

the eventual result is a series of numbers presumed to represent the actual auditory threshold. The extent of the inexactness cannot be concluded from the numbers themselves. By this a greater exactness is supposed than is really the case. The continu audiogram, however, by abnormally large deviations or abnormal straightness of the curve, immediately betrays that the necessary reserve must be exercised in reading it.

Not every patient appeared to be able to notice the auditory threshold with the same facility. In cases of undamaged hearing this caused generally more difficulties than in cases with loss of hearing. Patients, suffering from perception deafness and regression, can very easily recognize the auditory threshold by means of the rapid rise of the loudness-sensation in increasing energy.

Chemistry. — *The mechanism of isomerisations of unsaturated fatty acids by SO₂.* By J. H. DE BOER¹⁾, J. P. W. HOUTMAN²⁾ and H. I. WATERMAN³⁾.

(Communicated at the meeting of October 25, 1947.)

§ 1. Introduction.

Systematic investigations by WATERMAN and collaborators on the polymerisation of linseed oil⁴⁾ and of linoleic and linolenic esters by the action of SO₂ have shown⁵⁾ that prior to polymerisation there is a shift of one or more double bonds in the molecules. This isomerisation leads from a system of isolated double bonds to a system with conjugated double bonds. The reaction is restricted to those unsaturated fatty acids which have in their molecules a system of two double bonds separated by a central CH₂-group. As an example we mention the isomerisation of linoleic ester:



It is not easily understood why such an isomerisation should be catalysed by SO₂. It is the purpose of this note to discuss a possible mechanism which may offer an explanation. We will start our considerations with a short discussion of two other catalytic reactions by which this isomerisation can be performed.

§ 2. Conjugation by hydrogenation catalysts.

It is known that isomerisation of these molecules to form systems with conjugated double bonds also proceeds at the surface of hydrogenation catalysts, like paladium⁶⁾, nickel⁷⁾, platinum on active carbon or nickel on kieselguhr⁸⁾.

A hydrogenation catalyst, such as nickel, may give rise to a shift of the

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³⁾ Laboratory for Chemical Engineering, University, Delft (Holland).

⁴⁾ H. I. WATERMAN and C. v. VLODROP, *J. Soc. Chem. Ind.*, **55**, 333 T (1936).

⁵⁾ H. I. WATERMAN, C. v. VLODROP and M. J. PFAUTH, *Verfkroneik*, **13**, 130 (1940). British Patent 544, 482, April 15th 1942 (H. I. WATERMAN and C. v. VLODROP to I.C. I.).

⁶⁾ C. W. MOORE, *J. Soc. Chem. Ind.*, **38**, 320 T (1919).

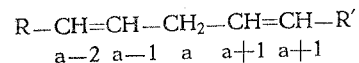
⁷⁾ H. I. WATERMAN, C. v. VLODROP and W. J. TAAT, *Chimie et Industrie*, **44**, 285 (1940).

⁸⁾ H. I. WATERMAN and M. J. v. TUSSENBROEK, *Chem. Weekblad*, **26**, 410, 566 (1929); **27**, 146 (1930).

H. I. WATERMAN and C. v. VLODROP, *J. Soc. Chem. Ind.*, **55**, 320 T (1936).

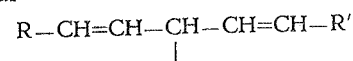
double bond in mono-unsaturated molecules also provided gaseous hydrogen is present⁹). For the conjugation isomerisation of the system of two double bonds, separated by a central CH₂-group the presence of gaseous hydrogen, however, is not necessary¹⁰).

The isomerisation may — formally — be understood in these cases to be caused by the transfer of a hydrogen atom of the central CH₂-group a of the typical grouping:

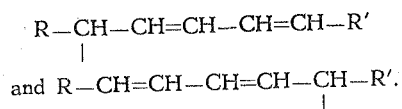


to the metal. It is known that metallic hydrogenation catalysts may easily take up hydrogen atoms as well as transfer them other molecules.

The resulting radical



may be considered as one of the forms of a resonance hybrid, other contributing forms of which are

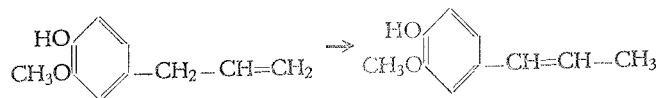


When this radical takes up a hydrogen atom from the metal again, we may, therefore, expect this hydrogen to be added either to carbon atom *a*-2, to *a* or to *a* + 2. An addition to *a*-2 or *a* + 2 is even more probable because of the resonance energy of the conjugated system in the resulting molecule¹¹).

Even if every molecule collides and reacts with the metal surface only once, we may already expect a product with more than 2/3 of the molecules in the conjugated form.

§ 3. Conjugation by alkali.

The isomerisation under consideration may also often be performed by the action of aqueous or alcoholic alkali, as is well known in the technically important isomerisation of eugenol to iso-eugenol by alkali¹²):



⁹) G. H. TWIGG, Proc. Roy. Soc., (London), A 178, 106 (1941).

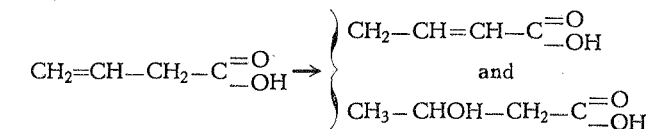
¹⁰) See for one of the latest articles: S. B. RADLOVE, H. M. TEETER, W. H. BOND, J. C. COWAN and J. P. KASS, Ind. Eng. Chem., 38, 997 (1946).

¹¹) The picture developed here runs completely parallel to the picture of the mechanism of oxidation of similar systems, as developed by FARMER and collaborators, see e.g. E. H. FARMER, H. P. KOCH and D. A. SUTTON, J. Chem. Soc., 1943, 541, and also § 4 of this article.

¹²) In a case like this, as in many others, the position of one of the double bonds of the system is fixed by being part of an aromatic ring, hence the shift can take place to one side only.

or in the transfer of *α*-carotene into *β*-carotene by heating in an alcoholic solution with sodium-ethylate¹³).

The isomerisation under the influence of alkali, which can also be obtained readily in the case of linoleic or linolenic acids¹⁴), is often considered to be performed by adding the elements of water: OH and H to e.g. the carbon atoms *a* + 1 and *a* + 2 respectively and by subsequently losing OH and H again by carbon atoms *a* + 1 and *a* respectively. In some, similar, cases the corresponding hydroxy compounds are isolated. Vinyl acetic acid, when boiled with caustic soda, is converted into crotonic acid and *β*-hydroxy-butyric acid¹⁵):

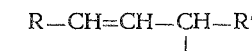


With a metallic hydrogenation catalyst, therefore, the reaction starts by taking away something of the molecule (a H-atom); with alkali-hydroxides as catalysts the first step seems to be to add something to one of the double bonds. Neither of the simple starting mechanisms seem to serve us, however, in the case of SO₂ as isomerisation catalyst.

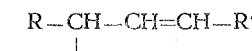
§ 4. Conjugation during oxidation.

Apart from the ability to be isomerised easily, the systems under consideration also show a higher rate of oxidation than other systems with double bonds. GUNSTONE and HILDITCH¹⁶) found that the ratio of the rates of oxidation by oxygen of the methyl esters of oleic-, linoleic- and linolenic acids at 20° C is 1:12:25.

Systematic investigations by FARMER and collaborators¹⁷) have suggested that oxidation of systems with nonconjugated double bonds leads to the formation of hydroperoxides at methylene groups adjacent to the double bonds. The autoxidation reaction proceeds as a chain-reaction of the radical type; the radical is formed by the loss of a hydrogen atom from this *α*-methylene group:



The radical, however, is a resonance hybrid, the other contributing form being:



¹³) P. KARRER and E. JUCKER, Helv. Chim. Act., 30, 266 (1947).

¹⁴) J. P. KASS and G. O. BURR, J. Am. Chem. Soc., 61, 3292 (1939); 62, 1796 (1940). T. F. BRADLEY and D. RICHARDSON, Ind. Eng. Chem., 32, 963 (1940); 34, 237 (1942).

¹⁵) It may be remarked that also in this example, where one of the double bonds is not a C=C- but a C=O double bond, the shift can only take place to one side.

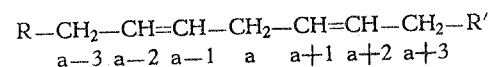
¹⁶) F. D. GUNSTONE and T. P. HILDITCH, J. Chem. Soc., 836 (1945).

¹⁷) See e.g. E. H. FARMER, Trans. Far. Soc., 38, 340 (1942); E. H. FARMER and A. SUNDRALINGAM, J. Chem. Soc., 121 (1942); 125 (1943); E. H. FARMER and D. A. SUTTON, J. Chem. Soc., 139 (1942); 119, 122 (1943).

When the radical is saturated by -OOH, it is easily seen that part of the resulting hydroperoxide-molecules have the double bond at the original position; in part of them, however, the double bond is shifted.

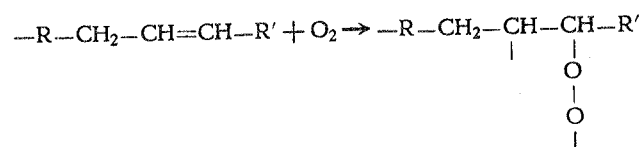
When applied to the system of two double bonds, separated by one CH₂-group, the result of the oxidation is that part of the formed hydroperoxides possess a system of conjugated double bonds¹⁸). It is interesting to note that also in the enzymitic oxidation of linoleic acid and of esters of linoleic- and linolenic acids by lipoxidase, a high proportion of oxidation products with conjugated double bonds is formed¹⁹).

As BOLLAND²⁰) points out, the most likely formation of the starting radical is by losing a hydrogen atom from the central CH₂-group (carbon-atom *a* in our notation), because the resonance energy associated with the resulting radical (three contributing forms with the "free" valency at carbon atoms *a*-2, *a* and *a* + 2 respectively) is much higher than when the radical is formed by losing a hydrogen atom from either carbon atom *a*-3 or *a* + 3:



In these latter cases there are only two contributing forms to the resonance hybrids, namely either a free valency at one of the carbon atoms *a*-3 and *a*-1 or at one of the carbon atoms *a* + 3 and *a* + 1; the resonance energy is estimated to be 18.7 Kcal/mol in this case, as against 30.5 Kcal/mol when the hydrogen is taken from carbon atom *a*²¹), ²²).

Before the autoxidation of α -methylene groups to hydroperoxides can proceed, radicals with free valencies on these α -methylene groups have therefore to be formed. It is not until such radicals are formed that the real chainreaction sets in. FARMER²³) suggests that the initial reaction starts with the addition of an oxygen molecule to one of the carbon atoms of a double bond, thus leading to a bi-radical: —



¹⁸) E. H. FARMER, H. P. KOCH and P. A. SUTTON, loc. cit. 11); J. L. BOLLAND and H. P. KOCH, J. Chem. Soc., 445 (1945).

¹⁹) S. BERGSTRÖM, Arkiv Kemi, Mineral. Geol., 21 A No. 14 and No. 15 (1935), see R. T. HOLMAN, Archives of Biochemistry, 519 (1946).

²⁰) J. L. BOLLAND, Proc. Roy. Soc., A 186 218 (1946).

²¹) J. L. BOLLAND and W. J. C. ORR, I.R.I. Trans., 21, 133 (1945).

²²) This result is completely in harmony with the well-known fact that such a central CH₂-group is an "active" one, the hydrogen of which is "mobile". This is especially the case when the CH₂-group is situated between C = O double bonds, as in acetyl-acetone, malonic ester, etc., or between one C = C and one C = O double bond.

²³) E. H. FARMER, Trans. Far. Soc., 42, 228 (1946).

Subsequent collisions of such a bi-radical with other molecules may then lead to the transfer of a hydrogen atom of the α -methylene group of these other molecules to the free valencies of the bi-radical, thus leaving a free valency at the α -methylene group behind.

§ 5. Differences between the action of oxygen and of SO₂.

When we compare the reaction with oxygen and the action of SO₂ we must bear in mind a few significant differences. Firstly there is no SO₂-containing ultimate product isolated in these reactions, secondly SO₂ produces a shift of double bonds only in those systems where two double bonds are separated by a central CH₂-group, thirdly there are no signs that the reaction with SO₂ has an autocatalytic character. Let us look into each of these three points separately:

1. The ultimate products do not contain SO₂. This, of course, does not mean that SO₂ could not be temporarily added and split off again during the reaction. Addition of SO₂ is known to occur at systems with conjugated double bonds, cyclic sulphones are isolated and well studied; they all lose SO₂ at higher temperatures, thus leaving the original hydrocarbons behind²⁴). Although a careful examination of the crystal structure of one of these compounds (β -isoprene-sulphone) has revealed that the structure is probably a resonance hybrid of several forms, it is nevertheless certain that the compound is formed by sulphur-carbon bonds and not by oxygen-carbon bonds²⁵).

2. SO₂ produces only a shift of double bonds in a system with two double bonds, separated by a central CH₂-group. As we have discussed above, oxygen produces hydroperoxides with shifted double bonds already from compounds with one double bond only.

SO₂, however, though leaving the double bond in its place, may produce a cis-trans-isomerisation, in a system with one double bond. Whilst the shift of double bonds to produce a conjugated system in linoleic acid proceeds at temperatures of about 180° C—200° C in liquid SO₂, oleic acid is transformed into elaeidic acid when heated with liquid SO₂ at 100° C—140° C for a longer time. This latter reaction is a strong indication that a temporary addition compound of SO₂ to one of the carbon atoms of the double bond may be formed.

3. There are no signs that the reaction has an autocatalytic character. From the study of the reaction one gets the impression that every con-

²⁴) J. BÖESEKEN and E. DE R. VAN ZUYDEWIJN, Rec. trav. chim., 56, 1047 (1937); 57, 445 (1938). H. J. BACKER and J. A. BOTTEMA, Rec. trav. chim., 51, 294 (1932); H. J. BACKER and J. STRATING, Rec. trav. chim., 53, 525 (1934); 54, 618 (1935); H. J. BACKER, J. STRATING and A. J. ZUTHOFF, Rec. trav. chim., 55, 761 (1936); H. J. BACKER and C. C. BOLT, Rec. trav. chim., 54, 538 (1935); H. J. BACKER, J. STRATING and C. M. H. KOOL, Rec. trav. chim., 58, 778 (1939).

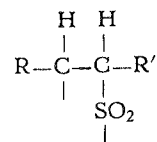
²⁵) E. G. COX and G. A. JEFFREY, Trans. Far. Soc., 38, 241 (1942).

version goes via a direct action of SO_2 rather than via a chain-reaction which is initiated by SO_2 .

§ 6. *Suggested mechanism for the cis-trans-isomerisation.*

The above considerations lead us to the following suggestions for the explanation of the cis-trans-isomerisation of oleic acid by SO_2 :

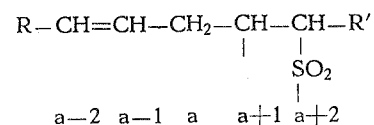
SO_2 may be added to one of the carbon atoms of the double bond, forming a bi-radical with one free valency on the sulphur and a second one on the other carbon atom of the original double bond:



In this bi-radical there is not only a single bond between the two carbon atoms, but one of these carbon atoms carries only three substituents. If, therefore, the period of existence of the SO_2 -addition product is long enough, rearrangements of the mutual position of the two carbon atoms and of the substituents on one of them may occur²⁶). When subsequently SO_2 splits off again the double bond may be restored in such a way that either a cis- or a trans-position of the two large substituents R and R' will result. Consequently a partial cis-trans-isomerisation may have taken place as determined by the energy relations of the resulting products. It is not necessary that the large substituents R and R' actually rotate round the temporarily single bond.

§ 7. *Suggested mechanism for the SO_2 catalysed conjugation.*

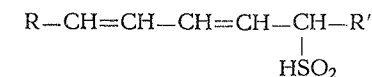
The catalytic action of SO_2 in the conjugation isomerisation starts probably in the same way. In the resulting bi-radical in this case, however, there is a CH_2 -group (a) left, still "activated" by the other remaining double bond:



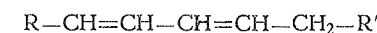
The transfer of a hydrogen atom from CH_2 -group a to the sulphur atom, attached to carbon-atom a + 2 seems to be quite feasible, also from sterical considerations. The resultant free valency on carbon atom a and the free valency on carbon atom a + 1 would saturate each other and form a

²⁶) The cis-trans-isomerisation by bromine atoms in the case of maleic- and fumaric acids is also caused by the formation of radicals, in which one of the carbon atoms carries only three constituents, see e.g. W. HÜCKEL, *Theoretische Grundlagen der Organische Chemie*, Leipzig 1931, Band I, page 269.

double bond which is conjugated with the one between carbon atoms a - 2 and a - 1:



This sulphone, in splitting off SO_2 , gives:

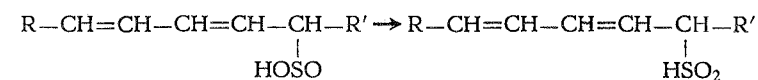


§ 8. *Influence of the orientation by polar forces.*

It may be asked whether the polar character of SO_2 might play a role in this suggested mechanism. SO_2 carries a relatively large dipole, the moment of which is 1.61 Debye-units. The positive pole is on the sulphur side of the triangular molecule (valency angle O-S-O about 125° , distance O-S 1.37 Å). The combination of a double carbon-carbon-bond and an adjacent CH_3 - or CH_2 -group also gives rise to local dipole moments which, depending on the symmetry conditions, may or may not result in a total dipole moment of the molecule as a whole. The CH_3 - or CH_2 -groups form the positive poles of such partial dipoles, the negative charges are more or less located on the carbon atoms of the double bond.

In the mutual attraction of the molecules, prior to the addition of SO_2 to an isolated double bond, the sulphur of the SO_2 will therefore be directed towards one of the C-atoms of the double bond. This is in accord with the experimental fact that in such an addition (and also in the addition of bisulphite) C—S links are always formed and not C—O links.

In systems of two double bonds, separated by one $-\text{CH}_2-$ group, this central CH_2 -group is the site of a positive charge and the carbon atoms a + 2 or a - 2 are to be considered as the sites of negative charges. When SO_2 is added, the sulphur atom is directed either to carbon-atom a + 2 or to a - 2 and will be added to one of these C-atoms. One of the oxygen atoms of SO_2 is orientated into the direction of the central CH_2 -group and the possibility might be considered for one of the hydrogen atoms to be added to such an oxygen atom, rather than to the sulphur-atom as in our consideration above. The resultant sulphinic acid would, however, easily transfer into the corresponding sulphone²⁷):



or it would, when losing SO_2 , transfer its hydrogen to the carbon atom to which it is attached.

The polar properties of SO_2 , therefore, assist the addition mechanism to follow the suggested course. The typical feature of the catalytic action of SO_2 in the cis-trans-isomerisation and in the conjugation isomerisation is,

²⁷) T. P. HILDITCH, *J. Chem. Soc.*, 93, 162 (1908).

in our opinion, however, a radical reaction. This radical reaction does not start a chain reaction, as in the case of oxygen.

Summary.

SO₂ catalyses the cis-trans-isomerisation of unsaturated fatty acids, such as oleic acid. At somewhat higher temperatures it also catalyses the conjugation of linoleic and linolenic acids.

Both catalytic reactions may be explained by assuming that SO₂ forms an addition product, which has the character of a bi-radical. Intra-molecular rearrangements and subsequent splitting off of SO₂ result in the isomerisations.

When the typical features of this and other isomerisation catalysts are compared, the following differences may be pointed out:

a) In the isomerisation by a heterogeneous catalyst a hydrogen atom is taken away from the molecule and when another hydrogen atom is added to the resultant radical this addition may take place at another carbon atom.

b) In the isomerisation by means of alkali, a OH-group and a H-atom may be added to a double bond, whereupon the OH-group and a hydrogen atom from another carbon atom are removed.

c) In the isomerisation by SO₂, a molecule of SO₂ is added to the double bond and performs the transfer of a hydrogen atom of one carbon atom of the molecule to another carbon atom.

Chemistry. — Contribution to the explanation of motory and desintegration phenomena in complex coacervate drops in the electric field.

By L. DE RUITER and H. G. BUNGENBERG DE JONG.

(Communicated at the meeting of September 27, 1947.)

A. Introduction.

In a previous article ¹⁾ it was suggested that local changes in the interfacial tension (σ) coacervate-medium might play an essential part in the occurrence of the motory and desintegration phenomena, which have been observed in complex coacervate drops in the electric field and in diffusion fields of substances, which have a swelling or densifying influence on the coacervate.

It was supposed that the assumed σ -changes in the electric field would be due to variations of pH caused by polarisation of the surface of the drops. No immediate data however were available at that time concerning the influence of diverse variable factors on σ .

No more had the postulated pH changes been directly demonstrated.

Some data concerning the value of σ and the influence thereon of mixing proportion and salt concentration in gum arabic (A)-gelatine (G) systems have since been obtained ²⁾.

In the present article some experiments will be mentioned, which were carried out on gum arabic-gelatine systems in order to demonstrate the postulated pH changes. Although we did not succeed therein (which may be due to the fact that we worked with buffered systems), we found indications for the existence of another factor, which may be responsible for the assumed changes of σ , viz. a local shift of the composition of the coacervate in the electric field.

Finally it will be undertaken to give, in the light of these recent data, a more detailed explanation of the phenomena observed in coacervate drops in electric and diffusion fields.

B. Description of phenomena in the electric field.

In our experiments we used systems prepared by mixing 2% A- and 2% G sols at 40° C. These stock sols had been buffered with a mixture of sodium acetate and acetic acid at pH 3.7 ³⁾ and were of the following composition:

20 gr. G, resp. A, (airdry)
50 cc 0,1 n. sodium acetate
50 cc 1 n. acetic acid
920 cc dest. water.

¹⁾ H. G. BUNGENBERG DE JONG and E. G. HOSKAM, Proc. Ned. Akad. v. Wetensch., Amsterdam, 44, 1099 (1941).

²⁾ L. DE RUITER and H. G. BUNGENBERG DE JONG, Proc. Kon. Ned. Akad. v. Wetensch., Amsterdam, 50, 836 (1947).

³⁾ H. G. BUNGENBERG DE JONG and E. G. HOSKAM, Proc. Ned. Akad. v. Wetensch., Amsterdam, 45, 585 (1942).