarbon, and that they maintain the pH at a favorable level. Sodium and ammonium nitrites and ammonium persulfate can replace oxygen in promoting the reaction of bisulfite with styrene but they are no more efficient, 30 mole per cent or more of these substances being required for a 15 to 25 per cent yield of total sulfonates. With these oxidizing agents, no unsaturated sulfonate (II) whatever was found, the proportion of both addition product and hydroxysulfonate being increased.

All three types of sulfonates were isolated in the pure state. No one of them is converted into any other under the conditions of the styrene–bisulfite reaction, and all are stable to hot dilute acids and bases. Therefore all three are thought to be primary products.

Since the presence of an oxidizing agent is necessary for the formation of all three sulfonates, and since in all of them the sulfur is attached to the terminal carbon atom, the three reactions are easily correlated by the assumption that the sulfonate-ion radical formed by reactions 22 and 23 is an intermediate common to all. If such is the fact, then the low yields of addition product (I) prove that only a small proportion of the sulfonate-ion radicals formed undergo reaction 24, whereas the large amount of oxidizing agent consumed in the styrene reaction suggests that this agent reacts with the sulfonate-ion radical. The unsaturated sulfonate may be

formed through reaction 25, oxygen being the only oxidizing agent known to give this result:

$$\underset{\bullet}{\text{R}}\text{CHCH}_2\text{SO}_3^- + \text{O}_2 \rightarrow \text{RCH=CHSO}_3^- + \text{HO}_2\bullet \qquad (25)$$

The $HO_2\bullet$ radical may react with bisulfite. The hydroxysulfonate (III) is formed in the presence of oxygen, nitrite, or persulfate:

$$\underset{\bullet}{\text{R}}\text{CHCH}_2\text{SO}_3^- + \text{oxidant} \rightarrow \underset{+}{\text{R}}\text{CHCH}_2\text{SO}_3^- + \text{oxidant}^- \qquad (26)$$

$$\underset{+}{\text{R}}\text{CHCH}_2\text{SO}_3^- + \text{H}_2\text{O} \rightarrow \text{RCHOHCH}_2\text{SO}_3^- + \text{H}^+ \qquad (27)$$

The difference between styrene and the alkenes apparently lies in the ease with which the sulfonate-ion radical reacts with bisulfite (reaction 24). The aliphatic free radicals apparently need little or no activation energy in order to undergo this reaction, and since the concentration of bisulfite is much higher than that of oxygen, the simple alkenes give long chains. The substituted benzyl radical formed from styrene obviously reacts sluggishly with bisulfite, but much more easily with oxygen, considering the low concentration of the latter in solution. If the slow reaction of bisulfite with the substituted benzyl radical is due to the stabilization of the latter by resonance, then this stabilization has little or no effect on the ability of the radical to react with oxidizing agents.

Except for compounds containing carbonyl groups, cinnamyl alcohol seems to be the only styrene derivative whose reaction with bisulfite has been investigated. The reaction depends upon the presence of oxygen (75), but no products have been identified.

V. The Peroxide Effect in Rearrangements

A. Rearrangement of 1-bromo-2-butene and 3-bromo-1-butene

The peroxide effect in the rearrangement of 1-bromo-2-butene and 3-bromo-1-butene was discovered (66) during a study of the addition of hydrogen bromide to butadiene, of which the bromides in question are the two addition products:

$$\text{CH}_2\text{=CHCH=CH}_2 + \text{HX} \begin{cases} \nearrow \text{XCH}_2\text{CH=CHCH}_3 \text{ (“crotyl halide”, IV)} & (28) \\ \searrow \text{CH}_2\text{=CHCHXCH}_3 \text{ (“secondary halide”, V)} & (29) \end{cases}$$

It was shown by Winstein and Young (166) that either bromide when pure undergoes, on standing at room temperature, an allylic rearrangement to an equilibrium mixture of 85 per cent crotyl bromide (IV) and 15 per cent secondary bromide (V). Later, it was shown in this laboratory (66)

that under the combined influence of hydrogen bromide and ascaridole, rearrangement, even at −12°C., is rapid and complete. Under the same conditions, ascaridole alone has no effect; hydrogen bromide alone causes only slight rearrangement. Young and Nozaki (169) have since employed hydrogen bromide and benzoyl peroxide to accelerate these rearrangements, but the reviewers know of no other application of the early finding. The rearrangements of some homologs of these bromides are reported to be highly susceptible to the effects of traces of unspecified catalysts (170). It is probable that the peroxide effect is widespread in allylic rearrangements of bromides, and that therefore the additions of hydrogen bromide and bromine to conjugated systems need reinvestigation.

That the allylic rearrangement sometimes has a molecular or ionic mechanism is shown by a study of the behavior of 1-chloro-2-butene (IV) and 3-chloro-1-butene (V) (71). As expected, peroxides and air have no effect on their rearrangements, which are very slow except in the presence of a catalyst. Small amounts of anhydrous ferric chloride or of a mixture of cuprous and hydrogen chlorides cause isomerization of either chloride to an equilibrium mixture containing about equal proportions of each isomer. This isomerization is rapid with the former reagent, somewhat slower with the latter. A large proportion of hydrogen chloride alone causes slow rearrangement to a different equilibrium mixture, indicating that this acid forms a complex with one or both of the organic halides. These phenomena show that the rearrangements of these chlorides have much in common with the normal addition of halogen acids to alkenes.

The facts that small amounts of both hydrogen bromide and peroxides are required for a very rapid rearrangement of bromides, and that allyl-type chlorides are not susceptible to corresponding influences, suggest that the peroxide-catalyzed rearrangement of bromides proceeds by a chain mechanism involving bromine atoms or free radicals. On this meagre basis, two such mechanisms are tentatively suggested:

$$CH_2{=}CHCHBrCH_3 + Br\bullet \rightleftarrows CH_2BrC\overset{\bullet}{H}CHBrCH_3 \rightleftarrows CH_2BrCH{=}CHCH_3 + Br\bullet \quad (30)$$

$$CH_2C{=}H\overset{\bullet}{C}HCH_3 \text{ (indistinguishable from } \overset{\bullet}{C}H_2CH{=}CHCH_3) + CH_2BrCH{=}CHCH_3 \rightleftarrows CH_2{=}CHCHBrCH_3 + \overset{\bullet}{C}H_2CH{=}CHCH_3 \quad (31)$$

There are two difficulties with the first mechanism. One is that in the addition of a bromine atom to 1-bromo-2-butene the bromine atom might not attach itself to the 3-carbon atom,[20] as required for rearrangement.

[20] This difficulty may not arise if it is assumed that the bromine atom adds to the ethylene bond to give the more stable free radical.

The other difficulty is that, wherever a bromine atom adds to either isomer, subsequent separation of a bromine atom from the free radical formed may be too endothermic for a chain reaction. The second mechanism avoids both of these objections. The energy change involved in reaction 31 is very close to zero, and if the exchanges proceed through a chain reaction, the activation energies must also be small. The free radical necessary to start the chain may be formed as follows:

$$CH_2BrCHCHBrCH_3 \text{ (}cf.\text{ reaction 30)} + CH_2BrCH{=}CHCH_3 \rightarrow CH_2BrCHBrCHBrCH_3 + {\bullet}CH_2CH{=}CHCH_3 \quad (32)$$

The conditions for the rearrangement of the products having been established, the addition of hydrogen chloride and hydrogen bromide to butadiene may be considered. As mentioned in the discussion accompanying table 1, the addition of hydrogen chloride to butadiene gives, over a wide range of temperatures (71), 75 to 80 per cent of secondary chloride (V) and 20 to 25 per cent of crotyl chloride (IV). Isomerization of the products under the conditions of addition is negligible. Addition of hydrogen bromide under conditions most favorable for the normal addition (presence of an antioxidant, absence of air, temperature −78°C.) gives within experimental error the same proportion of isomers. As the temperature of addition is raised to 25°C., the proportion of crotyl bromide formed increases to 56 per cent. If the addition is carried out in the presence of a peroxide, only 40 to 45 per cent of crotyl bromide is formed at −78°C., but 70 to 80 per cent of this bromide (approximately the equilibrium mixture) is formed at −12°C.

Since the addition of hydrogen chloride shows no temperature effect, and since at low temperatures in the presence of antioxidants essentially the same results are obtained with hydrogen bromide, it is concluded that the normal addition of a halogen acid to 1,3-butadiene gives about 80 per cent 1,2-addition and 20 per cent 1,4-addition. In additions of hydrogen bromide at room temperature, or in the presence of peroxides, some or all of the additional crotyl bromide found is due to isomerization of secondary bromide first formed by 1,2-addition. The possibility that addition by an abnormal mechanism increases the proportion of direct 1,4-addition has not been ruled out, but the failure to find any 4-bromo-1-butene excludes the possibility that appreciable abnormal 1,2-addition has occurred in any experiment made to date.

B. REARRANGEMENT OF α-BROMOACETOACETIC ESTERS

It has been shown by Hantzsch and coworkers (33) that α-bromoacetoacetic ester rearranges slowly at room temperature to γ-bromoacetoacetic ester, that this change is accelerated by hydrogen bromide, and that

it is inhibited by water. However, the α-bromo ester, in spite of its instability at room temperature, can be distilled four or five times *in vacuo* at 100°C. without change. The effect of hydrogen bromide explains the differences between the methods for preparing the two esters directly (21). When acetoacetic ester is brominated in the presence of ice and water, pure α-bromo ester is immediately obtained. When slow bromination lasting several hours takes place in carbon disulfide solution, the γ-bromo ester is formed. If, in the latter preparation, hydrogen bromide is removed by intermittent washings with water, mixtures are obtained. This result suggests that the γ-bromo ester is formed by rearrangement of the α-bromo ester. The α- and γ-bromo derivatives of methyl α-methylacetoacetate have been similarly prepared. Ethyl α-chloroacetoacetate has no tendency to rearrange, even in the presence of hydrogen chloride (21). This difference between the α-chloro and α-bromo esters suggested the possibility of a peroxide effect in the rearrangement of the bromo esters.

By a series of experiments, each lasting only a few hours and carried out in glacial acetic acid solution, it was found that air, a peroxide, or light greatly accelerated the rate of rearrangement of the α-bromo ester by hydrogen bromide (68). In the absence of hydrogen bromide, no rearrangement took place in the presence of a peroxide and light, either with or without hydrogen chloride. In glacial acetic acid, the bromination of ethyl acetoacetate in the absence of air, peroxides, and light gave more than 90 per cent α-bromo ester; in the presence of any one of these agents, 80 per cent or more of the γ-isomer was formed. The bromination of ethyl α-methylacetoacetate was very similar, except that rearrangement was more rapid.

The effects of oxygen, peroxides, and light on the rearrangement of α-bromoacetoacetic esters by hydrogen bromide and the stability of the corresponding chloro esters suggest that the rearrangement has much in common with the rearrangements of the butenyl halides and the addition of hydrogen bromide to alkenes. Probably a part, if not all, of the rearrangement takes place through a chain mechanism in some stage of which bromine atoms are involved. Stability of the bromo esters in the presence of a suitable inhibitor would indicate whether the isomerization is exclusively a chain reaction and whether the chain carrier is the same as in the abnormal addition of hydrogen bromide to alkenes. Such experiments have not yet been performed; consequently any discussion of a mechanism is admittedly speculative. Only in order to show that a simple chain can be written is the following mechanism ventured:

$$\bullet CH_2COCH_2COOC_2H_5 + CH_3COCHBrCOOC_2H_5 \rightleftarrows CH_2BrCOCH_2COOC_2H_5 + CH_3\dot{C}OCHCOOC_2H_5 \quad (33)$$

$$CH_3\dot{C}OCHCOOC_2H_5 \rightleftarrows \bullet CH_2COCH_2COOC_2H_5 \quad (34)$$

The mode of formation of bromine atoms has been indicated in an earlier section. These atoms may attack ester molecules to yield the free radicals necessary to start chains. Since the bromination of acetoacetic ester is reversible, the bromine atoms may attack a bromo ester molecule to give either bromine or hydrogen bromide. Like the second mechanism proposed for the rearrangement of the butenyl bromides, the chain here suggested consists of the transfer of bromine atoms from a molecule to a radical; the chain carrier is not a bromine atom, but a radical which can isomerize. Whatever the mechanism of the rearrangement, the product should be an equilibrium mixture of the γ-bromo ester with a small proportion of the α-isomer.

C. CIS–TRANS ISOMERIZATIONS

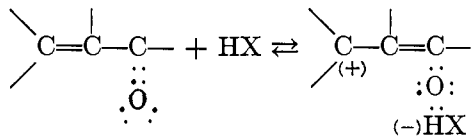
A thorough discussion of the rearrangement of geometrical isomers is beyond the scope of this review on the peroxide effect. Except for recent work, the subject has been covered by both R. Kuhn (24) and Dufraisse (28). In order that isomerization may occur, the resistance of the double bond to free rotation must be overcome. The assumption by some investigators that all such isomerizations take place by a single mechanism has led to some confusion, for at least four distinct mechanisms will be cited for the conversion of a *cis*-ethylene derivative to its *trans*-form.

The first mechanism is associated with the simplest reaction, represented by the homogeneous, apparently unimolecular, rearrangement of dimethyl maleate in the vapor phase (119, 147). This reaction has a fairly high activation energy and requires a temperature of around 300°C. The uncatalyzed liquid-phase isomerizations of isostilbene and its α-chloro derivatives (149) are also unimolecular. They require a temperature of at least 200°C. and have activation energies of about 35 kg-cal. These isomerizations apparently depend on violent collisions to effect rotation about the double bond.

Ultraviolet radiation is known to cause isomerization of ethylene derivatives in the absence of other catalysts. According to Mulliken (118a), absorption of such radiation by an ethylene derivative causes a transition to an excited electronic state in which the perpendicular configuration of the groups placed about the double bond is more stable than the planar configuration characteristic of the unexcited state.

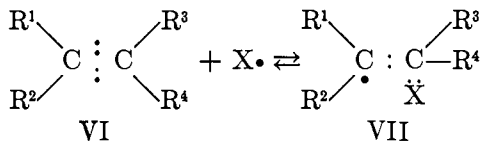
A third type of mechanism is associated with a catalyst which can donate a proton or accept a pair of electrons. Mineral acids (24, 28, 137, 138, 149) are known to be effective in many instances and ineffective in others; primary and secondary, but not tertiary, amines rapidly isomerize dimethyl maleate (18); aluminum, ferric, and zinc chlorides have been effective with the same ester (26); boron trifluoride has been found to rearrange isostilbene, but not dimethyl maleate (127). Various workers have

suggested that one of the doubly bound carbon atoms shares a pair of electrons with the catalyst, leaving the other previously doubly bound carbon atom with a positive charge and free to rotate about the axis of the former double bond. After such rotation, dissociation from the catalyst permits reëstablishment of the double bond and consequent formation of the geometrical isomer. If a carbonyl group is conjugated with the double bond, association of the catalyst may take place at the carbonyl group, but then the double bond is shifted and rotation between the carbon atoms previously doubly bound becomes possible:



(35)

Most of the remaining observations on the effects of catalysts suggest that a fourth type of mechanism involves catalysts with two unpaired or an odd number of valence electrons. For the sake of brevity, it will be assumed that all such catalysts act through a single mechanism, although future work may show that this class of substances should be subdivided. The general scheme is represented by reaction 36:



(36)

VI VII

As in the proton-catalyzed mechanism, rotation about the double bond in the intermediate is possible, but the intermediate here is a free radical. Its stability is unknown. The catalysts include univalent atoms, free radicals, molecules with odd electrons, and paramagnetic substances in general. One class of catalysts which has been assumed to function in this manner consists of the alkali metals (24); these cause isomerization without much reaction on the part of the metal. That the isomerization of isostilbene by stilbene disodium (in the absence of free metal) involves free radicals or metal atoms is possible, but doubtful in view of the statement by Ziegler and Wollschitt (171) that isomerization takes place on regeneration of the ethylene compound (after exchange of metal), but not on the appearance of a single free valence. Platinum and palladium blacks have been found to isomerize maleic acid (148) and its methyl ester (24). Paramagnetic metal ions are also said to isomerize the acid (148). The weak effect of oxygen in accelerating both the vapor-phase (147) and liquid-phase (146, 148) isomerizations may be partly due to the paramagnetism of this substance, but in the isomerization of isostilbene (149) the

effect of oxygen has been ascribed to the fact that it causes the formation of catalytically active acids. Since nitrogen oxides (24, 27, 146) are better catalysts than oxygen for some isomerizations, the probability that they function through a free radical addition product is somewhat greater. A combination of hydrogen sulfide and sulfur dioxide causes isomerization of maleic acid, although neither gas alone is effective. Heating with aqueous bisulfite has caused rearrangement of erucic acid. In both cases the effect has been attributed (24) to the colloidal sulfur formed. More recent work has shown that a combination of aqueous sulfur dioxide and manganese dioxide (120) rearranges maleic acid, its esters, and citraconic acid. In additions of mercaptoacetic acid and glutathione to maleic acid (118), part of the unreacted maleic acid was isomerized to fumaric acid. Glutathione would neither add to, nor rearrange, *cis*-cinnamic acid; hence it was concluded that the sulfhydryl group must be able to add to a double bond in order to cause isomerization. The close analogy between all of of these observations and those on the addition of mercaptans and bisulfites suggests that free radicals (formed as intermediates in the oxidation of bisulfites or hydrogen sulfide by air, peroxides, or manganese dioxide) are the active agents for the observed isomerizations.

This fourth type of mechanism is closely related to the peroxide effect, because halogen atoms can cause the reactions in question. Wachholtz (159) found that the photochemical isomerization of dimethyl maleate by bromine in carbon tetrachloride solution depended only on the quanta absorbed by the bromine, and that quantum yields as high as 600 were obtained. The isomerization was thought to proceed according to reaction 36, but an exchange of bromine atoms between the free radicals (VII) and the unsaturated molecules (VI) seems more likely than a dissociation. Even higher conversions were obtained when bromine atoms, the presumably active agents, were generated by chemical means (160). In water solution, the action of ferrous sulfate on bromine, hypobromous acid, or bromic acid isomerized 10,000, 1000, and 500 molecules, respectively, of maleic acid per atom of bromine formed. Iodine in the light (24, 28) and at elevated temperatures (167) has been found to catalyze other isomerizations; here iodine atoms seem to be the active agent.

Since it is well established (24, 37) that bromine atoms can cause *cis–trans* isomerizations proceeding through chain reactions, the fact that hydrogen bromide can cause similar isomerizations under conditions favorable for previously described peroxide effects is strong support for the contention that, where hydrogen bromide is thus effective, bromine atoms are involved. The peroxide effect in the rearrangement of geometrical isomers was observed in this laboratory in 1937, but only the first portion of this work has yet appeared. Urushibara and Sinamura have subsequently

published several papers in this field; their observations agree with, and extend, those made here. The following description is intended to bring out the relations indicated above and to show how the principal mechanism of isomerization changes with the structure of the unsaturated compound.

In the absence of air and light, the isomerization of stilbene (93, 67, 150) by hydrogen bromide or hydrogen chloride in benzene solution is very slow, requiring several days. The isomerization by hydrogen bromide is accelerated by light, air, peroxides, or by reduced iron or nickel. The accelerating effect of these agents can be overcome by catechol, less effectively by diphenylamine. The isomerization by hydrogen chloride is unaffected by light or peroxides. These results show that there is a slow isomerization by acids through a molecular or ionic mechanism, but that the isomerization by hydrogen bromide proceeds through a much more rapid chain mechanism. That this chain mechanism involves bromine atoms is suggested by the known ability of such atoms to cause isomerizations, together with the fact that small proportions of stilbene dibromide are formed as a result of the oxidation of hydrogen bromide in the presence of air and light (93, 150). α,α-Dichlorostilbene is isomerized by a combination of hydrogen bromide and oxygen, but not by halogen acids alone (149).

In the isomerization of maleic acid and some of its derivatives when the halogen acids are present, rearrangement by the bromine-atom chain mechanism is negligible compared with that by the ionic or molecular mechanism. Sinamura (137) found that the isomerization of dimethyl maleate by hydrogen bromide is unaffected by oxygen or antioxidants and that hydrogen chloride is nearly as effective as hydrogen bromide in producing the reaction. Kharasch, Mansfield, and Mayo (93) found that isomerization of maleic acid, maleic ester, and bromomaleic acid in air was catalyzed to about the same extent by both hydrogen bromide and hydrogen chloride.

Further work by Sinamura (138) shows that the behavior of methyl allocinnamate is intermediate between that of maleic ester and stilbene with respect to both mechanisms. With this compound, hydrogen chloride is distinctly less effective than hydrogen bromide, and the isomerization by hydrogen bromide is only moderately accelerated by oxygen or partially inhibited by catechol. Work in this laboratory (93) shows that isomerization of the labile form of α-phenylcinnamic acid to the stable form by hydrogen bromide is accelerated by air and light, whereas the apparently slower isomerization by hydrogen chloride is not.

From the foregoing discussion it seems probable that acids usually cause isomerization of a *cis*- to a *trans*-ethylene derivative. This mechanism is

most important when the ethylene bond is conjugated with one or more carbonyl groups. Probably any type of ethylene derivative can also isomerize by the atom or radical type of mechanism. Examples of the isomerization of maleic acid derivatives by the bromine-atom mechanism have been cited, but two groups of workers have failed to observe any evidence of this mechanism in the presence of hydrogen bromide. It may therefore be concluded tentatively that, with maleic acid derivatives, the action of hydrogen bromide or hydrogen chloride through the polar mechanism is large compared with the action of the former reagent through the atom mechanism. The reverse is true for isostilbene, whereas the behavior of allocinnamic ester is intermediate.

Such considerations show also that the varying effectiveness of different reagents, which has often in the past been described as anomalous, may easily be fitted into a general scheme. Some *cis*-derivatives should be expected to rearrange easily by several mechanisms, whereas others may rearrange with difficulty by some or all mechanisms. Accordingly, it is not at all surprising that one group of investigators found no correlation between catalytic activity and magnetic susceptibility (26). In the large amount of experimental work required to permit comparisons between different alkenes or different catalysts, it will be necessary to establish the mechanism of each isomerization.

VI. Conclusion

In all the studies discussed in the foregoing review the experimental facts seem to be best explained by the hypothesis that the striking effects of oxygen and peroxides arise out of their ability to initiate chain reactions in which atoms or free radicals act as chain carriers. So-called solvent effects and inhibitory effects of traces of various materials are best interpreted as the result of their effects on chain reactions. Many discrepancies in observations recorded in the earlier literature are explained; many hitherto isolated phenomena are correlated; and many supposed abnormalities are reduced to parts of a logical pattern.

It is perhaps of even greater significance that a new and broader outlook on organic reactions in general is opened up by this hypothesis. The concept of chain reactions in solution, involving atoms or free radicals, will doubtless in many cases supersede earlier limited and inadequate notions which ascribed all reactions to simple unimolecular or bimolecular mechanisms. In any event, it now seems a necessary supplement to such ideas.

Even though future work may necessitate changes in the theoretical concepts of chain reactions, the present ideas have served as a powerful working hypothesis. Already they have been applied in this laboratory

to several classes of reactions other than those here discussed. Such applications are the following:

1. The bromination of phenanthrene (72), toluene (73), cyclopropane (78), cyclohexane, methylcyclohexane, isobutane (90), aliphatic acids, acid halides, and anhydrides (91).

2. The use of sulfuryl chloride (in the presence of a peroxide) as a chlorinating agent for aliphatic compounds (79, 82, 86).

3. The use of sulfuryl chloride (under illumination in the presence of pyridine) as a sulfonating agent for aliphatic compounds (80, 89).

4. The introduction of the —COCl group into aliphatic compounds by the use of a peroxide and oxalyl chloride (92), or by the use of light and either oxalyl chloride or phosgene (85).

5. The use of peroxides in accelerating the chlorination of hydrocarbons in the dark (88).

It is hoped that a review of these and related phenomena will be undertaken when sufficient data become available.

The principles discussed in this paper have been developed in collaboration with Prof. M. S. Kharasch over a period of several years. He has assisted in determining the scope of this review and has offered many helpful criticisms of its content. Dr. James K. Senior has greatly assisted the authors in the revision of the manuscript.

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