J. A. CHRISTIANSEN

SEVEN ESSAYS RELATING TO THE STEREOCHEMISTRY OF CYCLOHEXANE AND ITS VICINAL DI-DERIVATIVES

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BIANCO LUNOS BOGTRYKKERI A/S

Introduction

The accepted assignment of configurations to vicinal *di*-derivatives of cyclohexane dates back to a renowned paper by WERNER and CONRAD (1899)[1]. In the same paper the two authors believed to have decided the competition between BAEYER's[2] planar and SACHSE's[3, 4] puckered (chair-) form of cyclohexane in favour of the former.

About two decades later MOHR[5] revivified SACHSE's brilliant idea with the exception that he (M.) assumed the conversion of the two SACHSE-hexagons into each other to be fast. In that form SACHSE's idea has survived to the present day. However, if one scrutinizes WERNER and CONRAD's paper, it appears that they uncautiously replaced BAEYER's names from 1890[2] of the two isomers of his hexahydro phtalic acid, maleinoidic and fumaroidic, respectively by *cis*- and *trans*-. From BAEYER's paper it is clear that he chose his names to express that the maleinoidic isomer could easily be dehydrated and the fumaroidic one only with difficulty. BAEYER carefully uses these names throughout his paper and only once he mentiones in passing *cis*- and *trans*-. But if, in a contest between BAEYER's and SACHSE's hexagons, one replaces maleinoidic and fumaroidic by *cis*- and *trans*-, one has already implied the validity of BAEYER's planar form because SACHSE's chair form permits a *cis*(ea) and a *trans*(ee) configuration in which the distances between the two sites are equal (in the ideal models) and small enough to permit the formation of a five-membered ring coupled to the six-membered one. The *trans*(aa) form can not be expected to react at all in that way. The fact is that WERNER and CONRAD found that the fumaroidic isomer of BAEYER's acids could be separated into optical antipodes while the maleinoidic could not. This is certainly not sufficient evidence to denote the former as *trans*- and the latter as *cis*-. But, if MOHR's assumption be accepted, the *cis*(ea) form must be a racemic equilibrium mixture of its two optical antipodes and the isomer which can be separated into enantiomers was believed to be a mixture of the two *trans*-forms.

When MOHR wrote his paper, it was impossible, for lack of experimental data, to estimate the work of activation for the conversion in question, which is necessary to prove or to disprove the validity of his assumption. This assumption differed radically from SACHSE's, which he (S.) admittedly arrived at by intuition, namely, that his chair-model, on account of mechanical resistances, was rigid. But, after the surge of papers on RAMAN and a little later on infrared spectra which began in the thirties, estimates became possible, at least in principle. The present author[6, 7] has tried to perform such estimates, and his result is, that it is difficult, to say the least, to avoid the conclusion that SACHSE was right and MOHR wrong. Furthermore, a study of the conditions for the separability of the enantiomers by the method of diastereomers showed that the *cis*(ea) enantiomers must be much easier to separate than the *trans*(ee) and *trans*(aa) ones.[8]

Generally, all experiments known to the writer can, so far as he can see, more naturally be interpreted to mean that BAEYER's fumaroidic acid is *cis*(ea) and that the maleinoidic acid is *trans*(ee). Of course, different kinds of experiments have different weights, but in some of them the situation seems to be so clear, that the opposite assignment, the current one, cannot be maintained.

The whole problem has so many fascinating aspects that the writer has found it convenient for the reader and for himself to treat them separately in a number of essays. A group of such essays is published on the following pages.

2. The Configuration of Baeyer's Hexahydrogenated Phtalic Acids

In 1890 A. Baeyer[2] published an extensive paper in which he reported a great number of experimental results on the reduction products of phtalic acid obtained by his coworkers. In the same paper he presents his well known opinion that the hexahydrogenated benzene ring is plane, an opinion which most probably has been enhanced be his veneration for his old master Kekulé. Among many other facts Baeyer reports the discovery of two different hexahydrogenated phtalic acids, one melting between 182 and 192°C and another melting in the interval 215 to 221°C. The former looses water very easily, already just above the melting point. The latter, the isomer with the higher melting point, can be dehydrated, but only by use of a strongly dehydrating reagent. Baeyer's coworker whom he, as always, took great care to mention by name, used acetyl-chloride. Referring to the somewhat similar properties of maleic and fumaric acid he named them respectively maleinoid and fumaroid. Somewhere in the paper he mentions in passing the prefixes *cis* and *trans* but it is characteristic for Baeyer and his time that throughout the paper he speaks only about the maleinoidic and the fumaroidic acid, thus referring only to the factual properties of the two isomers and not to any hypotheses concerning their configuration as implied in the prefixes *cis* and *trans*.

In the same year, 1890, H. Sachse published[3] the first of his two renowned papers on the strainless carbon skeleton in alicyclic compounds, the most important examples being cyclohexane and its derivatives. The second one appeared[4] in 1892, but Sachse did not live to follow up his discovery of the strainless six-rings and to defend his ingenious ideas. He died in 1893, 31 years old. His first paper was abstracted in Chemisches Centralblatt by the organic chemist J. Wagner. The abstract is short and, to say the least, very cool. The second paper was abstracted by W. Nernst who was the junior of Sachse by two years. His abstract is longer and one gets the impression, that Nernst has seen the importance and the difficulties of Sachse's model.

For example he emphasizes that SACHSE's model in contrast to BAEYER's permits two monosubstitutes of cyclohexane, while only one was (and is) known.

After that it seems that silence fell upon SACHSE's idea and BAEYER's plane model was generally accepted as true. However, in 1899 the problem was taken up by A. WERNER in cooperation with H. E. CONRAD[1]. They believed to be able to settle the conflict between BAEYER's and SACHSE's views experimentally by using the following argument: If BAEYER is right, the *cis*-form of his hexahydro phtalic acid must be optically inactive and the *trans*-form active that is that isomer which can be separated into optical antipodes must be the *trans*-form. But if SACHSE is right it is the *cis* acid which has this property. (The two authors seem to have overlooked the fact that also the molecules of the *trans*-forms of BAEYER's acids are asymmetric if SACHSE's model (chair-form) is accepted). Now, what WERNER and CONRAD found was, that BAEYER's fumaroidic acid could be separated into optical antipodes and the maleinoidic not. But, unfortunately, they were less cautious than BAEYER and translated the latter's designations, which are free from hypotheses, into *trans*- and *cis*, expressions which refer to the middle plane of the molecule.

As well known a maleinoidic isomer of a dibasic acid must have the property of being able to loose water very easily, while the corresponding fumaroidic one looses water only with difficulty or not at all. When we say that the former has its two COOH groups near to each other and the latter far, or further, from each other, it is of course a hypothesis, but a hypothesis which is so well founded that its validity hardly can be doubted. If therefore we knew that BAEYER's planar form of cyclohexane were the right one we should certainly be justified in using WERNER's assignment of *cis*- and *trans*- to malenoidic and fumaroidic respectively. But, unfortunately, according to SACHSE's (chair) model there are, at vicinal C-atoms, one pair of *cis*-positions but two pairs of *trans*-positions, one (*aa*) and one (*ee*) This complicates the assignment as the distance between the *cis*(*ea*) sites in the (ideal) SACHSE model is exactly the same as that between the *trans*(*ee*) ones. Consequently, when we identify maleinoidic with *cis*- and fumaroidic with *trans*- we imply the validity of BAEYER's model, which means that the two authors in their proof have assumed what they intended to prove. Today, however, we know, with a probability approaching certainty, that SACHSE's model is the right one, and by reverting WERNER and CONRAD's argument we might therefore draw the conclusion from their experiments, that it is BAEYER's fumaroidic acid which is *cis*-.

The difficulty is, however, that not only the *cis* form but also the two *trans* forms are asymmetric. But, as will be shown later, we must expect that the difference in solubility between diastereomers which have been formed from a pair of *cis* enantiomers will be much greater than that between diastereomers formed from a pair of *trans* enantiomers.

The two authors express the result of their experiments in a strikingly cautious way. On the second page of their paper they say: " . . . so spricht das Resultat, unter Berücksichtigung der positiven Ergebnisse bei der Transsäure, doch dafür, dass die Annahme stabiler räumlicher Lagerungen der Hexamethylenkohlenstoffe nicht sehr wahrscheinlich ist. "It must be remembered that "der Transsäure" means "der fumaroide Säure". It is not quite evident what the authors mean by "stabile räumliche Lagerungen" but most probably the expression refers to the fact that SACHSE's model in contrast to BAEYER's is strainless.

One can only guess at the reason for this cautiousness, but it is certain, that contemporary chemists took WERNER and CONRAD's experiments as a proof that BAEYER was right, and it sems also certain that nobody observed the flaw in the logic of their argument. The proof of the former statement is that MEYER and JACOBSEN in their renowned LEHRBUCH der Organischen Chemie, Zweiter Band, ERSTER TEIL (1902) p. 860 use BAEYER's model and do not spend a single word on SACHSE's. In contrast to this one finds in the same volume p. 63 a rather detailed description of SACHSE's now nearly forgotten model of benzene. It may be mentioned in this connection, that it appears from articles in Chemiker Zeitung (1893) that professor MEYER highly venerated his deceased collegue and his work.

Before continuing the later history of SACHSE's model we shall discuss the assignment of configurations (cis-, trans-) to BAEYER's fumaroidic and maleinoidic hexahydrogenated phtalic acids by means of WERNER and CONRADS experiments from another point of view.

3. On the Possibilities of Separation of Racemic Mixtures of Vicinal Derivatives of Cyclohexane with two Equal Substituents

In stead of considering WERNER and CONRAD's experiments from the viewpoint of the possibility of optical activity of BAEYER's two acids one may discuss which of them may be expected to be best suited for separation by means of the difference in solubility in symmetric solvents, of their salts with an asymmetric base.

To investigate the conditions for the solubilities being different one must study the possibilities for interaction between the solvent molecules and those of the diastereomers.

In cyclohexane and its derivatives there are on the "surface" of the molecule twelve sites, namely 2×3 axial and 2×3 equatorial sites which are occupied either by hydrogen atoms or by substituents. In between there are twelve empty sites where solvent molecules may accommodate themselves. It must be such solvent molecules which mainly determine the interaction between the diastereomers and the solvent and therefore the solubility of the former in the latter.

Now, unfortunately, it is nearly impossible to illustrate the situation by means of drawings of the molecular models. In stead of that one must use some sort of projection from which the relative position of ligands and empty sites can be seen qualitatively. Table 1 represents a kind of "Mercator's Projection" in which the 24 empty and occupied sites are tabulated in four lines corresponding to the two groups of axial and two groups of equatorial sites, and in six columns corresponding to the six carbon atoms. It will be seen that there are around each ligand four empty sites, one above, one below, one to the left and one to the right. Now, an asymmetric ligand may be compared with a screw. As well known a screw has the property that its two ends are alike while there is a difference between its left and its right sides. This is true also for some kinds of asymmetric molecules, but for others there is only a qualitative and not an exact likeness between the two ends.

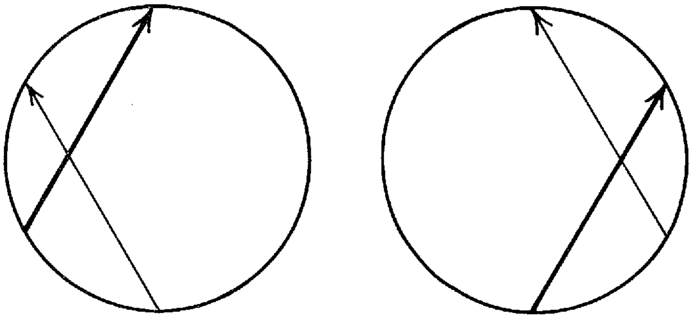


Fig. 1.

The figure to the left is meant to represent a fictive asymmetric molecule consisting of a regular cylinder provided with electrical permanent dipoles on both endfaces. Heavily drawn dipoles are meant to be nearest to the eye, if they are thinly drawn they are meant to be more distant. The "molecule" has the property of a lefthanded screw in so far as a screw-like motion of the upper dipole will cause its direction to coincide with that of the lower. The arrows point against the negative ends of the dipoles (by convention). When the translation is from the upper to the lower, end the rotation is to the left.

The figure to the right represents the same "molecule" turned through 180° around a vertical axis in the plane of the paper. It is seen that the negative ends of the two arrows point to the same side when the model is regarded, e.g. from the left, whether or not it is turned upside down. That it has the same screw-property seen from both ends is a matter of course.

For example, they may both contain dipoles, but the dipoles may be of different strength. However, the difference between the two sides is much more pronounced, as can be seen *e.g.* from fig. 1 where the left hand side is negative whether or not the model is turned upside down. If the upper and the lower ends of the asymmetric substituent are not equal, the two sites at the upper and the lower end of that substituent are not exactly equivalent, but the forces emanating from its two ends are still similar. They may for example both he dipole forces, which are not very different from each other. But the forces from the two sides, left and right, are qualitatively different and stronger than those from the ends. Consequently the difference between left and right around an asymmetric substituent is much more pronounced than that between above and below.

In the diagrams or "projections" Table 1 the empty sites are marked by asterisks and the asymmetric substituent is symbolized by the letter Z, because this letter has the same property in a plane as a screw has in space: it looks alike whether it is seen from below or from above, while there is a marked difference between sites which are to the left or to the right of it.

As the three isomers, cis(*ea*), trans(*ee*) and trans(*aa*) are all asymmetric, the three corresponding pairs of diastereomers with a common asymmetric substituent cannot be equal that is, there must be differences between the

Table 1.

Vicinal Derivatives of the Sachse Model of Cyclohexane With Two Equal Asymmetric Substituents

	3	2	1	6	5	4	3			3	2	1	6	5	4	3
	*	*	*	*	*	*	*			*	*	*	*	*	*	*
a	*	Z	*	H	*	H	*		*a*	*	H	*	H	*	Z	*
e	H	*	Z	*	H	*	H		*e*	H	*	H	*	Z	*	H
e	*	H	*	H	*	H	*		*e*	*	H	*	H	*	H	*
a	H	*	H	*	H	*	H		*a*	H	*	H	*	H	*	H
	*	*	*	*	*	*	*			*	*	*	*	*	*	*

cis (*ea*)

	3	2	1	6	5	4	3			3	2	1	6	5	4	3
	*	*	*	*	*	*	*			*	*	*	*	*	*	*
a	*	H	*	H	*	H	*		*a*	*	H	*	H	*	H	*
e	H	*	Z	*	H	*	H		*e*	H	*	H	*	Z	*	H
e	*	Z	*	H	*	H	*		*e*	*	H	*	H	*	Z	*
a	H	*	H	*	H	*	H		*a*	H	*	H	*	H	*	H
	*	*	*	*	*	*	*			*	*	*	*	*	*	*

trans (*ee*)

	3	2	1	6	5	4	3			3	2	1	6	5	4	3
	*	*	*	*	*	*	*			*	*	*	*	*	*	*
a	*	Z	*	H	*	H	*		*a*	*	H	*	H	*	Z	*
e	H	*	H	*	H	*	H		*e*	H	*	H	*	H	*	H
e	*	H	*	H	*	H	*		*e*	*	H	*	H	*	H	*
a	H	*	Z	*	H	*	H		*a*	H	*	H	*	Z	*	H
	*	*	*	*	*	*	*			*	*	*	*	*	*	*

trans (*aa*)

Table 2.

Empty Sites
in Diastereomers of Vicinal Disubstituted Cyclohexane

	cis(*ea*)		
*a*1	above Z(*e*), R	*a*5	above Z(*e*), L
*e*2	below Z(*a*), L	*e*4	below Z(*a*), R
	trans (*ee*)		
*e*2	above Z(*e*), L	*e*4	above Z(*e*), R
*e*1	below Z(*e*), R	*e*5	below Z(*e*), L
	trans (*aa*)		
*a*1	above H(*e*), R	*a*5	above H(*e*), L
*a*2	below H(*e*), L	*a*4	below H(*e*) ,R

diastereomers in each pair. The question is in which pair the difference in solubility is most pronounced. Now, as the solubility must be determined mainly by the location of the empty sites, where solvent molecules may locate themselves, and as differences in solubility must be expected to arise mainly from differences in location of the empty sites which are nearest to the asymmetric substituents, we must try to enumerate these differences by means of the "projections". This has been done in table 2.

As will be seen, one of the diastereomers is to the left, and the corresponding one to the right. Inspection of table 1 shows that, only empty sites in lines containing the symbol Z are different from those in their diastereomers that is, there are, in each pair of diagrams, only two lines to consider. Each site is indicated by the character of its line, axial (*a*) or equatorial (*e*), followed by the number of its column, which is the same as the number of the carbon atom in question.

For each site there are in table 2 two entries. Concerning the first one *e.g.* "above Z(*e*)" means that the empty site in question is in the same column but above an equatorial asymmetric substituent Z.

Concerning the second entry, R means that the empty site in question is to the right of an asymmetric substituent in the same line and similarly to the left if the entry is L.

In the cis(*ea*) pair of diastereomers it is seen that all four entries are different in the two members of the pair. All these differences may be called major because of the decisive difference between equatorial and axial positions.

In the case of the trans(*ee*) isomer, the difference between the diastereomers is much less. As will be seen, the only difference between the sites *e*2 and *e*5 is that, one is above and the other one below an equatorial Z. Similarly, the only difference between *e*1 and *e*4 is, that the former is below and the latter above an equatorial Z. Thus there are in this case only two differences between the diastereomers, and these differences are, according to what was said before, much less pronounced than the four differences in the cis case.

In the trans(*aa*) case the difference between the diastereomers is still less: It must be immaterial whether the site in question is above or below a hydrogen atom. Therefore, if only sites which are neighbours to asymmetric substituents are taken into account there is no difference between the diastereomers. It is only when forces between an empty axial site in the lower half of the molecule and an axial asymmetric substituent in the same column but in the upper half are taken into account, that a difference can be assumed to exist. Such forces must however be very weak, and as the situation concerning the empty axial site besides Z in the upper half of the molecule, is the same the difference between the trans(*aa*) diastereomers must be very small indeed.

In this way we arrive at the result that the difference in solubility of the diastereomers is much greater in the *cis*(ca)- than in the *trans*(ee)-case and that the difference in the latter case is again greater than that in the trans(*aa*)-case.

As now WERNER and CONRAD succeded in separating diastereomers of BAEYER's fumaroidic acid but were unable to separate diastereomers prepared from his maleinoidic acid, one can hardly avoid the conclusion that the former must be the cis-form and the latter one of the trans-forms, or a mixture of both. This is just the opposite of the result arrived at by the two authors, whose assignment of configurations to the two acids has been accepted by all chemists up till now.

4. Mohr's Assumption Concerning the Ease of Conversion of the Sachse Hexagon. Assignment of Configurations to Vicinal Cyclohexanediols

After the commencement of the 20'th century silence fell again upon SACHSE's idea, and it was so late as in 1918 that MOHR[5] saw the advantage of SACHSE's model as compared to BAEYER's, and his paper paved the road for its general acceptance by chemists. Many new chemical findings, most of them being due to W. HÜCKEL[9] and his coworkers, gave more and more experimental support to the chair conformation of the SACHSE-hexagon until finally X-ray and electronic diffraction experiments provided us with practically certain proofs of its validity. As one of the leaders, or as the leader, of the latter kind of experimental work O. HASSEL[10] (Oslo) should be mentioned, so much more as a great part of the work in his laboratory was carried out under the extremely difficult conditions prevailing in Norway during world war II.

Nevertheless, a fate of misunderstanding or of missing appreciation of the strength of SACHSE's arguments seemed still to cling to his fundamental work.

In the two papers[3, 4], particularly in the one from 1892, SACHSE emphasizes that strong mechanical forces (due to the deformation of valency angles) must resist the conversion ("Version" as proposed by SACHSE) of one of the chair forms into the other one and also the conversion of a boat form into the chair form and *vice versa*. To get an explanation of the circumstance which was at that time considered to be a fact, that the SACHSE model gave room for too many isomers, MOHR[5] simply reversed SACHSE's statement and assumed that the conversions in question could easily take place. MOHR seems to have been under the impression, that the only or at least the main forces which tend to hinder the said conversions are those arising from rotations around single bonds. This is certainly not true, as angular deformations must give an essential contribution to what we nowadays may denote as the work of activation. In this connection it may be of interest to note that SACHSE's first paper appeared only about one year after ARRHENIUS's[11] renowned work on the dependence of the velocity of chemical reactions on temperature, the paper in which the concept energy of activation is introduced. The present author has tried to calculate the work of activation for the conversion of the two chair forms into each other, as a sum of two contributions one from the rotations around single valence bonds and one from the deformation of valency angles[6, 7]. He arrived at the result, that the work in question was large enough to prevent, practically speaking, the conversion at not extremely high temperatures. However, after the publication of MOHR's paper, chemists accepted his assumption of easy conversion without further discussion.

Today, when one looks back at the situation in 1918 it seems a little surprising that MOHR was so convinced that SACHSE's model permitted too many isomers. The background for this remark is the following: Originally two and only two isomers of 1,2 cyclohexanediol were known, one which melted at 99° C and and one with m.p. 104° C. But in 1908 SABATIER with his coworker MAILHE[12] tried his method of catalytic hydrogenation on catechol and obtained an isomer of vicinal cyclohexanediol with m.p. 75° C. It is true that H. LEROUX[13] two years later reported that the low melting isomer could be formed by dissolving the two higher melting ones and evaporation, from which he concluded that the former was a chemical combination of the the two latter.

However, LEROUX's report, which may have released a sigh of relief from contemporary chemists, is contained in a few lines which are part of a comprehensive paper on hydrogenation products of naphtalene-β-diols. In this paper he describes three isomers which he denotes as cis-naphtanediol-β (m.p. 160° C), cis-trans naphtanediol-β (m.p. 141° C and (cis + cis-trans) naphtanediol-β (m.p. 125° C). The latter can be formed by mixing solutions of the two higher melting isomers and evaporating, and LEROUX emphasizes that it cannot be fractionated back into the two others. He considers it to be a compound of the two, notwithstanding the fact that a determination of the molecular weight gave him 177 g/mol (calculated for a single molecle 170 g/mol). He does not report any m.w. determination of the low melting cyclohexane diol. These results may not prove with certainty the existence of the three isomers permitted by the Sachse models, but much less do they prove the non-existence of a third isomer.

It is thus seen that in the case of the cyclohexanediol the number of isomers may agree with that predicted by the Sachse model.

As mentioned in the foregoing, two vicinal cyclohexane diols have been known for a long time, one with the melting point 104°C and another with melting point 99°C. The former can be separated into optical antipodes and the latter not.[14]

On this basis the 104° diol has been believed to be the trans-form and the other one the cis-form. The argument for this assignment is the following: According to Mohrs hypothesis the conversion of the Sachse hexagon takes place very easily and it is therefore impossible to separate the two enantiomeric *cis*-forms from each other, as they are transformed into each other by the conversion of the Sachse hexagon, in other words the lower melting diol should be a racemic *cis*-mixture. On the other hand, by the same conversion one of the two trans-forms must be transformed into the other one, or, in other words, the trans-form is an equilibrium mixture of *trans*(aa) and *trans*(ee), both of which are asymmetric and therefore separable into optical antipodes.

According to the considerations in the foregoing paragraphs this is improbable and, apart from that, it is seen that the whole argument rests on the validity of Mohr's assumption, that the work of activation for the conversion in question is small and the conversion therefore rapid. The validity of this assumption has been discussed by the writer in a note[6] and the result was that the work of activation must be rather high and the conversion therefore slow. Consequently conversion of the Sachse (chair) hexagon does not prevent the separation of the two enantiomeric *cis*-forms.

In consideration of the importance of the question of the work of activation it will be discussed in more detail in the next essay.

References to Essays 1–4

1. Werner, A., and Conrad, H. E., Ber. **32**. (1899) 3046.
2. Baeyer, A., Ann. d. Chem. **258** (1890) 145.
3. Sachse, H., Ber. **23** (1890) 1363.
4. Sachse, H., Z. physik. Chem. **10** (1892) 228.
5. Mohr, E., J. prakt. Chem. **98** (1918) 315.
6. Christiansen, J. A., Nature **211** (1966) 184.
7. Same author, Danske Vids. Selsk.
8. Same author, Danske Vids. Selsk.
9. W. Hückel. Theoretische Grundlagen der organischen Chemie, Leipzig, Erste Auflage (1931) and later editions.
10. O. Hassel and coworkers. Acta Chemica Scandinavica Vol. 1 (1947) with references to earlier publications.
11. Arrhenius, Sv., Z. physik. Chem. **4** (1889) 226.
12. Sabatier, P., and Mailhe, C. r. **146** (1908) 1154.
13. Leroux, H. Ann. de chim. et de phys. 8^{ieme} ser. **21** (1910) 541.
14. Böeseken, J., van Giffen, J., and Derx, Rec. trav. chim. **39** (1920) 183.

5. Transition State and Work of Activation at the Inversion of the Sachse (Chair) Hexagon

For reasons mentioned in a note in NATURE it is assumed that all intermediates between the two Sachse (chair) hexagons can be inscribed on the surface of a regular hexagonal prism, and that their angles and their sides are all equal, the sides being constant in length. Consequently the transition form is assumed to be BAEYER's planar regular hexagon. The work of activation for the inversion ("Version" as SACHSE named it) of one of the SACHSE (chair) forms into the other one is then calculated, *a.* at 176.2 kJ/mol (directly from the frequency 384.1 cm^{-1} in the Raman spectrum of cyclohexane) and *b.* at about 173 kJ/mol (indirectly by adding 101.4 kJ/mol calculated from the methane frequency 1520 cm^{-1} to six times PITZER's maximum for the work of twisting the C–C bond in ethane. This means that SACHSE was right when he intuitively deemed it to be difficult or impossible to invert his puckered hexagon, the reason being mechanical resistances.

In a note in *Nature*[1] it was pointed out that it is hardly possible to avoid the conclusion that the transition state between the two (congruent) forms of SACHSE's (chair) model [2,3] of cyclohexane must be BAEYER's planar model of the same substance. When this is taken for granted the work of activation for the conversion of one of the two forms into the other one can be calculated by classical mechanics.

It is assumed that the molecule behaves as a system of atoms bound to each other by bonds of constant length, so that only the deformation of the bond angles determine the potential energy of the molecule in a given configuration.

When BAEYER's "Spannungshypothese" is taken into account, it is seen that the two SACHSE forms are at minima of the potential energy and therefore stable. They are separated by the BAEYER form which is at a maximum and unstable. The difference between the two extreme values of the potential energy must then be the required work of activation.

From the standpoint of quantum theory it might be argued that this difference must be the difference between two "eigenvalues" of the energy of the molecule. But this is not so certain as it sounds. Many years ago the present writer and H. A. KRAMERS wrote a paper on chemical kinetics[4]. In this paper KRAMERS pointed out that the active state (as it was called at that time) might not be a state in the quantum-theoretical sense of the word.

A few years later J. FRANCK[5] drew attention to a phenomenon observed by V. HENRI[6] who named it "Prädissoziation". HENRI observed that lines in a band spectrum often became diffuse and the more so the shorter their wavelength. He interpreted the phenomenon as a beginning dissociation, a predissociation.

FRANCK explained the phenomenon by means of potential curves, corresponding to the force-field which produced the vibrations in question. FRANCK's theory is described *e.g.* in the book of his coworker H. SPONER[5]: Molekulspektren und ihre Anwendung auf chemische Probleme vol. II. In the meantime HEISENBERG's uncertainty relation had come to light and following FRANCK, SPONER uses this to connect the breadth of the diffuse lines with the life-time of at least one of the two states involved in the quantum-jump in question. As the life of the transition state must be very short indeed its state must be very ill defined. This is the same result as that maintained by KRAMERS several years before the advent of quantum-mechanics. It is clear that this uncertainty in the quantum mechanical definition of the transition state prevents a contradiction between that and the classical mechanical one, Consequently it must be permissible to calculate the work of activation in the classical way.

Calculation of the work of activation in the SACHSE *hexagon.*

We consider a particle of mass m which is located relative to the rest of the molecule at a certain equilibrium position. Let the displacement of the particle in a certain direction from the equilibrium position be x. Assuming the validity of HOOKE's law the force in the x direction will then be

$$F_x = -Dx \tag{1}$$

where D is the restoring force at unit displacement of the particle in the direction considered. We have from the law of motion

$$m(\mathrm{d}^2/\mathrm{d}t^2)x = -Dx \tag{2}$$

(2) describes a vibration with frequency ν connected to D by the equation

$$m(2\pi\nu)^2 = D. \tag{3}$$

Thus, if m is known and the frequency ν has been measured, D can be calculated. Furthermore, if z is the displacement in a direction which is perpendicular to that of x and the force constant D is independent of the direction, the force in the z direction becomes

$$F_z = -Dz. \tag{4}$$

If the forces from (1) and (4) are the only ones which act on the particle its potential energy V is given by

$$2V = D(x^2 + z^2). \tag{5}$$

Now, in the chair form of the SACHSE model of cyclohexane the six carbon nuclei are at the corners of what might be called a quasiregular hexagon, meaning a hexagon in which all the sides and all the angles are equal and which can be inscribed on the surface of a regular hexagonal prism. If the angles are equal to the tetrahedral angle

$$\omega = \arccos(-1/3) \tag{6}$$

the hexagon will, according to BAEYER's hypothesis, be strainless, but it is strained at all other values of the angle. The arguments in the note referred to above make it natural or even necessary to assume that also the strained forms of the hexagon have the property of being quasiregular.

If this be granted there is only one deviation from the tetrahedral angle to take into account, but this is not the only stress which contributes to the restoring force represented by D.

Years ago PITZER[7, 8] showed that there is in ethane a difference between the potential energies of the molecule in the two positions named "eclipsed" and "staggered" of the pair of valency triades. PITZER estimated this difference at about 3 kcal or about 12 kJ. If therefore we calculate D from the RAMAN spectrum of cyclohexane (the vibration in question is inactive in the IR-spectrum) we have already included both kinds of stress in our calculations. This was pointed out by LANGSETH and BAK[9] in their paper on the RAMAN spectra of cyclohexane and some deuterated cyclohexanes. However, for the application of the spectra to the determination of the restoring force it is unfortunate that neither LANGSETH and BAK nor other investigators of the cyclohexane spectrum have assigned types of vibrations to the different, surprisingly few, Raman lines. For the calculation of the work of activation relating to the transition from one chair form of the Sachse hexagon into the other one we are interested in that type of vibrations during which the hexagon remains quasiregular.

We shall assume that the Raman frequency to be assigned to that type of vibration is 384.1 cm^{-1}, the lowest one found by Langseth and Bak in their investigation, and in agreement with that found by a number of other authors. By comparison with their tables of Raman lines in the spectra of deuterated cyclohexanes it can be concluded with certainty that there are no lines with lower Raman shifts than the one at 384.1 cm^{-1} hidden in the strong light from the exciting mercury line. That the assignment is correct is admittedly a guess, but it is a guess which yields the lowest possible value of the work of activation which is compatible with the Raman spectrum.

The numerical value of D is to be calculated from (3). For this calculation the value of m is needed. We may at once replace m for one molecule by the molar mass. However, the vibrational movement of the molecule is more complicated than that on which equation (3) is based, and it is therefore not so easy to assign a certain value to m, but as a crude approximation it may be assumed that the CH^2 group vibrates as an entirety, and that its entire mass is located in the carbon nucleus. Using this approximation we get the value of D by putting m equal to 14 g. This and the wave number 384.1 molar from Langseth and Bak's paper yields, by insertion in (3),

$$D = 7.332 \times 10^{28}\ \text{g/s}^2. \tag{7}$$

Fig. 2 is intended to illustrate the calculations of the displacements x and z which are the same for all six CH^2 groups.

It shows the regular hexagonal prism on whose surface the quasiregular hexagon is inscribed, the prism being viewed from the side. Its upper end face contains the three uppermost corners of the hexagon and the lower endface the three other ones. The height of the prism may be denoted by h and its largest radius by r. If a is the side length of the Sachse hexagon we then get

$$r = a\sqrt{2(1 - \cos\omega)/3} \tag{8}$$

$$h = a\sqrt{(1 + 2\cos\omega)/3}\,. \tag{9}$$

From (8) and (9) we get in the first approximation for the displacements x and z caused by the deformation α of the angle ω

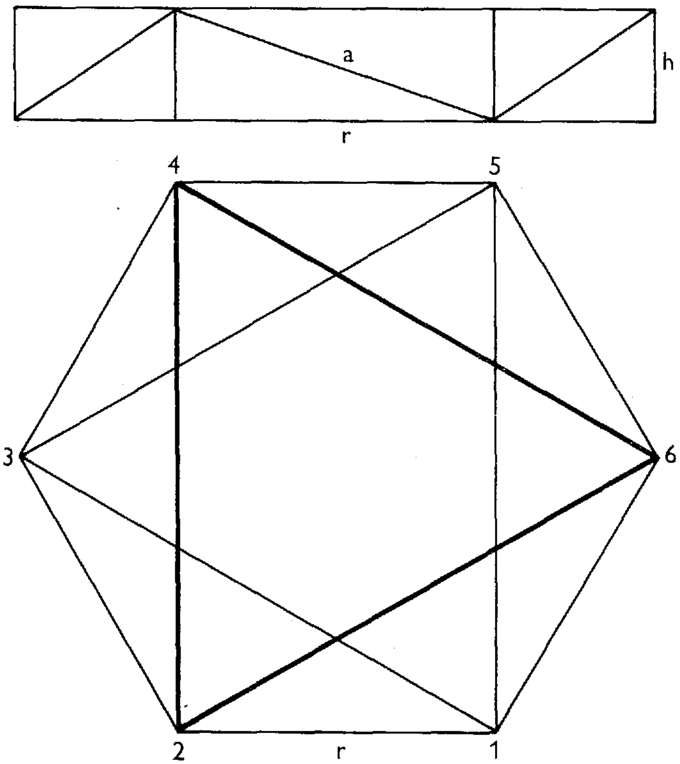


Fig. 2.

The drawing shows a regular hexagonal prism, with a SACHSE hexagon inscribed on its surface, in horizontal and in vertical projection respectively. The C-atoms in the corners are numerated as usual in hydrocarbon-chemistry but with C_6 in stead of O_5. The height of the prism is $a/3$ if a is the length of the side in the SACHSE-hexagon. The length of the side of the hexagon in vertical projection is then $2a\sqrt{2}/3$. The triangle drawn with thick lines connects the three uppermost C-atoms, 6, 2, and 4, and the one drawn thinly connects the three lower ones. The triangles are helpful in visualizing the possible ways in which the SACHSE-hexagon can be deformed.

$$x = \alpha(\mathrm{d}/\mathrm{d}\omega)r \tag{10}$$

and

$$z = \alpha(\mathrm{d}/\mathrm{d}\omega)h \tag{11}$$

In connection with (11) it must be remembered that a certain decrease of the six tetrahedral angles displaces the upper endface of the prism upwards by a certain amount and its lower endface downwards by the same amount. Consequently the six radial and the six axial displacements will cancel each other and there will result neither a displacement of the center of gravity nor a rotation of the SACHSE hexagon, conditions which necessarily must be fulfilled for any permitted type of internal motion of the molecule.

Insertion of $\omega = \arccos(-1/3)$ in (10) and (11) yields

$$x^2 = a^2\alpha^2/9 \tag{12}$$

and

$$z^2 = 8a^2\alpha^2/9. \tag{13}$$

Consequently

$$2V = A\,\alpha^2 \tag{14}$$

where

$$A = Da^2. \tag{15}$$

From many sources it is known that a, the C–C distance, is very nearly $1.54\ 10^{-8}$ cm. Insertion of this and (7) in (15) yields

$$A = 1739\ \mathrm{kJ/radian}^2 \tag{16}$$

for one "mol of angles".

If α is taken to be the difference between 120° and the tetrahedral angle

$$\alpha = 0.1838\ \mathrm{radian}. \tag{17}$$

Insertion of (16) and (17) in (14) yields

$$2V = 58.72\ \mathrm{kJ} \tag{18}$$

where V is the work required to increase one angle from the tetrahedral value to 120° plus the work required to twist one pair of valency triades from its most favorable into its least favorable position. For the total work of activation of the SACHSE hexagon G* we thus get

$$G^* = 6V = 176.2\ \mathrm{kJ/mol}. \tag{19}$$

When it is remembered that RT at 300°K equals 2.5 kJ/mol it is seen that the conversion of the hexagon must be extremely slow at ordinary temperatures. This disagrees completely with the assumption originally introduced by MOHR, that the conversion is fast enough to make the two states tautomeric whenever they have been made different by substitution of at least one of the twelve hydrogen atoms by some other atom or radical. Even today MOHR's assumption is generally accepted and it is therefore desirable or necessary to look for other ways of calculating G*.

It is evidently the force constant which measures the angular restoring force of the aliphatic C–C–C angle which is decisive. Let the force constant be denoted by B. As the C–C and the C–H bonds are both two-electronic we may expect them to have about the same "stiffness" or about the same B. Now, according to H. SPONER[10] there is in methane a vibration with the wave number 1520 cm^{-1} which she ascribes to a synchronous vibration of the four C–H bonds of such a kind that they do not effect the position of the carbon nucleus. She gives the distance C–H at $1.1\ 10^{-8}$ cm.

With $m = 1.008$ g/mol we get from (3) and (15)

$$D = 8.266\ 10^{28}\ \mathrm{g/s^2} \tag{20}$$

and

$$B = 1001\ \mathrm{kJ/mol\ rad^2}. \tag{21}$$

With these values we get for the work of distortion of six angles through 0.1838 radian

$$6V = 101.40\ \mathrm{kJ/mol} \tag{22}$$

To get the work of activation in question we must add to this about 72 kJ/mol which is the work required to twist six pairs of valency triades from the staggered into the eclipsed position. In this way we get

$$G^{*} = 173.4\ \mathrm{kJ/mol} \tag{23}$$

On account of the different approximations which we have used the close agreement between the results (23) and (19) may be fortuitous but so much seems to be certain that the conversion in question must be very slow indeed. Qualitatively the same result was arrived at in the authors note in *Nature*[1] but quantitatively there is a marked difference. In the note, WESTHEIMER's[11] value 8×10^{-12} erg/radian² was used for the *molecular* constant A in (14). This lead to the the value 48.84 kJ for the *molar* value of $6V$, which is a little less than half of that from (22). WESTHEIMER's value is nearly identical with that given by KAARSEMAKER and COOPS[12] who have $7.97\ 10^{-12}$ erg/rad² molecule.

For this value they refer to T. P. WILSON's paper[13] on the IR and RAMAN spectra of cyclobutane. From his spectra WILSON has calculated a number of force constants which are tabulated in his Table V. Among these constants is a constant f_γ which relates to deviations from the C–C–C angle (90°). The table gives for this constant $0.767\ 10^{-11}$ erg/radian², but it has a footnote saying: "The interaction constants given here are taken from matrix expressions for the potential energy. For use in the quadratic form of this quantity they should be multiplied by 2". It is not clear to the present author whether or not the footnote means that, when the potential energy V is given by $2V = A\gamma^2$, A should equal $2f_\gamma$. If that is so the difference between the value of V derived from the spectra of cyclohexane and methane on one side and that derived from the cyclobutane spectrum on the other side would practically disappear.

At any rate, all three ways of calculating the activation potential lead qualitatively to the same result, that SACHSE was right when he maintained, by intuition, that the inversion in question ("Version" as he named it), on account of mechanical resistances, does not take place. This however leaves us with the necessity to explain the old puzzle, why fewer isomers of substituted cyclohexanes have been found than are permitted by the model.

Post Scriptum

Some months ago ANET and BOURN[14] objected against my note in *Nature* that I had not taken a paper by K. S. PITZER and coworkers[15] into account. These authors calculated the height of the potential barrier between a SACHSE chair form and one of the boat forms of cyclohexane at about 14 kcal/mol. They based this calculation on the existence of a line at 231 cm^{-1} in the spectrum of the substance in question. They state, however, that a line of this frequency had been found, neither in the infrared nor in the RAMAN spectrum and that it "was selected to fit the experimental entropy of cyclohexane". To the present writer this seems to be an insecure foundation on which to build far reaching conclusions. Furthermore, I am in agreement with PITZER and coworkers when, in the foregoing, I have assigned the RAMAN frequency at 384.1 cm^{-1} (PITZER has 382 cm^{-1}) to a motion leading from one chair conformation through the BAEYER planar form to the other chairform. If that be accepted, there are in the motion six angular strains acting on six C-atoms. On the other hand, in the motion to which PITZER and coworkers assign the frequency 231 cm^{-1} there are two angular strains acting on one C-atom. To me this would suggest that the latter type of motion corresponds to a vibration whose frequency is greater and not less than that of the former. The present writer, therefore, does not believe that his calculations can be upset by PITZER and coworkers considerations.

References

1. Christiansen, J. A., *Nature* **211**, (1966) 184.
2. Sachse, H., *Ber.* **23**, (1890) 1363.
3. Sachse, H. *Z. physik. Chem.* **10**, (1892) 203.
4. Christiansen, J. A., and Kramers, H. A. *Z. physik. Chem.* **104**, (1923) 451.
5. Sponer, H. *Molekülspektren und ihre Anwendung auf chemische Probleme.* II. J. Springer, Berlin (1936).
6. Henri, V., and Teves, M. C. *Nature* **114**, (1924) 894.
7. Pitzer, K. S., *Science* **101**, (1945) 672.
8. Pitzer, K. S. *Discussions, Faraday Society* **10**, (1951) 66.
9. Langseth, A., and Bak, B., J. *Chem. Physics* 8, (1940) 403.
10. Sponer, H., Ref. 5. vol. I. Tabelle 13. p. 82.
11. Westheimer, F. H. in *Steric Effects in Organic Chemistry* edit. by Newman, M. S. (1956) 533.
12. Kaarsemaker, S., and Coops, J. *Rec. Trav. chim.* **71**, (1952) 261.
13. Wilson, T. P. *J. Chem. Physics.* **11**, (1943) 369.
14. Anet, F. A. L., and Bourn, A. J. R. *J. Amer. Chem. Soc.* **89**, (1967) 760.
15. Beckett, C. W., Pitzer, K. S., and Pitzer, R. *J. Amer. Chem. Soc.* **69**, (1947) 2488.

6. A Hypothesis on the Cause of Coalescence of Multiplets in NMR Spectra of Cyclohexane and Related Compounds at Increasing Temperatures

It is assumed that the coalescence of signals due to equatorial and axial protons is caused by the onset at higher temperatures of angular vibrations of the C–H bonds. Calculations based on the HERZFELD-EYRING expression for the rate constant of unimolecular reactions at the coalescence temperatures of $C_6D_{11}H$ and $C_5H_{10}O$ agree with this assumption.

The generally accepted explanation of the well known phenomenon of coalescence at increasing temperatures, of doublets or multiplets in the n.m.r. spectrum of cyclohexane into a singlet is that the interconversion of the two SACHSE chair forms of that compound becomes so fast at the coalescence temperature that the slightly different signals from the axial and the equatorial protons merge into one. To the writers knowledge however, it has never been proved that this conversion is the only possible cause of the coalescence. If it were, there would be a hopeless clash between the work of activation calculated from optical spectra on one side and that calculated from from the n.m.r. spectra on the other side.[1, 2]

Now, it is well known that vibrations of not too low frequency are "frozen" at low temperatures and may be "thawed" at higher ones. It is also known that C–H bonds, *e.g.* in cyclohexane, perform angular vibrations whose frequency can be read from the optical (infrared or RAMAN-) spectra of the compound in question. The protons bound to the C-atoms behave like spinning tops and in classical physics one should say, that they perform a precessing motion, when they are placed in the magnetic field of the n.m.r. spectrograph. In the language of quantum mechanics somewhat different expressions are used but the difference is so small that the writer may be permitted to use the older language. The precession is a motion in which the axis of the spinning proton performs a conical motion whose frequency depends on the strength of the magnetic field.

At available field strengths it is so low that it can come into resonance with radio waves which are fed into the spectrograph and whose frequency, usually 40 or 60 MHz, is fixed. Whenever resonance between the variable frequency of precession and the fixed radio-frequency obtains, a peak will appear on the screen of the spectrograph.

At low temperatures the protons in cyclohexane and similar compounds are known to produce double or multiple peaks which in all probability is due to the existence of both equatorial and axial bonds in the molecule. If now the two kinds of C–H bonds are exited to angular vibrations it seems probable that the directions of the spin axes of the two kinds of protons are perturbed so much that their frequencies of precession become equal, *e.g.* so that both kinds of spin axes become perpendicular to the threefold rotational symmetry axis of the molecule. It is natural to suppose that the condition for the perturbation to be strong enough to extinguish the difference between equatorial and axial protons is that the molecule sufficiently often during one revolution of the precessing spin axis takes up an energy-quantum, *e.g.* once for each C-atom in the Sachse hexagon.

The probability pro second, w, for this to happen can easily be calculated if we accept the Herzfeld-Eyring value of the pre-exponential factor and if the frequency ν of the vibration in question is known. The familiar expression is

$$w = (kT/h)\exp(-h\nu/kT) \tag{1}$$

where T must be understood as the coalescence temperature. On account of the resonance the frequency of revolution of the precessing spin axis equals the radiofrequency f which is characteristic of the spectrograph and therefore known. The quantity to be determined is then, according to the preceding text w/f, which is the number of "hits" during one revolution of the precessing spin axis. We calculate the frequency ν from the wave number 1445.1 cm^{-1} which Langseth and Bak[3] determined from the Raman spectrum of cyclohexane. This frequency must in all probability be assigned to the angular vibrations of the C–H bond. Anet and Bourn[4] chose a particularly clear-cut example for their recent investigation, namely the substance $C_6D_{11}H$, where only one nucleus, the proton, has a spin. For this substance they determined the coalscence temperature at $-61{,}4°\text{C} = 211{,}75°\text{K}$. With $2{,}9978 \cdot 10^{10}$ cm/s for the speed of light and $h/k = 4{,}7984 \cdot 10^{-11}$ s.deg we get from (1)

$$w = 18{,}707 \cdot 10^{7}\ \text{s}^{-1} \tag{2}$$

The radio-frequency in ANET and BOURN's spectrograph was $f = 6.10^7\,\mathrm{s}^{-1}$ and consequently

$$w/f = 3{,}118 \tag{3}$$

Another recent example is that investigated by GATTI, SEGRE and MORANDI[5]. Their object was tetrahydropyrane, $C_5H_{10}O$, and their experimental methods are somewhat similar to those of ANET and BOURN. They found a coalescence temperature at $-65°C = 208{,}15°K$. With the same value of ν as that used above one gets

$$w = 15{,}467\ .\ 10^7\,\mathrm{s}^{-1} \tag{4}$$

and

$$w/f = 2{,}578. \tag{5}$$

That the ratio w/f (3) is just above three at the coalescence-temperature may mean that the molecule is hit about three times for each revolution of the precessing spin axis by a quantum $h\nu$ and that this is enough to secure that the single C–H bond is set in vibration. This might seem to agree with the fact that the mother-substance, cyclohexane, has a three-fold symmetry-axis and that it therefore has, so to speak, three equivalent compartments. This is however not sufficient because the molecule has also three two-fold symmetry axes which means that there should be six and not only three equivalent ways in which it can be hit, corresponding to the fact, that the six C atoms are equivalent if we ignore the difference between the two possible directions of the three-fold symmetry axis of cyclohexane. It follows that to secure that the single C–H bond in $C_6D_{11}H$ is excited to vibration the molecule should be hit six times. We learn therefore from the experimentally determined value 3,12 of w/f that w means the number of times the molecule is hit from one side pro second and that it must be multiplied by two to get the whole number of "hits" pro second. Similarly the number of hits which is necessary to extinguish the difference between equatorial and axial protons in tetrahydropyrane is, according to the experiments, 5,16 for each turn of the precesseing spin axes, while the expected value is five.

To test the validity of these considerations, the coalescence-temperatures for the same substances should be determined at other radio-frequences, *e.g.* 40 MHz in stead of 60, but unfortunately the present writer is unable to do this as he retired some nine years ago. But it seems important to him if someone else would undertake the job. It would not only be important to know whether or not the ratio w/f is independent of the radio-frequency, but if so, the result would be a rather strong proof of the validity of the HERZFELD-

EYRING value for the preexponential factor in the expression for the unimolecular velocity-constant in reaction kinetics. It goes without saying that the clash concerning the work of activation for the conversion of the two forms of the SACHSE chair hexagon into each other, calculated on one hand from optical and on the other hand from n.m.r. spectra would disappear simultaneously.

References

1. CHRISTIANSEN, J. A., *Nature* **211**, (1966) 184.
2. CHRISTIANSEN, J. A., *Kgl. Danske Vid. Selsk.* this issue p. 16.
3. LANGSETH, A., BAK, B., *J. Chem. Physics* **8**, (1940) 403.
4. ANET, F. A. L., and BOURN, A. J. R., *J. Amer. Chem. Soc.* **89**, (1967) 760.
5. GATTI, G., SEGRE, A. L., and MORANDI, C., *J. Chem. Soc. B*, (1967) 1203.

7. Hypotheses on Tautomerism of Conformational Isomers of Vicinal Derivatives of Cyclohexane

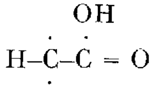
The fact that Sachse's rigid model of cyclohexane permits „too many" isomers must be caused by some sort of tautomerism. As calculations based on spectral evidence of work of activation have corroborated that Sachse's hexagon is rigid, the flexibility must be caused by changes in some of the angles in the hexagon. Such changes can be brought about *e.g.* by displacement of a H-atom geminal to a carboxyl-group or by displacement of a proton geminal to a hydroxyl group. In both cases the corresponding ring-angle will change from about the tetrahedric angle to about 120°. In that case experiments with models of the space-filling type show that mutual transformations of the two *trans* forms, (*ee*) and (*aa*), of vicinal disubstituted compounds must be relatively easy while racemization of the *cis* (*ea*) forms is difficult.

The classical objection against the rigid chair form of the Sachse model of cyclohexane is that it permits more isomers than are actually known. For example, it permits two monosubstitutes, one axial (*a*) and one equatorial (*e*), while no cases of more than one substance of the composition of a monosubstitute are known. Concerning vicinal disubstituted cyclohexanes the model permits three isomers, apart from enantiomers, namely *trans*(aa), *trans*(ee) and *cis*(ea). However, only two vicinal dicarboxylic acids derived from cyclohexane are known. Concerning vicinal diols the situation is more complicated. As a matter of fact three different substances of that kind have been isolated, two with melting points at respectively 104°C and 99°C and one which melts at 75°C.

The latter was prepared by Sabatier and Mailhe by catalytic hydrogenation of catechol[1]. Leroux[2] found that a substance with the same melting point could be prepared from a mixed solution of the two former ones and he believed it to be a compound of them.

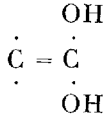
However, so far as known to the present author a determination of the molecular weight of the 75° diol has never been performed, and this is necessary before Leroux's assumption can be finally accepted. The need for a determination of the m.w. of the 75° diol is so much more needed as Leroux himself by catalytic hydrogenation of a certain naphtalene diol got three isomers of which the low melting one could be prepared from a mixed solution of the two others, in analogy with his results for the cyclohexane derivatives. Here, however, he performed a m.w. determination and found that the low melting compound was a monomer.

In his paper from 1918 Mohr[3] took it for granted that only two disubstituted and one monosubstituted cyclohexane were known and he assumed therefore that the mutual conversion of the two chair forms of the Sachse model was fast enough to make some of the isomers pairwise tautomeric. That tautomerism must occur seems certain enough but, as shown in a preceding paper, an easy conversion of the two chair forms into each other can hardly be the explanation. In the search for other explanations we may begin with the cyclohexane monocarboxylic acid. The configuration around the carbon atom which is implied in the substitution is usually assumed to be the one indicated by (I)



$$\mathrm{H{-}\overset{\cdot}{\underset{\cdot}{C}}{-}\overset{\overset{OH}{\cdot}}{C}=O} \qquad \text{(I)}$$

But, many years ago, Aschan[4,5] explained certain reactions in camphor chemistry by assuming an enolization of the carboxylgroup as indicated by (II)



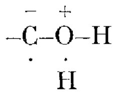
$$\overset{\cdot}{\underset{\cdot}{\mathrm{C}}}=\overset{\overset{\mathrm{OH}}{\cdot}}{\underset{\underset{\mathrm{OH}}{\cdot}}{\mathrm{C}}} \qquad \text{(II)}$$

From many investigations of different kinds it has been concluded that the directions of two single and one double bond around a carbon atom form angles of about 120° with each other. If we now build models corresponding to (I) and (II) of cyclohexane carboxylic acid from atomic models of the Stuart Briegleb type it turns out that the one corresponding to (I) is rigid but that the one corresponding to (II) is flexible in so far as the $C = C(OH)_2$ group can be turned relative to the rest of the molecule between two extreme positions which correspond roughly to the equatorial and the axial positions respectively. The movement is not free from resistance but it can be performed without breaking the ring, while a similar movement is impossible with the model corresponding to (I). Consequently, when one of the two hydrogen atoms in (II) migrates back into the position indicated by (I) it depends on chance whether it becomes fixed axially or equatorially. In this way the tautomerism of the (*a*) and (*e*) forms of the monocarboxylic acid may be understood.

The case of the monosubstituted hydroxy derivative is somewhat different, but it may nevertheless be treated in a similar way: The tertiary proton in (III)

$$\mathrm{H}-\underset{\cdot}{\dot{\mathrm{C}}}-\mathrm{OH} \qquad \text{(III)}$$

may migrate to the OH group which thus acts as a base as indicated in (IV)

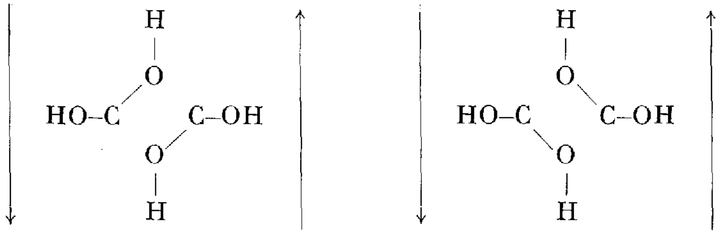


$$-\underset{\cdot}{\overset{-}{\mathrm{C}}}-\underset{\underset{\mathrm{H}}{\cdot}}{\overset{+}{\mathrm{O}}}-\mathrm{H} \qquad \text{(IV)}$$

By this exchange of charges both the carbon and the oxygen atom become nitrogen isosters and may be expected to have three valency bonds each[6]. As these bonds must be expected to form angles of approximately 120° with each other, the situation may be much the same as that described above in the case of the monocarboxylic acid, that is, the (*e*) and the (*a*) forms may be expected to be tautomeric. The case of vicinal disubstituted cyclohexanes is more complicated. Experiments with the STUART-BRIEGLEB models show that, if two neighbouring carbon atoms in the ring have double bonds pointing outwards, the ring becomes even more flexible than in the case of the monosubstitute, in so far as these carbon atoms can then be turned relative to each other in opposite directions, but not in the same direction. In one of the extreme positions where the substituents have been turned as far as possible relative to each other they approach the *trans*(aa) conformation and in the other extreme position they approach the *trans*(ee) form. When now the migratory hydrogen atoms return to their normal sites on the ring carbon atoms it depends on chance which one of the two conformations will result, and we may therefore understand that the two *trans*-forms are mutually tautomeric.

But to transform one of the *cis*(ea) forms into its mirror image the two substituents must be moved to the same side and experiments with the model shows this to be impossible. Therefore we cannot expect that racemization of the optical antipodes is easy.

Concerning the *trans*-forms of the vicinal dicarboxylic acid the model shows that there is a difficulty. It seems that steric hindrance must prevent the two $= C(OH)_2$ groups in passing by each other. This is, however, probably of no great consequence because the two colliding HO groups, one from each of the two enolized carboxyl groups can change over from one carbon atom to the other by small changes in their electronic clouds and without large displacement of the nuclei. The two diagrams (*V*) are intended to show the situation. If the relative movements of the two groups and the distribution of the valencies are as shown to the left the two groups cannot pass each other. If however the valency clouds around the two oxygen atoms are rearranged so as to produce the valency distribution indicated to the right the movement can continue in the same direction as before the two groups met, without mutual hindrance.



(V)

Of course the two diagrams are schematic, but a comparison with the model shows it to be more realistic than such diagrams usually are. It must be understood that the diagrams are intended to visualize the positions and the movements of the enolized carboxylic groups seen from the outside of a model whose axis is vertical. In this way tautomerism between the two *trans* forms can be understood, but, as mentioned before, to transform the enantiomeric *cis* forms into each other, the trivalent atomic models must be turned in the same direction, which is difficult or impossible. Therefore even enolization of the carboxyl group cannot lead to a racemization of one of the optical antipodes of the *cis* compound. In case the compound considered is a vicinal cyclohexane diol the transition state may be one in which two tertiary protons have been displaced as indicated in (IV) so that we get two neighbouring negatively charged nitrogen isosters, which again may be assumed to be centers for three single bonds. The situation is then about the same as in the case of the cyclohexane dicarboxylic acid, and we are lead to expect tantomerism between the two *trans* forms but not between the enantiomeric *cis* forms.

The activation potential may be expected to be twice the work necessary to transform (III) into (IV) where one proton has been displaced. Similarly, the work of activation for the transformation of the two *trans* forms of the dicarboxylic acids into each other may be expected to be twice the difference between the potential energies of (II) and (I), where a hydrogen atom has been displaced. As this may be expected to be less, than when a proton is displaced it seems natural that it is possible to isolate two *trans* forms of the diol, but not of the dicarboxylic acid.

References

1. SABATIER, P., and MAILHE, *C. r.* **146**, (1908) 1154.
2. LEROUX, H., *Ann. de Chim. et Phys.* [8] **21**, (1910) 541.
3. MOHR, E., *J. prakt. Chem.*, [2] **98**, (1918) 315.
4. ASCHAN, O., *Liebigs Ann.* **387**, (1912) 17.
5. HÜCKEL, W., *Theoretische Grundlagen der organischen Chemie*, Erster Band. Leipzig (1931) 256.
6. CHRISTIANSEN, J. A., *J. Coll and Interface Science* **22**, (1966) 2.

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