

FRACTIONATION OF SULFUR ISOTOPES  
IN THE BISULFITE ADDITION REACTION

By

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### ABSTRACT

The equilibrium constants for the isotopic exchange of  $S^{32}$  and  $S^{34}$  have been measured for the equilibrium reaction of bisulfite ion with eight different carbonyl compounds. This was accomplished by comparing the mass spectrometric measurements of the  $S^{32}/S^{34}$  abundance ratios of the reacting bisulfite ion and the addition compound. The  $S^{34}$  was found to concentrate to the extent of 1-2% in the addition compound. These equilibrium constants have been put to a unique use to confirm that the addition compound has a carbon-sulfur bond structure rather than a carbon-oxygen-sulfur structure.

An attempt has been made to measure the isotope effect in the formation of the carbon-sulfur bond under conditions which favour an unidirectional process. The effect appeared to be zero. It is proposed that the initial product of the reaction has the carbon-oxygen-sulfur structure and that this compound is then rapidly converted to the more stable carbon-sulfur bond form, fractionation of the sulfur isotopes occurring in the latter process only.

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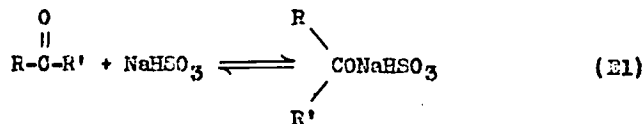
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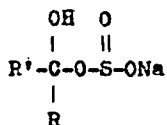
## INTRODUCTION

The reaction of aldehydes and ketones with alkali bisulfites to form an addition compound has long been investigated since the mechanism of formation and the structure of the products have presented an interesting field of research.



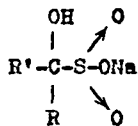
where R, R' are alkyl, aryl, or hydrogen.

Until the 1920's there was considerable controversy about the structure of this compound. Early evidence supported a structure that involved a carbon-oxygen-sulfur linkage:



Structure I

During the last three decades, however, physical and chemical evidence has been presented which strongly supports a structure involving a carbon-sulfur bond:



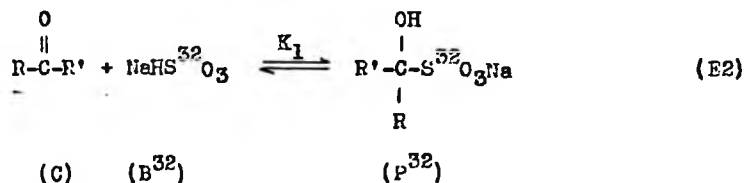
Structure II

This more recent evidence, supporting the latter structure, is indicative but not completely conclusive.

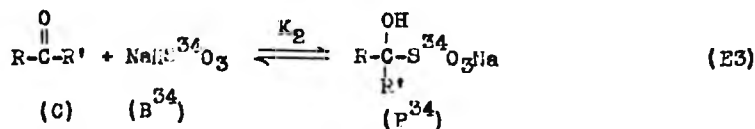
As a main objective, this thesis presents conclusive evidence for the carbon-sulfur bond structure by a unique use of isotope exchange equilibrium constants.

For a carbon-sulfur bond structure, the ratio of the two most abundant isotopes, S<sup>32</sup> and S<sup>34</sup>, in the addition compound formed under equilibrium conditions from an excess of bisulfite should differ measurably from the ratio in the remaining bisulfite, as shown in the following explanation. The reaction for each isotopic species may be written as follows:

for S<sup>32</sup>,



and for S<sup>34</sup>,



Using C, B<sup>32</sup>, P<sup>32</sup>, B<sup>34</sup>, and P<sup>34</sup> to represent the concentrations in the above equations as designated, the equilibrium constant, K<sub>1</sub>, for the S<sup>32</sup> species may be expressed as:

$$K_1 = \frac{P^{32}}{C \times B^{32}}$$

and similarly for the S<sup>34</sup> species the equilibrium constant, K<sub>2</sub>, is given by:

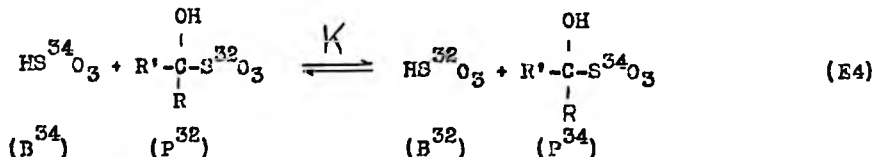
$$K_2 = \frac{P^{34}}{C \times B^{34}}$$



Dividing  $K_2$  by  $K_1$ , the following expression is obtained:

$$K = \frac{K_2}{K_1} = \frac{P^{34}/B^{34}}{P^{32}/B^{32}} = \frac{B^{32}/B^{34}}{P^{32}/P^{34}} \quad (M1)$$

where  $K$  is the equilibrium constant for the isotopic exchange reaction:



The ratio  $P^{32}/P^{34}$  gives the  $S^{32}/S^{34}$  abundance ratio in the addition compound and  $B^{32}/B^{34}$  abundance ratio in the bisulfite at equilibrium with the addition compound. When a large excess of bisulfite is used, the  $S^{32}/S^{34}$  abundance ratio of the original bisulfite may be used for the  $B^{32}/B^{34}$  ratio in the equilibrium reaction expression  $\frac{M1}{\Lambda}$  without introducing an appreciable error.

Theoretically it has been shown that the fractionation of isotopes in equilibrium processes depends on the change in the ratio of the partition functions for the two isotopic species in going from reactant to product. This is better understood when partition functions are defined in terms of the vibrational frequencies of the molecules involved; then a change in bonding about a certain atom changes the vibrational frequencies for the isotopic species by different amounts, causing a fractionation of the isotopes of the elements concerned between reactants and products. If a carbon-sulfur bond is formed in the addition product then the bonding about sulfur is different than in the bisulfite ion. The isotopic exchange reaction constant,  $K$ , which may be expressed in

terms of partition functions by the expression,

$$K = \frac{Q_{B^{32}}}{Q_{B^{34}}} \bigg/ \frac{Q_{P^{32}}}{Q_{P^{34}}}$$

will then differ appreciably from unity. The Q's in this expression are the partition functions of the isotopic species indicated. If, on the other hand, a carbon-oxygen-sulfur bond is present in the addition compound, then the bonding about sulfur is essentially the same as in the original bisulfite. The partition function ratio above will be very close to unity and no appreciable fractionation of the isotopes should occur. In this way, it should be possible to establish the structure of the bisulfite addition products.

The isotopic exchange equilibrium constant for eight aldehydes and ketones, namely, heptaldehyde, benzaldehyde, anisaldehyde, acetone, methyl ethyl ketone, methyl isobutyl ketone, methyl n-amyl ketone, and methyl n-hexyl ketone, have been measured and found to have values ranging from one to two per cent, with the S<sup>34</sup> concentrating in the addition compound. This value is of the same order of magnitude as the equilibrium constant for the sulfur dioxide-bisulfite ion exchange reaction. In the latter a sulfur-oxygen bond that is present in the bisulfite is not found in the sulfur dioxide; in the bisulfite addition reaction the bonding of the sulfur atom has apparently been changed in converting from the bisulfite ion to the carbonyl addition product.

In order to confirm the theoretical conclusion stated above, namely, that there should be no fractionation of the sulfur isotopes if the bonding of the sulfur atom is unchanged during the reaction, the

fractionation of the sulfur isotopes in the reaction of propene with sulfuric acid producing diisopropyl sulfate (in which a carbon-oxygen-sulfur bond is known to be present) has been studied under equilibrium conditions. As predicted, only a very small fractionation, 0.2%, was observed.

The study of the variation of isotopic equilibrium constants for the bisulfite addition reaction with complexity and molecular weight of the carbonyl reactant has been made. The results indicate that the magnitude of the equilibrium constant is greatest for the carbonyl compounds of low molecular weight. This may be explained in terms of the influence of isotopic mass of the sulfur atom on the vibrational frequencies of bonds in the carbonyl component.

A further aspect of the present investigation has involved a determination of the magnitude of the isotope effect in the formation of the bisulfite addition product under conditions which favour an unidirectional (non-equilibrium) process. This has been accomplished by shaking the carbonyl component with a large excess of saturated bisulfite solution for as short a period as possible and removing the first small amount of precipitated addition compound formed. The results obtained indicate that the unidirectional isotope effect in what was thought to be carbon-sulfur bond formation is zero. The rate with which isotopic equilibrium was attained was also studied and the results obtained, in conjunction with the zero isotope effect result, are accounted for by a theory that postulates the rapid formation of an  $\alpha$ -hydroxy sulfite ester (structure I) followed by a slow conversion to the

thermodynamically more stable  $\alpha$ -hydroxy sulfonic acid (structure II).  
Fractionation of the sulfur isotopes would be expected to occur only  
as the second structure forms.

## HISTORICAL INTRODUCTION

### Bisulphite Addition Compounds

Since the discovery of the bisulfite addition compounds about 1850, there has been considerable disagreement concerning their structure. By the beginning of our present century, however, it had been established that this structure was either an  $\alpha$ -hydroxy sulfite ester type:



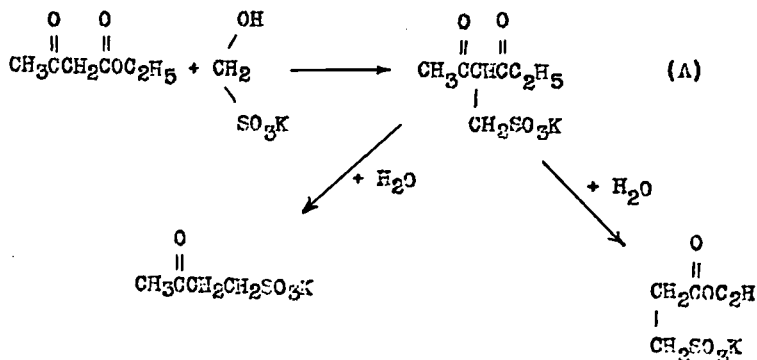
or an  $\alpha$ -hydroxy sulfonic acid type:



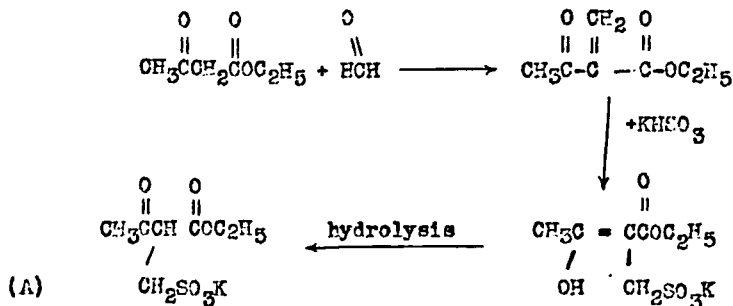
Müller (1) prepared what he considered to be hydroxy methane sulfonic acid,  $\text{HO-CH}_2\text{-SO}_3\text{H}$ , by sulfonating methyl alcohol and showed that this product had entirely different properties from the formaldehyde bisulfite compound. Other so-called  $\alpha$ -hydroxy sulfonic acids were also prepared (2,5) and shown to be different from the corresponding bisulfite addition compounds. From work initiated by Knoevenagel (3) it was thought that the formation of  $\alpha$ -hydroxy nitriles from potassium cyanide and the bisulfite addition compounds was characteristic of the C-O-S-O<sub>2</sub>H grouping of the first structure.

Raschig and Prah1 (4) in 1926 showed that the compound obtained by Müller was actually symmetrical acetone disulfonic acid

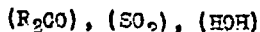
$\text{EOSO}_2\text{-CH}_2\text{-C(=O)-CH}_2\text{-SO}_2\text{OH}$ , formed from the sulfonation of acetone present as an impurity in the methyl alcohol of that period. They showed that methyl hydrogen sulfate,  $\text{HOCH}_2\text{OSO}_2\text{H}$ , the actual product from the sulfonation of methanol, was an isomer of hydroxy methane sulfonic acid. With this false evidence for structure I removed, they presented the following reaction as evidence for structure II:



The products formed by hydrolysis of compound A were definitely established as sulfonic acids. However Schroeter (5), the main opponent of structure II in the 1920's, suggested that this reaction might well follow another course:

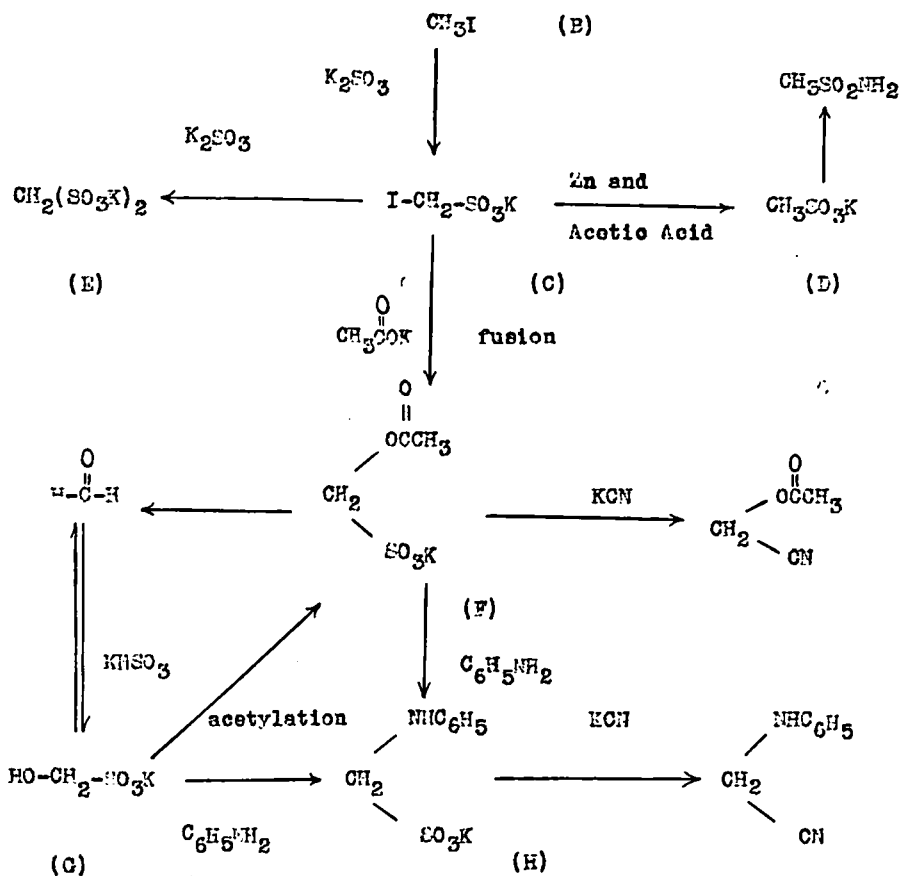


where the free formaldehyde added to the acetoacetic ester with the splitting out of water, followed by a 1, 4 addition of potassium bisulfite to yield the sulfonic acid. Schroeter suggested a stable "trimolecular" formula of type:



Becker and Mulder (6) produced further independent evidence for structure II by treating the bisulfite addition compound with ammonia to give aminomethane sulfonic acid,  $NH_2CH_2SO_3H$ , the structure of which was established by chlorination with nitrosyl chloride in water to produce chloromethane sulfonic acid,  $ClCH_2SO_3H$ . The structure of the latter was considered to have been previously established as a sulfonic acid type by a synthesis involving the reaction of dichloromethane with a sulfite. Schroeter (7) cast some doubt upon the structure of the aminomethane sulfonic acid in a preliminary communication that was not confirmed by additional publication.

Lauer and Langkemmerer (8) presented an excellent piece of chemical evidence for the existence of structure II by carrying out the following series of reactions:

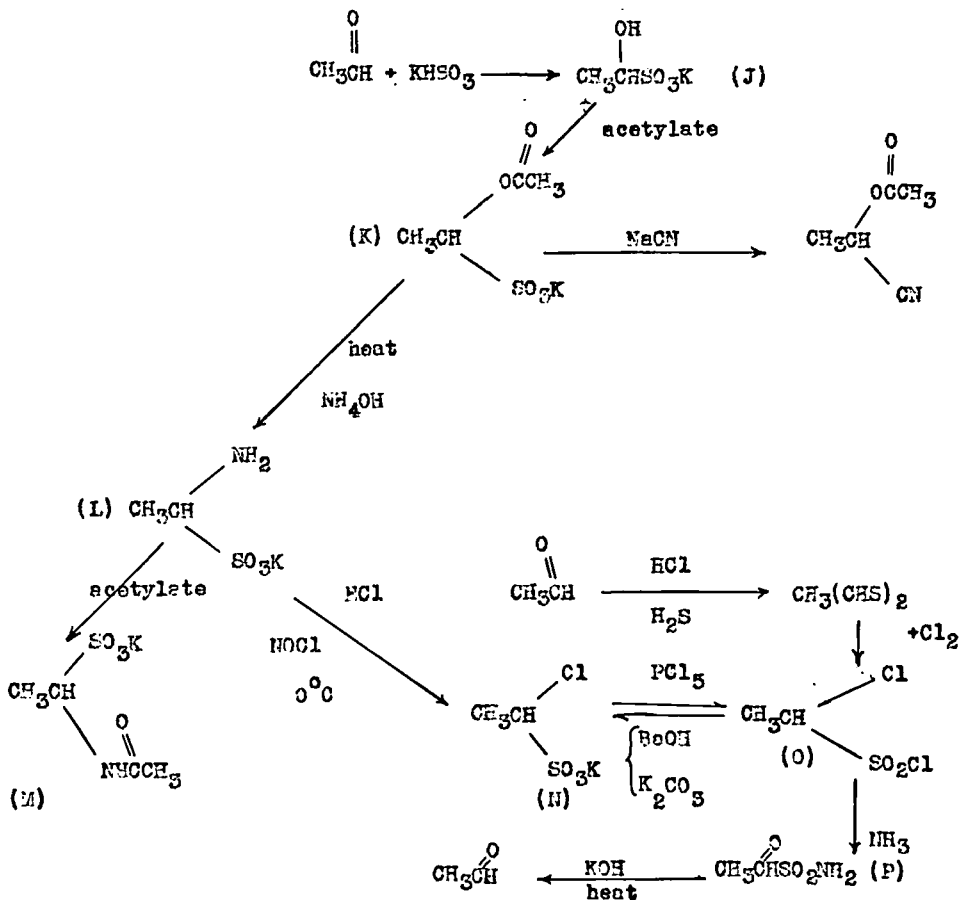


Iodomethane sulfonic acid, C, is definitely a sulfonic acid since it can be transformed into methionic acid, E, of known structure and into methane sulfonic acid, D, whose structure is proven by forming a sulfonamide. Fusion (about 200°C) of compound C with potassium acetate, and acetylation of the formaldehyde bisulfite addition compound, G, each yields acetoxymethane sulfonic acid, F. Preparation of compound H provides evidence for the structure of compounds F and G since replacement



of the  $\text{SO}_2\text{K}$  group (in H) by cyanide to form a nitrile derivative is indicative of the sulfonic acid. The compound F may also be converted to a nitrile. They presume that the addition compound of formaldehyde is typical of all carbonyl bisulfite addition compounds.

Shriner and Land (9) have added chemical evidence to the  $\alpha$ -hydroxy sulfonic acid structure by investigating the structure of the addition compound of acetaldehyde and potassium bisulfite using the following series of reactions:



The bisulfite addition compound, J, was acetylated to give compound, K, which was in turn converted to  $\alpha$ -aminoethane sulfonic acid, L, by heating K with ammonium hydroxide. The structure of L was established by forming an acetylated derivative, M, and also by a series of reactions whereby it was converted through  $\alpha$ -chloroethane sulfonic acid, N, to  $\alpha$ -chloroethane sulfonyl chloride, O. The structure of the latter was proven by synthesis from acetaldehyde, as indicated, and by decomposition to acetaldehyde through the intermediate sulfonamide, P.

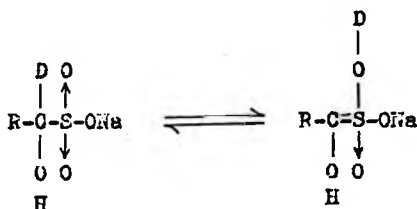
Although this chemical evidence appears to be conclusive, there is always the possibility that unknown and unexpected rearrangements in one or other of these reactions would invalidate the results. Hence more substantial proof for the carbon-sulfur bond structure is needed.

Some physical evidence has also been presented in support of structure II. Stalling (10) found that the absorption band of formaldehyde and acetone bisulfite compounds occurs at 4992.0  $\mu$ , that of sulfonic acid at 4992.2, that of alkyl sulfites at 4996.0, and that of dialkyl sulfites at 4997.7  $\mu$ . Hence, he logically concludes that bisulfite addition compounds have the constitution of the  $\alpha$ -hydroxy sulfonic acid structure.

Caughlen and Tartar (11) made use of Raman spectra in structure studies of the addition compounds. The band frequencies of the addition compounds of the four aldehydes, C<sub>1</sub> to C<sub>4</sub>, and acetone were measured and frequencies corresponding to a carbon-sulfur bond were observed. There was a disappearance of the frequency characteristic of the carbonyl group, thus eliminating Schroeter's "polymolecule" type. Because of the presence of the frequency characteristic of the carbon-sulfur bonds these results

indicate that structure II is the true one. However this again is not conclusive proof since some of the characteristic carbon-sulfur bond frequencies were observed for the free aldehydes themselves. This raises the question as to how precisely, in the present case at least, it is possible to assign a certain frequency to a given bond only.

Additional, but certainly not conclusive, physical evidence was presented by Thompson and Cronwell (12) using deuterium enriched aldehydes. They found that the deuterio aldehydes would not exchange their deuterium with conductivity water, whereas deuterio aldehyde bisulfite compounds would. They interpreted these results with regard to mechanism and structure in two ways. First, that there was an enolization of the sulfonic acid type compound:



which they suggest, could only take place if the sulfur is bonded to the carbon. They suggested, as an alternative explanation for their results, that the sulfur attached to the carbonyl carbon serves to mobilize the deuterio atom by withdrawing the electrons of the carbon-deuterium bond slightly from the deuterium. However, if this were the mechanism then it would be expected that the more electronegative oxygen would draw electrons even more effectively than the sulfur. Hence, it would appear that the latter mechanism would tend to support a carbon-oxygen-sulfur structure.

### Isotope Fractionation

Although isotopes have been known for half a century, it is only in the past twenty years that they have occupied a foremost position in scientific research. In equilibrium processes, a fractionation of isotopes results because of slight differences in thermodynamic properties of molecules containing the different isotopic species. This property has been used chiefly to concentrate the rarer isotopes for study and tracer work. In unidirectional processes, an isotope effect results because of the differences in reactivity of the isotopic species. This latter arises from differences in zero point energy in both reactants and activated complex for the isotopic species.

Isotope fractionation in the lighter elements was realized in the early 1930's when it was first calculated and then experimentally found that deuterium oxide ( $D_2O$ ) electrolyzed less readily than water ( $H_2O$ ). Here the difference in thermodynamic properties is well pronounced because of a large percentage mass difference. However for heavier elements small differences in properties between the isotopes might be expected, with this difference becoming increasingly smaller the heavier the element.

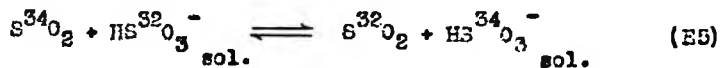
In 1935, Urey and Greiff (15) calculated equilibrium isotopic exchange constants for many reactions involving elements in the first period of the periodic table. They based their calculations on slight differences in the thermodynamic properties of the isotopic species. One typical example was:



for which the equilibrium constant was calculated to be 1.044 at 0°C. In other words the  $O^{18}$  isotope concentrates in the carbon dioxide to the extent of 4.4%. In 1947, Urey (14) presented a noteworthy paper entitled, 'The Thermodynamic Properties of Isotopic Substances', in which he compares theoretical and experimental equilibrium constants of most known isotopic exchange reactions, showing excellent agreement in every case.

Thode et al. (15) have presented an excellent discussion of sulfur isotopes with regard to their mass spectrometric measurement and natural fractionation. Thode and Tudge (16) have discussed thoroughly the thermodynamic properties of isotopic compounds of sulfur, calculating, by use of partition functions, the equilibrium constants for many reactions involving sulfur isotopes.

The reaction:



has been found experimentally (15) to have an equilibrium constant of 1.019 at 25°C., meaning a 1.9% concentration of  $S^{34}$  in the bisulfite ion. The reaction is consistent with others where it has been shown that the heavier isotope concentrates in the most highly oxidized form of the element concerned, or if the reaction is not one involving oxidation, in the form involving the greatest number of valence bonds. In the bisulfite addition reaction, which is being studied here, there is a greater number of valence bonds in the addition compound than in the original bisulfite and fractionation might be expected to be of the order of that for the bisulfite-sulfur dioxide reaction (equation

E4 in the introduction may be compared to E5 above). Unfortunately the equilibrium constant for neither of these reactions can be calculated theoretically because of the lack of data on vibrational frequencies for bisulfite ion and the bisulfite addition compound.

During the past ten years a number of papers have been published on isotope effects in unidirectional reactions. Some early work reported isotope effects involving hydrogen and deuterium bonds in dissociation reactions by electron impact in a mass spectrometer. Delfose and Hipple (17) found that dissociation of di-deutero-ethylene,  $\text{CFD}=\text{CHD}$ , by electron impact produced twice as many CD ions as CH ions, indicating that a carbon-hydrogen bond will rupture in preference to a carbon-deuterium bond. Further evidence of isotope effects in dissociation by electron bombardment has been presented for the isotopes of hydrogen, carbon and nitrogen (18, 19, 20).

Yankwich and Calvin (21) studied the decarboxylation of malonic acid containing  $\text{C}^{14}$  in one carboxyl group and reported a 12% preferential rupture of the  $\text{C}^{12}-\text{C}^{12}$  bond over the  $\text{C}^{12}-\text{C}^{14}$  bond. Bigeleisen and Friedman (22) and later, in this laboratory, Lindsay, Bourns and Thode (23) both working with normal malonic acid found only a 2% effect with  $\text{C}^{13}$ . Although this was much lower than expected on the assumption that the effect for  $\text{C}^{13}$  should be half that for  $\text{C}^{14}$ , it nevertheless agreed closely with a theoretical value calculated by Bigeleisen. Recently, Roe and Hellman (24) repeated the work with  $\text{C}^{14}$  malonic acid and found a  $6\% \pm 2\%$  effect, which approaches the 4% theoretical value. This above effect is described as intramolecular compared to an intermolecular isotope effect in which the ratio of rate of formation of  $\text{C}^{12}\text{O}_2$  from

from malonic acid containing only  $C^{12}$  has been compared to twice the rate of formation of  $C^{13}O_2$  from the acid containing a  $C^{13}$  in one carboxyl group. Bigeleisen and Friedman (22) have reported this as a 3.7% effect, whereas Lindsay et al. (23) have published a value of 4.6%. However, Lindsay in recent and more precise work in this laboratory has obtained a value of 3.7%. An isotope effect of approximately the same magnitude has been reported in the decarboxylation of normal mesitoic acid (25) and normal trichloroacetate ions (26). From these results, Bigeleisen concludes that the isotope effect is not appreciably influenced by the nature of the acid nor the medium.

Stacey (27), in this laboratory, has measured the nitrogen isotope effects involved in the thermal deamination of normal phthalamide. He has shown a preferential splitting amounting to 1% - 1.5% of the  $C^{12} - N^{14}$  bonds compared to the  $C^{12} - N^{15}$  bonds in phthalamide - $N^{14}N^{15}$  molecules (the intramolecular effect), but found that the rates of decomposition of phthalamide molecules containing only  $N^{14}$  atoms and those containing a single  $N^{15}$  atom were approximately equal (intermolecular effect). He accounted for this on the basis that an isotope effect in the formation of the new carbon-nitrogen bond was equal and opposite to that occurring in bond rupture.

Bigeleisen (28) used a theoretical approach to predict the isotope fractionation in decomposition reactions. He stated that the  $k_1/k_2$  ratio, where  $k_1$  and  $k_2$  are the rate constants for the reaction of the light and heavy isotopes respectively can be calculated from the following equation:

$$\frac{k_1}{k_2} = \frac{K_1}{K_2} \cdot \frac{f}{f^\ddagger} \cdot \left[ \frac{m_2^\ddagger}{m_1^\ddagger} \right]^{\frac{1}{2}},$$

where  $K_1$  and  $K_2$  are the respective transmission coefficients whose ratio closely approximates unity,  $f$  and  $f^\ddagger$  are the respective functions for reactants and transition states involving the fundamental vibrational frequencies of the two molecular species, and  $m_1^\ddagger$  and  $m_2^\ddagger$  are the respective reduced masses for the light and heavy isotopes involved in the bond being broken.

It would be theoretically possible, in our case, to calculate the isotope effect in the reverse bisulfite addition reaction in which a carbon-sulfur bond is being broken as bisulfite addition compound decomposes to carbonyl and bisulfite. However the vibrational frequencies for neither the bisulfite nor the bisulfite addition compound are known and most certainly those for the transition state cannot even be predicted. Hence, a relatively large error must be introduced by approximating  $f/f^\ddagger$  to unity for calculation of  $k_1/k_2$ . Considering the two bonds being broken as  $C^{12} - S^{32}$  and  $C^{12} - S^{34}$ , the approximate isotope effect, as calculated on the basis of the reduced masses alone, turns out to be 1.008, meaning the  $C^{12} - S^{32}$  bond decomposes 0.8% more readily than the  $C^{12} - S^{34}$  bond. This value is no doubt low. Bigeliesen, however, has had considerable success using this method since he has been able to make a reasonable assumption concerning the  $f/f^\ddagger$  ratio even though he had no definite data on the vibrational frequencies of the transition state.



Isotope effects in formation of bonds have never been measured directly, since the bond forming reactions so far studied have always involved a mechanism that required breaking of old bonds as the new bonds were formed. On the basis of the theory that isotopic species react at different rates and of the experimental work by Stacey (27), some isotope effect in bond formation should be expected. This expectation is further supported by considerations of the experimental work by Lindsay and Thode (29) on malonic acid (23) and oxalic acid (30) decomposition reactions.

A consideration of activation energies for isotopic species would also lead to a prediction of isotope effects in bond formation. The activation energy in the formation of a bond would be expected to vary for the isotopic species because of differences in zero point energy for reactants and activated complex, the latter having partially assumed the configuration of products. The smaller the activation energy of a reaction, the smaller the difference in energy for the isotopic species, and the less the fractionation that would result. In the bisulfite addition reaction, only a small activation energy is required for aldehydes compared to that for ketones and hence fractionation of the sulfur isotopes might be expected to be less for the aldehyde bisulfite reaction. However, a sulfur isotope effect in the formation of the carbon-sulfur bond would be expected to be measurable for the reaction of both aldehydes and ketones with bisulfite.

## EXPERIMENTAL

### General

Sodium bisulfite of natural isotopic abundance was used in the investigation. This was possible since the abundance of the  $S^{34}$  isotope in nature is of the order of 4% and, furthermore, errors arising from contamination of samples are very much smaller than would be the case using enriched material. The natural abundances of the sulfur isotopes,  $S^{32}$ ,  $S^{33}$ ,  $S^{34}$ , and  $S^{36}$  are in the ratio of the numbers 95.1, 0.74, 4.2 and 0.016. The isotopic fractionation between  $S^{36}$  and  $S^{32}$  is approximately twice that between  $S^{34}$  and  $S^{32}$ ; however, because of the difficulties in mass spectrometric measurement of the very low abundances of  $S^{36}$ , it was decided to measure the fractionation between  $S^{32}$  and  $S^{34}$  isotopes only.

As outlined in the Introduction, the equilibrium constant,  $K$ , is given by:

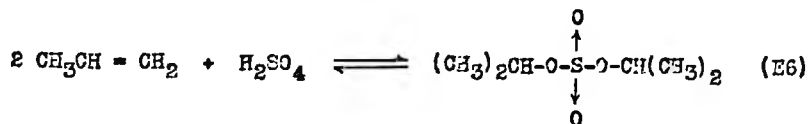
$$K = \frac{K_1}{K_2} = \frac{B^{32}/B^{34}}{P^{32}/P^{34}} \quad (11)$$

where the  $P^{32}/P^{34}$  ratio is the relative abundance of  $S^{32}$  and  $S^{34}$  in the product and the  $B^{32}/B^{34}$  ratio is the relative abundances of  $S^{32}$  and  $S^{34}$  in the excess bisulfite remaining at the end of the reaction.

A saturated solution of bisulfite was prepared and the carbonyl compound added in such quantities as to have an excess of bisulfite. The reaction mixture was shaken for at least a week to establish

isotopic equilibrium and the addition compound which precipitated was separated and decomposed completely to sulfur dioxide gas which was analyzed on the mass spectrometer for  $S^{32}$ ,  $S^{34}$  abundance giving the  $P^{32}/P^{34}$  value. The  $B^{32}/B^{34}$  ratio was not readily obtainable since the remaining bisulfite could not be separated from the bisulfite addition compound that remained dissolved. However the  $S^{32}/S^{34}$  ratio in the original bisulfite could be obtained by mass spectrometric analysis of the sulfur dioxide produced by its complete decomposition. Since the extent of reaction and the original concentration of carbonyl compound and bisulfite were known together with the abundance of the sulfur isotopes in the original bisulfite and in the addition compound, it was possible to calculate the correct equilibrium constant,  $K$ . If a large excess of bisulfite was used, this correction is almost negligible, since the depletion of  $S^{34}$  from the bisulfite is very small.

In the diisopropyl sulfate reaction, where a carbon-oxygen-sulfur bond is formed:



the fractionation of the sulfur isotopes under equilibrium conditions can be measured by a similar procedure as used with the bisulfite addition compounds. The diisopropyl sulfate was formed by reacting propene with an excess of concentrated sulfuric acid under equilibrium conditions at low temperatures. It was separated from the remaining acid by benzene extraction and vacuum distillation, and its sulfur was

obtained as barium sulfate by complete hydrolysis in aqueous barium chloride solution. The remaining sulfuric acid was also precipitated as barium sulfate and conversion of the barium sulfate from each to sulfur dioxide was accomplished by a standard procedure (31). Mass spectrometric analysis of the sulfur dioxide gave the  $S^{32}$ ,  $S^{34}$  abundance ratios for the diisopropyl sulfate product and the excess sulfuric remaining at the end of the reaction. Substitution of these ratios in equation M1 gave the equilibrium constant,  $K$ . It is to be noted that no correction is necessary here because analysis could be conducted on the sulfuric acid in equilibrium with organic sulfate.

#### Materials

Sodium Bisulfite (meta), Baker and Adamson, and Nichols, both reagent grade anhydrous powder 95.9% assay, was used without further purification. n-Heptaldehyde, Eastman Kodak grade, was used without further purification.

Benzaldehyde, Eastman Kodak grade, was purified by washing with sodium carbonate solution and water followed by vacuum distillation, b.p. 61 - 62°C.\* at 10 mm. The product was stored in a dark bottle under a nitrogen atmosphere.

Anisaldehyde, Eastman Kodak grade, was distilled, b.p. 106.5 - 108°C. at 5 mm.

Acetone, Nichols N.F. grade, was distilled, b.p. 56°C.

Methyl ethyl ketone, Eimer and Amend technical grade, was distilled, b.p. 77 - 79°C.

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\* All temperatures reported in this thesis are uncorrected.

Methyl isobutyl ketone, Eastman Kodak practical grade, was distilled, b.p. 114.5 - 115°C.

Methyl n-amyl ketone, Eastman Kodak grade, was distilled, b.p. 148 - 149°C.

Methyl n-hexyl ketone, Eastman Kodak practical grade, was distilled b.p. 169.8 - 170.9°C.

Isopropyl alcohol, Shell commercial grade, was distilled, b.p. 81-81.5°C.

Sulfuric acid, C.I.L. C.P. grade, 95%  $H_2SO_4$  was used without further purification.

#### Bisulfite Addition Reaction

##### Preparation of bisulfite addition compounds.

A saturated solution, containing 5.15 moles of bisulfite per litre of solution, was prepared. To a 40 ml. aliquot of this saturated solution was added the carbonyl compound normally in such quantity as to give as large an excess of bisulfite as possible, within certain limits. The reaction mixture, contained in a tightly stoppered flask, was placed on an agitating machine surrounded by a constant temperature box maintained at 25°C.  $\pm$  0.5°C. and shaken until isotopic equilibrium had been established (see page 28). The finely crystalline bisulfite addition product was removed by suction filtration, washed with ethanol and ether and finally dried.

The eight carbonyl compounds used were, heptaldehyde, benzaldehyde, cinnaldehyde, acetone, methyl ethyl ketone, methyl isobutyl ketone,

methyl n-amyl ketone and methyl n-hexyl ketone. A precipitate of addition compound could be obtained using ten equivalents of bisulfite in saturated solution to one equivalent of all of these carbonyl compounds except acetone and methyl ethyl ketone. For these two ketones it was found that their addition compounds were soluble in the bisulfite solution to the extent that a maximum of only two equivalents of sodium bisulfite could be used with acetone and 2.8 equivalents with methyl ethyl ketone and obtain a precipitate. With such a small excess of addition compound a correction, described later, for depletion of  $S^{34}$  in the remaining bisulfite was necessary. Unfortunately the high solubility in saturated bisulfite solution of the addition compounds of the aldehydes of molecular weight lower than butyraldehyde made their use impractical.

Extent of reaction.

The data on extent of reaction was necessary along with the other data stated on <sup>page</sup> 21 in order to calculate the isotopic exchange constant,  $K$ .

This extent of reaction for aldehyde reactants was taken as 100% because of the following considerations. First, well over 95% yield of precipitated addition compound was obtained with the aldehydes used. Second, a general quantitative procedure for determination of aldehydes is by titration with standard bisulfite solution. This latter fact indicates clearly that the reaction proceeds essentially to completion.

The position of chemical equilibrium for the ketone bisulfite

reaction is not nearly as far in the direction of the products as with the aldehydes, and the higher the molecular weight of the ketone the less the percentage yield of addition compound when equimolar quantities of ketone and bisulfite are used (32). It was found, however, that methyl n-hexyl and methyl n-amyl ketone produced yields of precipitated addition compound which were 98 to 99% with only four equivalents of bisulfite in excess. With the lower molecular weight ketones only two or three equivalents of bisulfite could be used to one of carbonyl compound because of the high solubility of the addition compounds of these ketones in saturated bisulfite solution. However the less reactive methyl n-amyl ketone gave a 97% yield when the molar ratio of bisulfite to ketone was two to one. Hence the logical assumption was made that the extent of reaction for acetone and methyl ethyl ketone under the conditions used was 97%.

In order to substantiate these conclusions concerning the extent of reaction for the lower molecular weight ketones, acetone, methyl ethyl ketone and methyl isobutyl ketone, analysis were conducted for free ketone remaining after establishment of chemical equilibrium, using conditions similar to those used for isotopic equilibrium studies. The free ketone was isolated by repeated extraction with ether and analysis for ketone was conducted using the method described by Smith and Mitchell (33). Only 5% of ketone at the most was isolated and part of this may well have resulted from dissociation of addition compound during the extraction.

It should be noted that an error of 10% in the value for extent of reaction for acetone and methyl ethyl ketone would introduce

an error of only 0.1% in the value of the isotopic exchange constant. This is of the same order of magnitude as the error in the mass spectrometer abundance measurements. It is unlikely that the data on the extent of reaction for these compounds is in error by more than 5% and the values calculated for the equilibrium constant may be considered to be well within the limits of the mass spectrometric error.

For the aldehydes and higher molecular weight ketones, the total correction applied to obtain the equilibrium constant is only at the most slightly larger than the 0.1% error, and a 10% error in the values assumed for the extent of reaction for these compounds will make no significant difference in the value of the equilibrium constant.

#### Validity of procedures.

Since some of the addition compound remained dissolved in the excess bisulfite solution, it is possible that sulfur isotope fractionation between the solid addition compound and that in solution might occur and this would invalidate the results. It was not possible to ascertain the extent of this fractionation with the addition compounds themselves because of their partial dissociation in solution. However the extent of the fractionation was determined between solid sodium bisulfite and bisulfite in solution in the following manner. Twenty grams of solid sodium bisulfite was shaken with 40 ml. of saturated bisulfite solution for about seven days. The saturated solution was decanted and the solid bisulfite remaining was dried by removal of excess solute using suction filtration followed by washing



with ethanol and ether. Sulfur dioxide samples were prepared from each of the two phases using the method outlined in the following section. Mass spectrometric analysis gave the following results:

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	64/66 mass abundance ratio
SO <sub>2</sub> from solid bisulfite	21.28 ± 0.02
SO <sub>2</sub> from bisulfite in solution	21.27 ± 0.02

---

It is readily seen that no measurable fractionation of the sulfur isotopes had occurred between the two phases. This result is to be expected since the small difference in molecular weight of the isotopic bisulfite molecules should have a negligible influence on their solubility. For the larger bisulfite addition compound molecule this difference is even less and fractionation between the two phases should be very slight indeed.

The technique of washing the precipitated addition compound, after suction filtration, with alcohol and ether undoubtedly caused the precipitation of some sodium bisulfite from the mother liquor clinging to the crystals of the addition compound. This might be expected to introduce an error in the values obtained for the equilibrium exchange constants. That this error is not significant has been demonstrated in the following way. A precipitate of the benzaldehyde bisulfite addition compound prepared in the usual way was divided into two portions. One was washed with ethanol and ether only, the other with cold water (to remove bisulfite solution adsorbed on the addition compound), ethanol and ether. The following results were obtained

for the abundance of the sulfur isotopes in samples of sulfur dioxide prepared from each part:

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	64/66 mass abundance ratio compared to the standard or 21.30.
Portion #1, washed with water, ethanol and ether	21.08 ± 0.02
Portion #2, washed with ethanol and ether only	21.09 ± 0.02

---

Since the difference between the two results falls within the precision of the mass spectrometric analysis, the procedure which omits the water wash can be considered satisfactory. The disadvantage of the longer method lies in the fact that the water tends to dissolve a large quantity of the addition product.

In order to insure that isotopic equilibrium had been established in the times used, similar reactions were shaken for various periods of time ranging from a few hours to 24 days. It was found (see Tables I and III in section on Results and Discussion) that the isotopic equilibrium was established within a one week maximum period for all the compounds studied.

Preparation of sulfur dioxide samples for mass spectrometer analysis.

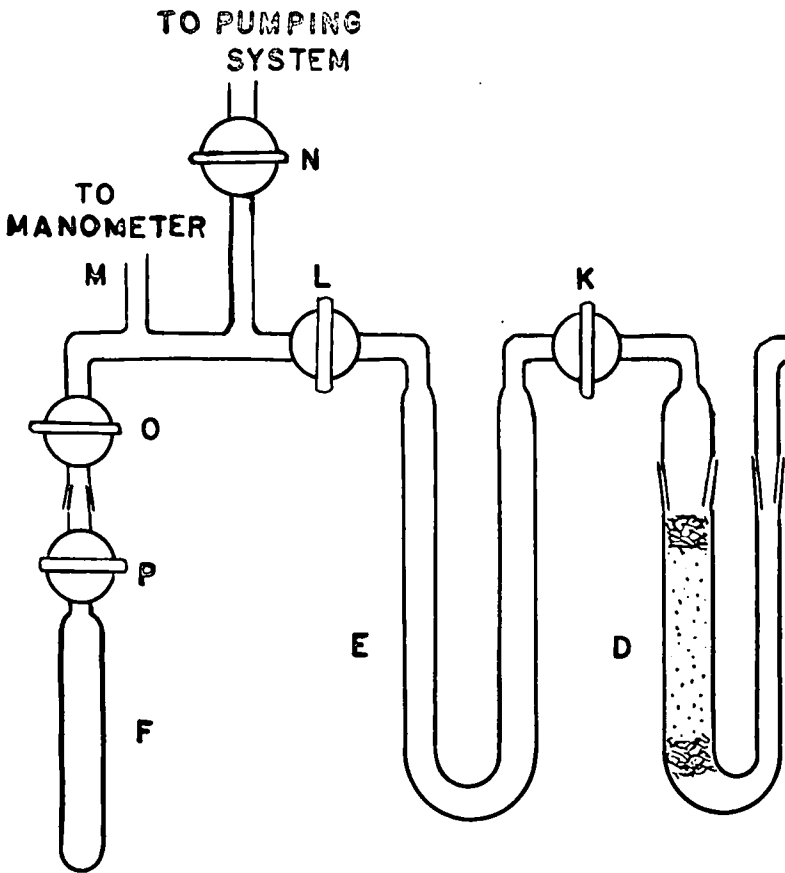
The apparatus used for the preparation of sulfur dioxide samples for mass spectrometric analysis is shown in Figure I. A quantity of solid sodium bisulfite addition compound,  $6 \times 10^{-4}$  moles, was placed in bulb B and a solution containing 0.5 ml. of 85% syrupy

phosphoric acid (reagent grade) dissolved in 0.5 ml. of distilled water was pipetted into bulb A, this being turned to position a. Both bulbs were surrounded with liquid-air baths and evacuated to a pressure of  $10^{-5}$  mm. of mercury or better (all stopcocks were open during this process). Stopcocks H and J were closed and bulbs A and B warmed by means of hot water. Bulb A was then turned to position b so that the aqueous acid ran into bulb B, thus decomposing the addition compound to give free sulfur dioxide. Complete reaction was achieved in five to ten minutes using a water bath temperature of 85 - 95°C. The reaction mixture was permitted to stand at room temperature for a period of two hours to permit equilibration of the oxygen isotopes of the sulfur dioxide with the oxygen of 'normal' water, the latter being in hundred fold excess of the sulfur dioxide<sup>\*</sup>.

At the end of the equilibration period, a liquid-air bath was placed around trap E, a salt-ice bath on trap C and a hot-water bath (90 - 95°C.) on bulb B; stopcocks G, J and K were opened, and L and H closed. The sulfur dioxide rapidly distilled into trap E, the greater part of the water vapour being partly condensed in the cold trap C and completely removed in the phosphorus pentoxide tower D. When all the sulfur dioxide had distilled into trap E, some water vapour began distilling past trap C, and its reaction with the phosphorus pentoxide in tower D could be observed. Sulfur dioxide would tend to remain

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\*Although no data was available on rate of equilibration of  $SO_2$  with  $H_2O^{18}$ , the  $CO_2$ ,  $H_2O^{18}$  equilibration reaction is complete in approximately thirty minutes at room temperature. Analysis of standard sulfur dioxide samples prepared under 1.5, 2.0 and 2.5 hour equilibration periods gave the same 64/66 mass ratio, within the experimental error of the instrument. The equilibration time was standardized to 2 hours  $\pm$  5 minutes.



TO PUMPING  
SYSTEM

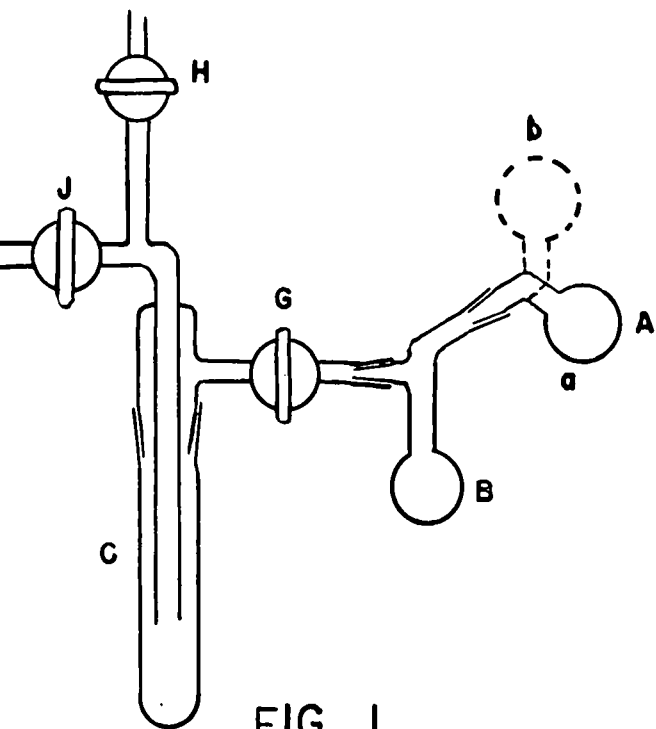


FIG. 1

in the cold water collected in trap C and hence, to insure its complete removal, stopcock J was closed and a liquid-air bath was used to distil the water and any free carbonyl compound back to flask B. The procedure for removing the sulfur dioxide from the aqueous solution was carried out three times in all, with the water condensate that collected in C being returned to the reactor B each time. At the end of the first operation a pressure of approximately six cm. of sulfur dioxide was recorded on the manometer when stopcocks L and J were closed, K opened, and trap E warmed to room temperature; after the second operation an increase of 0.1 - 0.2 cm. was noted and after the third time no pressure change could be observed, indicating that the sulfur dioxide had been quantitatively removed.

Trap E was now surrounded with a dry ice-acetone bath, stopcock N opened, and any carbon dioxide impurity present in the sulfur dioxide was removed by pumping on this trap for a few seconds; N was then closed. Sulfur dioxide has a vapour pressure of five mm. at the temperature of this bath, but it has been established that no fractionation occurs between the sulfur dioxide remaining and that pumped off with the carbon dioxide (15). Sample tube F was then surrounded by a liquid-air bath, stopcocks I, P and O opened and the sulfur dioxide partially distilled into this tube. Any free aldehyde or ketone that might have distilled into trap E with the sulfur dioxide will remain condensed at the dry ice temperature together with a small amount of sulfur dioxide. (Again there has been shown to be no fractionation of the sulfur isotopes by this procedure.) The sample tube containing the solid sulfur dioxide at liquid air temperature was sealed from

the line when a vacuum of  $10^{-6}$  mm. of mercury was attained.

Samples of the original bisulfite from which the addition compounds had been prepared were decomposed completely to sulfur dioxide which was collected and purified by exactly the same procedure as above. In this preparation, however, an aliquot of the saturated bisulfite solution containing  $6 \times 10^{-4}$  moles of bisulfite (0.12 ml.) was pipetted into flask B and a solution of 0.5 ml. of phosphoric acid and 0.38 ml. of water was pipetted into A. These samples were used as standards in the mass spectrometric analysis and it was found that the 64/66 mass abundance ratios of several samples prepared from one bisulfite solution remained constant within the error of measurement.

#### Mass spectrometric analysis.

The relative abundance ratios were obtained using both a  $90^\circ$  and a  $180^\circ$  direction focusing Nier type mass spectrometer equipped with an automatic recorder (15,34). The majority of the analyses were on the  $90^\circ$  instrument; it was found, however, that the same analysis was obtained for a given sample on each, so that no discrepancies resulted in going from one machine to the other.

The ion currents from the  $\text{SO}_2^+$  ion species were measured, thus giving the 64/66 mass abundance ratio. Although absolute abundance ratios can be determined to no better than  $\pm 0.5\%$  over a period of time, a relative precision of  $\pm 0.05\%$  can be obtained by comparing each sample to a standard. The standard, the sample, and the standard were analyzed

as quickly as possible in that order and the values accepted if the two sets of results for the standard agreed within 0.1%. The sulfur dioxide from the bisulfite solution was used as standard and all 64/66 abundance ratios in the addition compound were relative to the 64/66 ratio in the bisulfite. Since the standard varied from day to day an intermediate value of 21.000 was chosen for the 64/66 mass abundance ratio in it and all results were normalized to this value.

Calculations.

The 64/66 mass abundance ratios were converted to  $S^{32}/S^{34}$  ratios using the formula given by Thode (15):

$$\frac{S^{32}}{S^{34}} = \frac{1}{66/64 - 2(O^{18}/O^{16})}$$

which takes into account the  $O^{18}$  abundance ratio that contributes to the 66 mass peak for sulfur dioxide. The normal  $O^{18}/O^{16}$  abundance was taken as 0.00208, the value given by Thode (15) for tank oxygen. Any small difference from this value would be common to both standard and sample and would produce a negligible error in our results.

As shown previously, the equilibrium constant is given by:

$$K = \frac{B^{32}/B^{34}}{P^{32}/P^{34}} \quad (II)$$

where  $P^{32}/P^{34}$  is the  $S^{32}/S^{34}$  ratio in the addition compound and  $B^{32}/B^{34}$  the  $S^{32}/S^{34}$  ratio in the bisulfite at equilibrium. Use of the  $S^{32}/S^{34}$  abundances of the original bisulfite for the  $B^{32}/B^{34}$  ratio



does not give the correct value for  $K$  ; in order to distinguish this from the correct equilibrium constant it is designated in Table I as

$$\frac{(S^{32}/S^{34})_{\text{original bisulfite}}}{(S^{32}/S^{34})_{\text{products}}}$$

Calculation of the constant,  $K$ , applying the correction for depletion of  $S^{34}$  in original bisulfite, is best shown by the following example.

The data known is:

Equivalents of bisulfite to one of acetone: 2.0

Extent of reaction: 97%

$S^{32}/S^{34}$  abundance in original bisulfite: 23.01

$S^{32}/S^{34}$  abundance in product ( $P^{32}/P^{34}$ ): 22.77

The calculations are:

$$\%S^{34} \text{ in original bisulfite} = \frac{S^{34}}{S^{34} + S^{32}} \times 100\% = 4.165\%$$

$$\%S^{34} \text{ in product} = 4.206\%$$

Concentration of  $S^{34}$  in original bisulfite =

$$2.0 \times 0.04165 = 0.08330 \text{ gm-equiv.}$$

Concentration of  $S^{34}$  in the product =

$$0.97 \times 0.04206 = 0.04080 \text{ gm-equiv.}$$

Concentration of  $S^{34}$  in remaining bisulfite =

$$0.08330 - 0.04080 = 0.04250 \text{ gm-equiv}$$

Amount of bisulfite remaining = 1.03 equivalents.

$$\%S^{34} \text{ in bisulfite remaining} = \frac{0.04250 \times 100\%}{1.03} = 4.126\%$$

$$\frac{S^{32}}{S^{34}} \text{ in bisulfite remaining} = \left( \frac{100}{\%S^{34}} - 1 \right) = 23.24$$

( $B^{32}/B^{34}$  ratio)

$$K = \frac{B^{32}/B^{34}}{P^{32}/P^{34}} = \frac{23.24}{22.77} = 1.020$$

It is to be noted that the method of calculating the correct equilibrium constant should cause no error, even though a large correction is needed for acetone and methyl ethyl ketone. In confirmation of this statement that no error resulted in applying a large correction to determine  $K$ , it was found that the same equilibrium constant was determined for methyl isobutyl ketone with a comparatively small excess of bisulfite as with the large excess (see Table I).

#### Diisopropyl Sulfate Reaction

##### Preparation of diisopropyl sulfate.

Diisopropyl sulfate can be prepared by reacting concentrated sulfuric acid with propene (35) as shown in equation E6 given in the earlier section entitled 'General'. Propene was prepared by passing isopropyl alcohol over activated alumina catalyst at 450°C. The propene was dried by passage through first a salt-ice trap, then over phosphorus pentoxide and finally purified by distillation, collecting in a dry ice trap the middle fraction only. A weighed quantity of this propene (at dry ice temperature) was sealed in a glass bomb with a measured excess of concentrated sulfuric acid and the mixture allowed to warm to a temperature of -6 to -10°C. The reaction mixture was maintained at this temperature for sufficient time, seven or more days, to insure complete establishment of isotopic exchange equilibrium.

At the end of this period, the reaction mixture was poured over crushed ice and extracted three times with benzene to remove the diisopropyl sulfate. The benzene solution was then washed three times with ice water to remove all trace of acid. After removal of the benzene by low pressure distillation, the remaining material was vacuum distilled at 75 - 82°C. under a pressure of four mm. mercury (literature (35) 78 - 80°C. at 3.7 mm.). The yields were 12% for the two reactions conducted; these yields were not as high as reported but the use of 95% sulfuric acid instead of 98% sulfuric as recommended would possibly account for this fact.

Conversion to sulfur dioxide for mass spectrometric analysis.

The diisopropyl sulfate obtained as described in the previous section was hydrolyzed by refluxing with an aqueous solution of barium chloride (in large excess) for forty-eight hours. At the end of this time, the barium sulfate precipitate was separated by filtration; no further precipitation of barium sulfate was obtained by refluxing <sup>the filtrate</sup> with a fresh portion of barium chloride solution. The weight of barium sulfate obtained agreed closely with the theoretical value.

Samples of the original sulfuric acid and the excess sulfuric acid from the reaction were precipitated as barium sulfate by addition of a quantity of the barium chloride solution used above.

All barium sulfate samples were converted to sulfur dioxide for mass spectrometric analysis by a standard procedure reported previously by MacNamara (35). Briefly, the barium sulfate was oxidized to iron sulfide by heating with pure iron dust. This iron sulfide

was reacted with hydrochloric acid to form hydrogen sulfide gas which was bubbled into lead acetate solution to produce a lead sulfide precipitate. The lead sulfide, after filtering and drying, was burned in a stream of oxygen of standard  $O^{18}$  content and the sulfur dioxide formed collected and purified by usual vacuum line techniques.

The  $S^{32}/S^{34}$  abundance ratios were determined mass spectrometrically as previously described, the sulfur dioxide from the original sulfuric acid being used as standard. The calculation of the equilibrium constant was conducted by the method described previously using equation M1. Here, however, the  $P^{32}/P^{34}$  value was replaced by the  $S^{32}/S^{34}$  abundance in the diisopropyl sulfate and the  $B^{32}/B^{34}$  by the  $S^{32}/S^{34}$  abundance in the sulfuric acid remaining at equilibrium; no correction was needed because the  $S^{32}/S^{34}$  abundance in the acid remaining at equilibrium could be determined directly.

#### Unidirectional Process

A measure of the unidirectional isotope effect in the formation of a carbon-sulfur bond should be obtained by separating the first small amount of precipitated addition compound from the reaction of carbonyl compound with bisulfite and analyzing to obtain its  $S^{32}$ ,  $S^{34}$  abundance. If this material precipitates immediately and is separated before there is an opportunity for establishment of the reverse bond breaking process that is present under equilibrium conditions, then the isotope fractionation measured should be the true unidirectional effect for forming the carbon-sulfur bond. With certain of the

carbonyl compounds, no precipitate formed for at least a minute and there was opportunity for the reverse bond breaking reaction to commence. The true unidirectional effect could not be measured directly for these compounds; however, the rate of attainment of isotopic equilibrium could be noted by measuring the  $S^{32}/S^{34}$  abundance of precipitates formed at different time intervals, and a graph could be plotted from which the effect at zero time could be predicted by extrapolation.

The bisulfite addition compounds of n-heptaldehyde, benzaldehyde, anisaldehyde, methyl isobutyl ketone, methyl n-amyl ketone, and methyl n-hexyl ketone were prepared as described previously using ten equivalents of bisulfite in saturated solution to one equivalent of carbonyl compound. However, the time of shaking before suction filtration (followed by ethanol and ether washing) was varied from as short as possible to periods approaching the isotopic equilibrium condition. The conversion of the addition compound to sulfur dioxide and mass spectrometric analyses were conducted exactly as described in the previous section on the Bisulfite Addition Reaction. The final results are reported (in Table III) as the ratio

$$\frac{(S^{32}/S^{34}) \text{ original bisulfite}}{(S^{32}/S^{34}) \text{ products}} .$$

In an effort to explain the different rates with which isotopic equilibrium was attained, the solubilities of the addition compounds of the above six carbonyl compounds were measured in saturated bisulfite solution at 25°C. A weighed quantity of addition compound in

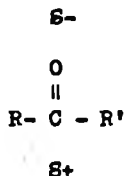
dry form was added to a 25.0 ml. aliquot of saturated bisulfite and shaken for several hours, maintaining a constant temperature of 25°C. When saturation of the solution with respect to the addition compound was assured, the remaining solid was filtered off and washed with ethanol and ether and dried. The difference between the original weight and the weight of compound remaining gave the solubility. The average value of several determinations by this method is reported as molar solubility.

## RESULTS AND DISCUSSION

### Isotopic Equilibrium Constants as Proof for the Carbon-Sulfur Bond Structure

In Table I are presented the isotopic equilibrium constants for the bisulfite addition compound reaction of eight carbonyl compounds. The equilibrium constant is noted to be of the order of 1.020 for lower molecular weight compounds, decreasing to 1.010 with increasing molecular weight; this is of the order of magnitude expected for a carbon-sulfur bond structure on the basis of the theoretical and experimental considerations discussed previously in the Introduction. Table II gives the equilibrium constant of 1.002 for the diisopropyl sulfate reaction. Since in this case a carbon-oxygen-sulfur bond is definitely involved, this result confirms the theoretical prediction that there is no appreciable fractionation of the sulfur isotopes when the bonding (electron distribution) about the sulfur atoms is unchanged in going from reactants to products.

To establish a firm basis for the above explanation of the results, the mechanism of formation of the addition compound from bisulfite and carbonyl compound must be considered. The carbonyl compounds have the structure:



which, on entering reaction with bisulfite ion or with other carbonyl addition reagents, becomes polarized in the manner indicated. The

TABLE I

EQUILIBRIUM CONSTANTS (AT 25°C.) FOR  $S^{32}$ ,  $S^{34}$  ISOTOPIC EXCHANGE IN THE BISULFITE ADDITION REACTION

Carbonyl Compound	Equivalents of $\text{NaHSO}_3$ to one of carbonyl compound	Time shaken (in days)	Extent of reaction (in %)	64/66 mass abundance ratio $1^{\#}$	$S^{32}/S^{34}$ ratio $1^{\#}$	$(S^{32}/S^{34})$ orig. bisulfite $(S^{32}/S^{34})$ prod.	Equilibrium Constant K
Acetone	1.9	24	97 $\pm$ 3	20.805 $\pm$ 0.014 <sup>2*</sup>	22.776	1.0103	1.021
	2.0	24	97 $\pm$ 3	20.803 $\pm$ 0.015	22.774	1.0104	1.020
	Average: <u>1.021<math>\pm</math>0.001</u>						
	1.9 <sup>3*</sup>	6	97 $\pm$ 3	20.816 $\pm$ 0.014	22.789	1.0097	1.020
	2.0 <sup>3*</sup>	6	97 $\pm$ 3	20.820 $\pm$ 0.028	22.794	1.0095	1.019
Methyl Ethyl Ketone	2.5	24	97 $\pm$ 3	20.752 $\pm$ 0.013	22.713	1.0131	1.022
	2.8	24	97 $\pm$ 3	20.737 $\pm$ 0.015	22.695	1.0139	1.021
	Average: <u>1.022<math>\pm</math>0.001</u>						
	2.5 <sup>3*</sup>	6	97 $\pm$ 3	20.739 $\pm$ 0.008	22.697	1.0138	1.023
Methyl n-amyl Ketone	10.0	7	99 $\pm$ 1	20.784 $\pm$ 0.014	22.751	1.0114	1.013
	10.0	14	99 $\pm$ 1	20.789 $\pm$ 0.018	22.757	1.0111	1.012
	10.0	24	99 $\pm$ 1	20.795 $\pm$ 0.011	22.765	1.0108	1.012
	Average: <u>1.012<math>\pm</math>0.001</u>						



TABLE I (cont'd.)

Carbonyl Compound	Equivalent of NaHSO <sub>3</sub> to one of carbonyl compound	Time shaken (in days)	Extent of reaction (in %)	64/66 mass abundance ratio <sup>1*</sup>	S <sup>32</sup> /S <sup>34</sup> ratio <sup>1†</sup>	$\frac{(S^{32}/S^{34}) \text{ orig. bisulfite}}{(S^{32}/S^{34}) \text{ prod.}}$	Equilibrium Constant K
Methyl Isobutyl Ketone	10.0	14	98 <sup>±</sup> <sub>2</sub>	20.663 <sup>±</sup> <sub>0.014</sub>	22.602	1.0179	1.020
	10.0	24	98 <sup>±</sup> <sub>2</sub>	20.684 <sup>±</sup> <sub>0.016</sub>	22.631	1.0168	1.019
	5.0	24	98 <sup>±</sup> <sub>2</sub>	20.680 <sup>±</sup> <sub>0.015</sub>	22.626	1.0170	1.019
	4.7 <sup>3*</sup>	5	98 <sup>±</sup> <sub>2</sub>	20.723 <sup>±</sup> <sub>0.012</sub>	22.678	1.0146	Average: <u>1.019<sup>±</sup>0.001</u> 1.019
Methyl n-Hexyl Ketone	10.0	14	99 <sup>±</sup> <sub>1</sub>	20.791 <sup>±</sup> <sub>0.014</sub>	22.759	1.0110	1.012
	8.0	24	99 <sup>±</sup> <sub>1</sub>	20.780 <sup>±</sup> <sub>0.012</sub>	22.746	1.0116	1.013
	10.0	24	99 <sup>±</sup> <sub>1</sub>	20.774 <sup>±</sup> <sub>0.018</sub>	22.739	1.0119	1.013
							Average: <u>1.013<sup>±</sup>0.001</u>
n-Heptaldehyde	10.0	8	100	20.768 <sup>±</sup> <sub>0.014</sub>	22.732	1.0122	1.014
	10.0	24	100	20.792 <sup>±</sup> <sub>0.017</sub>	22.761	1.0109	1.012
	10.0	24	100	20.781 <sup>±</sup> <sub>0.014</sub>	22.747	1.0116	1.013
							Average: <u>1.013<sup>±</sup>0.001</u>

TABLE I (cont'd.)

Carbonyl Compound	Equivalents of NaHSO <sub>3</sub> to one of carbonyl compound	Time shaken (in days)	Extent of reaction (in %)	64/66 mass abundance ratio <sup>1*</sup>	S <sup>32</sup> /S <sup>34</sup> ratio <sup>1*</sup>	(S <sup>32</sup> /S <sup>34</sup> ) orig. bisulfite / (S <sup>32</sup> /S <sup>34</sup> ) <sub>prod.</sub>	Equilibrium Constant K
Benzaldehyde	10.0	7	100	20.782 <sup>±</sup> 0.018	22.748	1.0115	1.013
	10.0	7	100	20.782 <sup>±</sup> 0.018	22.748	1.0115	1.013
	10.0	13	100	20.771 <sup>±</sup> 0.013	22.736	1.0121	1.013
	10.0	14	100	20.766 <sup>±</sup> 0.014	22.729	1.0124	1.014
	10.0	25	100	20.767 <sup>±</sup> 0.012	22.731	1.0123	1.014
Average: 1.013 <sup>±</sup> 0.001							
Anisaldehyde	10.0	17	100	20.824 <sup>±</sup> 0.012	22.799	1.0093	1.010
	10.0	24	100	20.824 <sup>±</sup> 0.029	22.799	1.0093	1.010
Average: 1.010 <sup>±</sup> 0.001							

1\* The S<sup>32</sup>O<sub>2</sub>/S<sup>34</sup>O<sub>2</sub> ratio for the original bisulfite was taken as 21.000; this gives an S<sup>32</sup>/S<sup>34</sup> ratio of 23.010.

2\* Average deviation of the mean.

3\* Temperature was only constant over range 25-30°C.

TABLE II

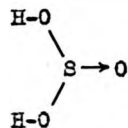
Equilibrium Constant (at -6 to -10°C.) for S<sup>32</sup>, S<sup>34</sup> Isotopic Exchange in the Diisopropyl Sulfate Reaction

Reaction time (in days)	Moles of propene	Moles of H <sub>2</sub> SO <sub>4</sub>	Equivalents of H <sub>2</sub> SO <sub>4</sub> to propene	Diisopropyl Sulfate		H <sub>2</sub> SO <sub>4</sub> remaining		Equilibrium Constant K
				<sup>64</sup> /66 ratio 1*	S <sup>32</sup> /S <sup>34</sup> ratio 1*	<sup>64</sup> /66 ratio 1*	S <sup>32</sup> /S <sup>34</sup> ratio 1*	
#1 7	0.167	0.175	2.1:1.0	20.991 ±0.013 <sup>2*</sup>	22.986	21.030 ±0.029	23.046	1.003
#2 19	0.136	0.195	2.9:1.0	20.984 ±0.014	22.991	21.001 ±0.030	23.011	1.001
Average								<u>1.002±0.001</u>

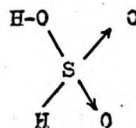
1\* The S<sup>32</sup>O<sub>2</sub>/S<sup>34</sup>O<sub>2</sub> ratio for the original acid was taken as 21.000; this gives an S<sup>32</sup>/S<sup>34</sup> ratio of 23.010.

2\* Average deviation of the mean.

structure of the bisulfite ion is not definitely established; however, there is fairly strong evidence that sulfurous acid is tautomeric, being a mixture of the two forms I and II:

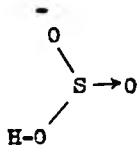


I

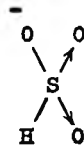


II

It is also possible to write two tautomeric formulae for the bisulfite ion:



III



IV

and in solution the bisulfite ion may exist as an equilibrium mixture of these two forms. The reaction of III with the carbonyl compounds would give the results previously predicted, namely a fractionation of sulfur isotopes for the carbon-sulfur bond form of the addition compound and none for the carbon-oxygen-sulfur bond type. If bisulfite were to react with the carbonyl compounds through structure IV, then fractionation of the sulfur isotopes might be expected for both the sulfonic acid and sulfite ester structures of the addition compound. For the latter, a sulfur-hydrogen bond would be broken, with the subsequent redistribution of the electrons about the sulfur that might result in some fractionation. However, it is highly unlikely that bisulfite ion exists to any appreciable extent in form IV, since, in this structure, the ionizable hydrogen is joined to a sulfur atom

having a formal positive charge of two. Therefore, this form should be thermodynamically much less stable than form III, in which the hydrogen is attached to oxygen and sulfur has but a unit positive charge.

It should be pointed out that kinetic studies (37) have indicated that the mechanism of addition of bisulfite to carbonyl compounds is complicated but involves the addition of sulfite ion rather than bisulfite ion. Since only one structure of sulfite ion,



, is possible, then there can be little doubt that the mechanism of formation of addition compound under equilibrium conditions is such that fractionation of sulfur isotopes only results if a carbon-sulfur bond is present in the addition compound.

The above results constitute conclusive proof for the existence of the sulfonic acid structure of the bisulfite addition compound formed under equilibrium conditions.

#### Variation of Isotopic Equilibrium Constant with Molecular Weight

The variation of the equilibrium constant from 1.022 for methyl ethyl ketone, to 1.010 for anisaldehyde is noted in Table I. These results are summarized as follows:

Carbonyl Compound	Molecular Weight (in grams)	Equilibrium Constant,
Acetone	58.1	1.021
Methyl Ethyl Ketone	72.1	1.022
Methyl Isobutyl Ketone	100.2	1.019
Benzaldehyde	106.2	1.013
n-Heptaldehyde	114.2	1.013
Methyl n-Amyl Ketone	114.2	1.012
Methyl n-Hexyl Ketone	128.3	1.013
Anisaldehyde	136.1	1.010

In general the fractionation of  $S^{34}$  into the addition compound is decreased by an increase in molecular<sup>weight</sup> and complexity of the reacting carbonyl. These results are as predicted and can be explained as follows. For simple low molecular weight molecules the vibrational frequencies of all carbon-to-carbon and carbon-to-hydrogen bonds would be somewhat affected by the formation of the new carbon-sulfur bond and the ratio of the partition functions would be reasonably large giving a large fractionation of the isotopes. For larger molecules, the vibrational frequencies of most of the carbon-to-carbon and carbon-to-hydrogen bonds are beyond the influence of the new bond and hence remain unaffected; this means a smaller overall difference in the vibrational frequencies for the isotopic species in going from reactants to products. The resulting partition function ratios are closer to unity and consequently less fractionation occurs.

This effect of variation of equilibrium constant with molecular weight is interesting and useful since it adds additional support to the theory relating to isotopic fractionation in chemical processes.

#### Unidirectional Isotope Effects

The results giving the fractionation of the sulfur isotopes in formation of the bisulfite addition compounds, under what were considered to be unidirectional conditions, are presented in Table III. The rates of attainment of isotopic equilibrium also are given in Table III and are illustrated graphically in Figure II. No fractionation occurred in the formation of the first small amount of heptaldehyde and benzaldehyde addition compounds, and it is apparent from Figure II that none would be found for the others if it had been possible to isolate a precipitate in the first few seconds. This result is surprising and unexpected on the basis of the considerations presented in the Historical Introduction.

If, as the results would indicate, there is a zero sulfur isotope effect in the formation of a carbon-sulfur bond, the results on the rates of attainment of isotopic equilibrium may be interpreted in terms of solubility of the addition products (presented in Table IV) and the structure of the carbonyl compounds. The less soluble addition compound will have a low concentration of addition compound in solution, and the position of the chemical equilibrium will consequently be almost completely towards the products; this means that the opportunity for conversion of product to original reactant,

TABLE III

Apparent Unidirectional Isotope Effects and Rates of Attainment of Isotopic Equilibrium

Carbonyl Compound	Time Shaken	64/66 Mass Abundance Ratio <sup>lx</sup>	S <sup>32</sup> /S <sup>34</sup> Ratio <sup>lx</sup>	(S <sup>32</sup> /S <sup>34</sup> ) <sub>orig.</sub>
				bisulfite (S <sup>32</sup> /S <sup>34</sup> ) <sub>prod.</sub>
Benzaldehyde <sup>2x</sup>	15 sec.	21.006±0.020 <sup>3x</sup>	23.017	0.9937
	20-25 sec.	20.973±0.014	22.978	1.0014
	40-45 sec.	20.918±0.013	22.912	1.0043
	60 sec.	20.903±0.015	22.897	1.0049
	2.5 min.	20.869±0.017	22.853	1.0068
	6 min.	20.854±0.017	22.835	1.0077
	10.3 min.	20.850±0.011	22.830	1.0079
	42 min.	20.838±0.013	22.816	1.0085
	1.7 hr.	20.839±0.010	22.816	1.0085
	6.2 hr.	20.806±0.014	22.777	1.0102
	25 hr.	20.797±0.014	22.767	1.0107
equil.	20.771±0.014	22.735	1.0120	
Anisaldehyde	35 sec.	20.966±0.015	22.969	1.0018
	45 sec.	20.940±0.015	22.938	1.0031
	2.5 min.	20.926±0.017	22.922	1.0033
	5 min.	20.925±0.009	22.920	1.0039
	equil.	20.824±0.012	22.799	1.0103



TABLE III (cont.)

Carbonyl Compound	Time Shaken	64/66 Mass Abundance Ratio <sup>Li</sup>	S <sup>32</sup> /S <sup>34</sup> Ratio <sup>Li</sup> *	$(S^{32}/S^{34})_{\text{orig. bisulfite}}$ $(S^{32}/S^{34})_{\text{prod.}}$
Methyl Isobutyl Ketone	1.5 min.	20.762±0.010	22.725	1.0125
	2.1 min.	20.731±0.015	22.687	1.0142
	3.3 min.	20.723±0.014	22.678	1.0146
	5.5 min.	20.699±0.012	22.649	1.0159
	equil.	20.674±0.012	22.619	1.0174
n-Heptaldehyde	30 sec.	21.000±0.016	23.010	1.0000
	50 sec.	21.019±0.015	23.032	0.9990
	3.3 min.	20.974±0.013	22.979	1.0013
	5 min.	20.963±0.011	22.966	1.0019
	10 min.	20.939±0.015	22.937	1.0032
	36 min.	20.949±0.019	22.949	1.0027
	3 days	20.820±0.013	22.794	1.0095
	equil.	20.781±0.014	22.747	1.0116
Methyl n-Amyl Ketone	40 sec.	20.956±0.021	22.957	1.0023
	45 sec.	20.970±0.017	22.974	1.0016
	70 sec.	20.969±0.015	22.973	1.0017
	3 min.	20.933±0.012	22.930	1.0035
	5 min.	20.910±0.017	22.902	1.0047
	equil.	20.790±0.011	22.758	1.0111

TABLE III (cont.)

Carbonyl Compound	Time Shaken	64/66 Mass Abundance Ratio <sup>1*</sup>	S <sup>32</sup> /S <sup>34</sup> Ratio <sup>1*</sup>	(S <sup>32</sup> /S <sup>34</sup> ) orig.
				bisulfite
				(S <sup>32</sup> /S <sup>34</sup> ) prod.
Methyl n-Hexyl Ketone	2.5 min.	20.920±0.030	22.914	1.0042
	2.8 min.	20.908±0.017	22.900	1.0048
	4 min.	20.876±0.018	22.861	1.0065
	equil.	20.782±0.012	22.748	1.0115

<sup>1\*</sup> The S<sup>32</sup>O<sub>2</sub>/S<sup>34</sup>O<sub>2</sub> ratio for the original bisulfite was taken as 21.000; this gives an S<sup>32</sup>/S<sup>34</sup> ratio of 23.010.

<sup>2\*</sup> Reactants ratio was standardized to ten equivalents of bisulfite to one equivalent of carbonyl compound for all results reported in this table.

<sup>3\*</sup> Average deviation of the mean.

TABLE IV

Solubilities of Disulfite Addition Compounds in Saturated Bisulfite Solution

Carbonyl Compound	Molecular Weight (in grams)	Gram Solubility per 25 ml. of Solution	Molar Solubility $\times 10^{-3}$ per 25 ml. of Solution.
n-Heptaldehyde	114.2	0.164 $\pm$ 0.009*	1.44
Benzaldehyde	106.2	0.217 $\pm$ 0.005	2.05
Anisaldehyde	136.1	0.07 $\pm$ 0.01	0.51
Methyl Isobutyl Ketone	100.2	0.62 $\pm$ 0.05	6.2
Methyl n-Amyl Ketone	114.2	0.060 $\pm$ 0.005	0.525
Methyl n-Hexyl Ketone	128.3	0.061 $\pm$ 0.004	0.475

\* Average deviation

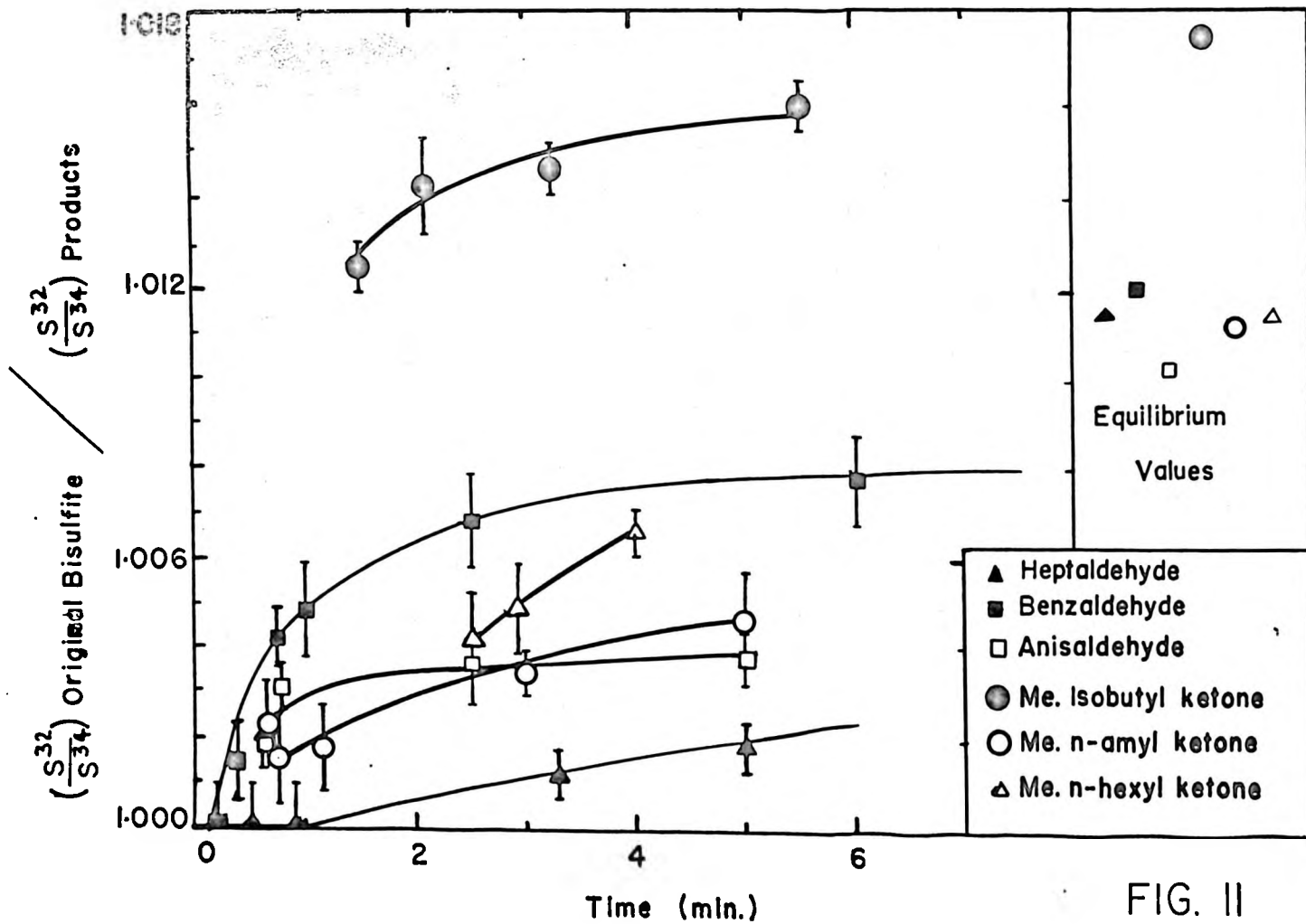
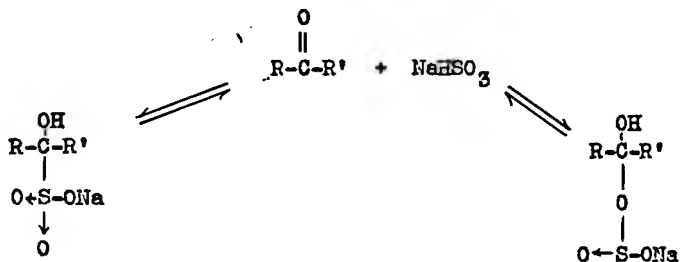


FIG. II

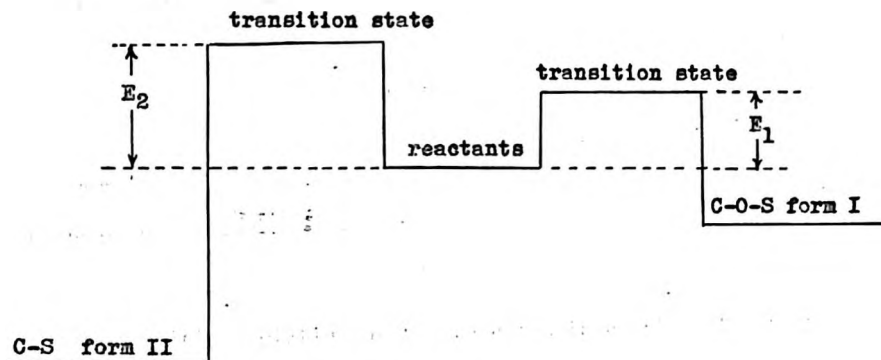
during which the fractionation is effected, is slower. Thus the carbonyl reactant with the least soluble addition compound would be predicted to attain isotopic equilibrium the slowest. That the structure of the carbonyl compounds also has a bearing in the rate of attainment of isotopic equilibrium is apparent from the following argument. The position of chemical equilibrium for aldehydes is such as to favour products to a much greater extent than is the case with ketones. In other words, the specific rate constant for the reverse process, the conversion of addition compound to carbonyl and bisulfite ion, is much smaller for aldehydes than for ketones. Since the fractionation has been assumed to occur in the bond breaking process only, isotopic equilibrium will then be attained much less readily for the former. A study of Figure II and Table IV indicates that the data is consistent with this interpretation.

A zero isotope effect in bond formation is difficult to accept, however, and an attempt has been made to develop a theory which avoids this interpretation and yet explains the results adequately. It is suggested that the first compound to separate is not the sulfonic acid type but the sulfite ester compound, formed with no fractionation of sulfur isotopes. This compound then is slowly converted, by dissociation to reactants followed by recombination, to the more stable sulfonic acid structure; fractionation of sulfur isotopes occurs in the latter process only. At chemical equilibrium, the greater part of the addition compound is present as the sulfonic acid form and the isotopic equilibrium value finally obtained is that of the equilibrium process involving the bisulfite ion and this form of the addition compound. This

explanation is shown more clearly by means of the following equation:

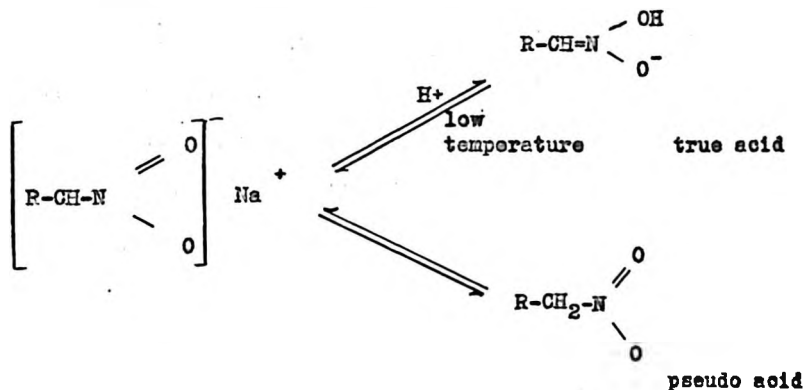


The interpretation of the reaction is consistent with the now generally accepted mechanism of carbonyl addition reactions, namely, that they involve the nucleophilic attack of the addendum on the carbon of the carbonyl group, the latter being somewhat positively charged by virtue of the greater electronegativity of the carbonyl oxygen. It would be expected that a lower energy of activation would be required for the reaction involving the attack on carbon of the negatively charged oxygen atom of the bisulfite than one involving the attack of the sulfur atom, since the sulfur carries a positive formal charge. The carbon-oxygen-sulfur bond structure should therefore form more readily. However, of the two addition products, the carbon-sulfur bond structure is the more stable (sulfonic acids are very much more stable than sulfite esters); therefore, when chemical equilibrium has been reached this form will predominate. In fact, it is probable that only an extremely small amount of the sulfite ester form is present in the equilibrium mixture. The following figure illustrates this explanation:



where  $E_1$  is the activation energy for the formation of the carbon - oxygen-sulfur bond form and  $E_2$  is the activation energy for the formation of the carbon-sulfur form. Since  $E_1$  is less than  $E_2$ , form I will be produced at more rapid rate than form II, and early in the reaction will be almost the exclusive product. Form II, however, is the thermodynamically more stable, and its concentration, relative to form I, will increase with time until it predominates at equilibrium.

This type of reaction has been noted previously. One example is the conversion of a primary or secondary nitro anion to the acid form by the addition of a strong acid.



The true acid is formed more rapidly and is almost the sole product on addition of oxonium ions at low temperatures. This form however, is the less stable and on standing slowly converts to the pseudo acid or nitro form.

Returning to the bisulfite addition reaction, the rates of attainment of isotopic equilibrium of the different carbonyl compounds can be readily explained in terms of this theory by consideration of their reactivity and the solubility of their addition compounds.

In considering the solubility effect, an assumption is made that the relative solubilities of the various addition compounds are the same for the sulfite ester structure as for those measured for the sulfonic acid form; this assumption is reasonably valid since, in the cases where the solubility effect is considered, there are very large differences in the solubilities of the addition compounds. The more insoluble the addition compound of the sulfite ester structure, the lower the concentration of this form in the solution, and therefore the less readily will the reverse reaction to reform reactants proceed. This will mean that the rate of conversion of sulfite form to sulfonic acid form will be slower for the reactions involving the more insoluble product, and, since fractionation occurs only in the reactions involving this latter structure, the rate of attainment of isotopic equilibrium will also be slower. In addition, a decreased solubility of the sulfonic acid form will also lower the rate of attainment of isotopic equilibrium since the maximum (equilibrium) isotopic effect will be reached only when the addition products and the reactants have been interconverted many times. The lower the concentration of the addition compound in solution the slower will be this interconversion,



The structure of the carbonyl compound will influence the rate of attainment of isotopic equilibrium by effecting the ratio  $E_1/E_2$ . The increment positive charge on the carbonyl carbon is smaller with ketones than aldehydes since the former contains two electron donating alkyl groups on this carbon and the latter only one. This should mean that the  $E_1/E_2$  ratio will be smaller for aldehydes since the greater positive charge on the carbonyl carbon, as compared with ketones, will lower the energy of activation,  $E_1$ , for the reaction involving attack of negatively charged oxygen and will raise  $E_2$ , the energy of activation for the attack of the relatively positive sulfur. Since all the fractionation is in the sulfonic acid form of the addition compound reaction, the aldehydes should be slower in reaching isotopic equilibrium.

In considering our results, it is seen that the solubility effect is well illustrated by the three ketones studied. Methyl isobutyl ketone, with a comparatively soluble addition compound, appears to attain isotopic equilibrium much more rapidly than the relatively insoluble methyl n-amyl and methyl n-hexyl ketones. The structure effect is demonstrated when the results for heptaldehyde are compared to those for the ketones. Heptaldehyde, a typical aliphatic aldehyde, attains isotopic equilibrium at a much slower rate than the less soluble methyl n-amyl and methyl n-hexyl ketones. The benzaldehyde and anisaldehyde results are also easily explained on the basis of structure and solubility. The electron density of the carbonyl carbon of benzaldehyde corresponds to that of ketones because

of the large donation of electrons from the benzene ring by virtue of resonance. Benzaldehyde is also more soluble than methyl n-amyl and methyl n-hexyl ketones and heptaldehyde and the two factors reinforce one another to facilitate attainment of isotopic equilibrium. In anisaldehyde the resonance effect is enhanced by the methoxy group in the para position and the donation of electrons to the carbonyl carbon is greater than for benzaldehyde; however this factor, that would alone result in more rapid approach of isotopic equilibrium, is opposed by a low solubility of its addition compound. This solubility factor appears to more than cancel the opposing structure factor, making the rate of attainment of isotopic equilibrium for anisaldehyde slower than for benzaldehyde.

In conclusion, it is suggested that further experimental work be conducted to substantiate the above theory. The results obtained so far, although all consistent with the explanation, are not sufficient to definitely establish this theory. Three suggestions are made for further work.

First, an attempt should be made to determine the rates of establishment of isotopic equilibrium for several more carbonyl compounds; the choice of these carbonyls should be carefully made so as to include compounds whose properties are such as to allow a definite prediction of the results, using the above considerations. A typical one suggested is p-nitrobenzaldehyde; the low solubility of its addition compound and the increased positivity of its carbonyl carbon should make it attain isotopic equilibrium even slower than heptaldehyde.

A second approach to the problem would be to measure the isotope effect in the breaking of the carbon-sulfur bond during the decomposition of the addition compound. By decomposing only a small amount of addition compound under unidirectional conditions, a measure would be given of the isotope effect in breaking a carbon-sulfur bond. From the considerations in the Historical Introduction, it would be expected that this effect might be approximately half that obtained for the equilibrium value, that is, the effect in bond breaking might be of the same order of magnitude as that in bond formation. On the other hand, if the isotope effect in the formation of a carbon-sulfur bond is actually zero, then the value measured for the breaking of this bond should be approximately that found for the equilibrium process.

Confirmation of this theory could only be accomplished by presentation of chemical or physical evidence for the existence of the carbon-oxygen-sulfur bond structure in the initial stages of the reaction. The third suggestion is to conduct Raman spectra measurements on a solution in which carbonyl compound is reacting with bisulfite. If line frequencies corresponding to a carbon-sulfur bond were found at the initiation of the addition compound reaction and if they disappeared as chemical equilibrium was established, then definite proof would be had for the postulation that the initial product is the sulfite ester form of the addition compound which converts readily to the thermodynamically more stable sulfonic acid form.

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