To
The Dean
of the
Faculty of Medicine
Edinburgh University

Competition Essay
for the
Gunning Prize in Chemistry

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7 Gayfield Square
Edinburgh

April 28th 1890.

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Tautomerism

The structural formulae which chemists have been led to give to the many bodies investigated, both inorganic and organic, show in general a close agreement with facts, and explain in a remarkably satisfactory way, the operations which go on when one substance reacts upon another. Even among isomeric substances there have been comparatively few instances where the theory in use failed to account for the observed appearances.

However, there are two classes of phenomena which the structure theory in its common acceptance does not succeed in explaining. In preparing certain organic bodies, it was found that in some cases a greater number of isomers were obtained than the possibilities of structural formulae allowed, that is, that one structural formulae belonged to several different bodies. This was notably the case with the Tartaric acids. The apparent contradiction has been satisfactorily met by the theory of Le Bel and van t'Hoff regarding the arrangement of atoms in space. This class of isomers are physical not chemical.

In this first class of exceptions facts overleap the theory of chemical structure, but in the second class theory overleaps the facts. It is with the latter class that this that this paper deals.

There are not a few cases known where substances act as if they possessed two structural formulae. For instance, some bodies answer either to the tests for phenols or ketones, others for phenols or imides, and so on, while one formula is able to account for only one or other of these conditions.

Or to put it otherwise, in certain reactions where we are led to expect isomers, one and the same body results.

Among the more important substances which behave in this manner may at present be mentioned, these, derivatives of cyanogen, hydrocyanic cyanates and isocyanates; isatine and similar bodies, phloroglucin and succinosuccinic ether.

For example, take the case of cyanides. Hydrocyanic acid has for its formula either $H-C\equiv N$ or $H-N=C:$ (or $H-N\equiv C$, but we shall regard the valency of the nitrogen to remain constant, while that of carbon changes).

If an alkyl iodide be treated with potassium cyanide the following takes place $RI+KCN=R-C\equiv N+KI$ ($R=$ alkyl), an alkyl nitril or cyanide is produced. That it possesses the formula assigned to it, is proved by its reaction with acid or alkali. When saponified, ammonia and an acid containing the same number of carbon atoms as the original nitril is produced. $R-C\equiv N+2H_2O=R-COOH+NH_3$. Also when treated with nascent hydrogen the amine of the next higher alcohol radicle is produced $R-C\equiv N+4H=R-\overset{H}{\underset{H}{C}}-N\begin{smallmatrix}H\\H\end{smallmatrix}$.

These and other reactions show that the

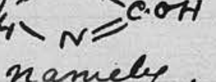
carbon is united to the alkyl and the nitrogen to it through the carbon, as in the given formula.

But now if instead of potassium cyanide we use silver cyanide, an altogether different body is obtained, viz, Alkyl Isonitril or isocyanide; $AgCN + RI = R{-}N{=}C + AgI$. That its constitution is $R{-}N{=}C$, is proved by the fact that when saponified the nitrogen and not the carbon remains attached to the alkyl. An alkyl ~~contain~~ amine containing a carbon less than the original isonitril is formed, along with formic acid, $R{-}N{=}C + 2H_2O = R{-}NH_2 + H{\cdot}COOH$. That formic acid is produced shows that the carbon was not attached to the alkyl directly, but only to it through the medium of a nitrogen.

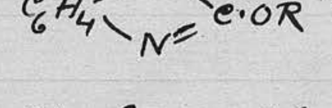
These two reactions are cases of double decomposition, and it is usual and natural to suppose, as in similar purely inorganic reactions, that when a metal or radicle is removed from a substance and ~~its place taken~~ another metal or radicle introduced instead, the thing introduced should occupy the same place and perform the same function as the original metal or radicle. If we suppose this, potassium cyanide comes to have the formula $K{-}C{\equiv}N$, and silver cyanide $Ag{-}N{=}C{:}$. These are both derivatives of hydrocyanic acid, but only one variety of it is known. Which formula $H{-}C{\equiv}N$ or $H{-}N{=}C$ is to be assigned to it? A similar difficulty arises with cyanic, sulphurous, and nitrous acids. In each of these cases there are derivatives corresponding to both of the possible representations of the acid.

Sulphurous acid forms a very interesting case. Sodium sulphite heated with ethyl iodide gives rise to sodiumethyl sulphonate, which has the constitution $C_2H_5-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-O-Na$, since it may be, indirectly converted into mercaptan; consequently sodium sulphite comes to have the constitution $Na-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-O-Na$. Silver sulphite behaves similarly to the sodium salt; ethyl sulphonate is best prepared from it. These metallic salts seem to correspond to a sulphurous acid $H-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-O-H$. But there is also a symmetrical ethyl sulphite of the constitution $C_2H_5-O-\underset{\underset{O}{\|}}{S}-O-C_2H_5$, as evidenced by its formation from thionyl chloride. Sulphurous acid itself arises from thionyl chloride and this points to the symmetrical constitution $H-O-\overset{\overset{O}{\|}}{S}-O-H$.

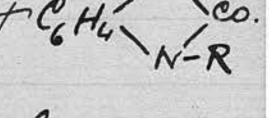
Here then there seems to be direct proof that sulphurous acid has the symmetrical form, that ethers of both forms exist, and that the metallic salts are unsymmetrical. The case of nitrous acid is very similar to this. The formation of nitrites and nitrobodies will however be spoken of later. Among the purely organic bodies showing this peculiarity, Isatin may be taken as an example. Baeyer has given to this body the formula



, but two classes of ethers exist, namely,

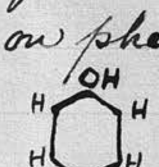


&

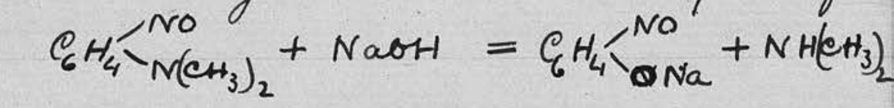


The isatin corresponding to the latter ether has never been prepared (i.e. if Baeyers formula is correct), and seems to be incapable of existence.

A very interesting example of the formation of one and the same substance, by reactions which would lead us to expect isomers, is that of nitrosophenols or quinoneoxims. By the action of nitrous acid on phenol we expect nitrosophenol to be formed.

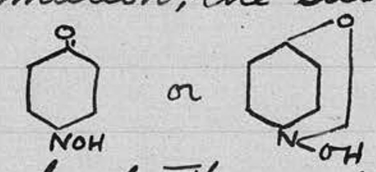


This is apparently the case, for on oxidising the product, nitrophenol is obtained. The product of the reaction also gives Liebermann's reaction with phenol and strong sulphuric acid (blue colour), and its formation from nitrosodimethyl anilin and caustic soda agrees with this conception of its constitution.

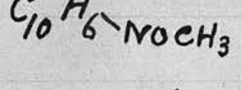


$$C_6H_4\begin{matrix}\diagup NO \\ \diagdown N(CH_3)_2\end{matrix} + NaOH = C_6H_4\begin{matrix}\diagup NO \\ \diagdown ONa\end{matrix} + NH(CH_3)_2$$

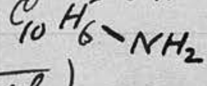
But the same body is produced by the action of hydroxylamine on quinone. According to this mode of formation, the substance should be represented by



This mode of representations finds support in the fact that by further action of hydroxylamine a dioxim is obtained, and in the case of the naphthol derivative, ethers exist which, by reduction, give amido naphthol.



$C_{10}H_6\begin{matrix}=O \\ \diagdown NOCH_3\end{matrix}$ is the ether and by reduction it gives



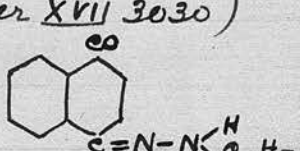
$C_{10}H_6\begin{matrix}\diagup OH \\ \diagdown NH_2\end{matrix}$. (N.B Isonitrosobodies do not answer to Liebermann's test).

These examples suffice for the present to show the nature of the question under consideration.

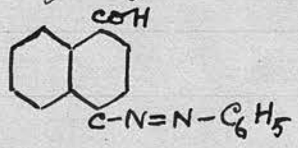
Baeyer first sought to give an explanation of such exceptions as are quoted above, in the case of isatin. (Ber XVI 2188.) According to him, the two classes of ethers which are met with in such cases, correspond to two different mother substances which are called "normal" and "pseudo" forms. Of these two, the normal alone is capable of existence under ordinary circumstances; the pseudo form represents an unstable grouping of the atoms, so that if any attempt is made to prepare it a molecular transformation takes place, the pseudo form passing at once into the normal form. This difference between the stability of the alkyl and the hydrogen derivatives, is accounted for by the much greater "mobility" of the hydrogen atom compared with the alkyl, so that, while there is usually a difference in the stability of the ethers, the radicle is not sufficiently easily moved about to assume, under ordinary conditions, the more stable arrangement, as the hydrogen does.

Opposed to this view of Baeyer's is the theory— enounced first with any great degree of concreteness by C. Laar (Ber XVIII 648, XIX 730),— which supposes that a compound exhibiting this twofold nature may, by the "wandering" of a hydrogen atom, exist sometimes in the one form, sometimes in the other, so that, according to the nature and conditions of the reaction, either one or other kind of derivative will result. The only difference between this view and that of Baeyer's is, that according to the former the hydrogen may move in either direction, while by the latter it only moves from the unstable to the stable position.

Previous to Laar's communication on this subject Zincke and Kekulé had expressed briefly, similar views as Laar. Zincke showed (Ber XVII 3030) that α naphthoquinonephenylhydrazide



was identical with phenylazo α naphthol



and stated, that in certain cases it was necessary to admit different formulae to the same body, according to circumstances. Kekulé likewise sought to explain such cases of identity by supposing the hydrogen atom to swing to and fro between the two possible positions, so that for the complete representation of the compound two formulae are necessary.

This property which these substances possess of exhibiting a double behaviour Laar designates as "Tautomerism", and bodies which have this property are said to be "Tautomeric".

Butlerow (Ann. Chem. Phar 189-76) mentions that in certain compounds it is not unlikely that isomeric changes are continually going on. These he would regard as due to inter-molecular change dependent on dissociation, not as Laar maintains to intra-molecular change. If the substance were an electrolyte with the hydrogen atom in question as one of the ions, then the change would at least be partly intermolecular. Whether the change be regarded as inter- or intra-molecular is of no consequence in the long run, as in the two formulae we have simply to deal with the change of the sphere of attraction of the hydrogen.

This change in the position of the hydrogen atom is necessarily associated with rearrangements in the linking of the atoms or changes in the valencies. Laar taking account of this, gave a classification of the types of tautomeric groups. A causual inspection of the possible tautomeric groups will show that they can all be reduced to two divisions, which he calls Triad or Perissad, and Dyad or Artiad divisions. The members of the peressad group contain an odd number of atoms united to oneanother by alternate double and single bonds, e.g. $-N{=}\overset{|}{C}{-}\underset{H}{O}$ or $-\underset{H}{N}{-}\overset{|}{C}{=}O$; Simultaneous with the wandering of the hydrogen atom, the single bonds change to double and the double to single. Types of more than three atoms may be regarded as condensed triads. In the artiad groups the hydrogen atom passes between two neighbouring atoms. Here there will be either a change in the valency if the type occurs alone, or a change in the position of the double bonds if it occurs condensed with other types.

Most tautomeric substances contain groups of the triad or perissad type; the dyad type occurs less frequently.

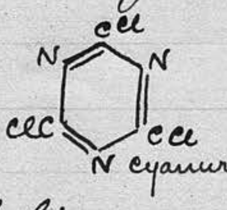
What the influence of the change in the position of the double bonds is we cannot say, as we have no clear conception of what they represent in the compound. It is easier in the conception of tautomeric changes to imagine instead of these double bonds mere blanks on the neighbouring atoms. We shall however for the sake of simplicity use the ordinary notation, as it is easier then to see where the blanks lie.

It is not necessary to go over Laar's types, more especially as the compounds belonging to many of them have not been sufficiently investigated, and besides, the arrangement of types is in no sense scientific, as by it compounds quite analogous to one another are put widely apart. We shall mention those classes of bodies where interesting cases of the socalled Tautomerism, or else actual isomerism, are to be found and discuss those cases to which ~~the~~ chemists have devoted their attention more especially.

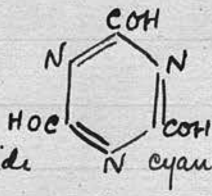
We may first consider bodies more directly connected with the cyanogen group.

Hydrocyanic acid has already been mentioned, but it may be added that there are two reactions which point more directly to the formula $H-C \equiv N$ for the acid itself; namely, its formation from chloroform and ammonia under pressure, and from ammonium formate.

It is doubtful which formula to assign to cyanic acid. The metallic salts give rise to iso-cyanic ethers of the form $O=C=N-R$, since these readily yield substituted ammonias. There are two classes of ethers, and of these the iso-ethers are the more stable. The greater stability of the iso-derivatives is seen better in the case of cyanuric acid. This acid from its relation to cyanuric chloride, contains probably three hydroxyls.

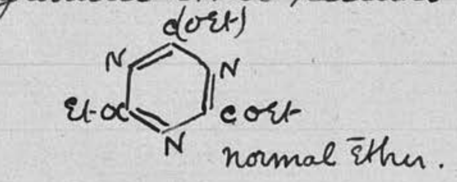


cyanuric Chloride

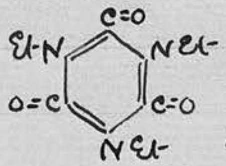


cyanuric acid

The normal ether $C_3N_3(OEt)_3$ results from the polymerism of cyanetholine $N \equiv C-O-Et$; while the isocyanuric ether results from the isocyanic ether .



normal Ether.



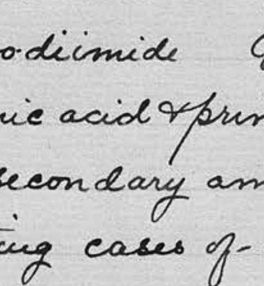
iso-Ether

There can be no doubt regarding the constitution of the ethers, the normal ethers split up giving alcohols, while the iso-ethers give primary amines. The normal ethers are much less stable than the isoethers into which form they readily pass. The connection between cyanic and cyanuric acid would point to the normal form $N\equiv C-O-H$ for cyanic acid, in that case the metallic salts would have the form $N\equiv C-O-K$, but they act as if they were $O=C=N-K$. The greater stability of the iso-derivatives has been used as an argument for the acid having the isoform $O=C=N-H$, both for this & for cyanuric aci

The case of thiocyanic acid is similar, the metallic salts however, unlike the cyanates, give rise to normal ethers $N\equiv C-S-C_2H_5$. These normal ethers are less stable than the iso ethers (mustard oils), into which they are converted by heating.

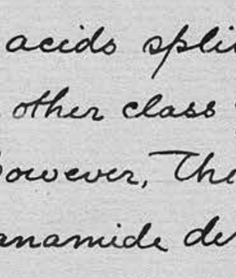
Cyanamide $N\equiv C-NH_2$ also has derivatives corresponding to a hypothetical isomer $HN=C=NH$ (carbodiimide). This isomer is known in derivatives chiefly in the aromatic series, eg. diphenyl carbodiimide $C_6H_5-N=C=N-C_6H_5$; acids split this up into carbonic acid & primary amine. The other class of ethers yield secondary amines. However, the most interesting cases of isomerism of cyanamide derivativ are found in its condensation compounds, eg. Melamine.

Melamine maybe represented by either of the two formulae



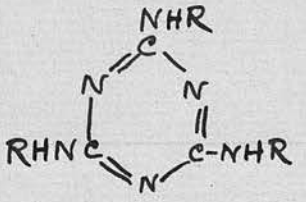
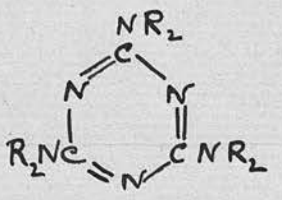
normal melamine

or.

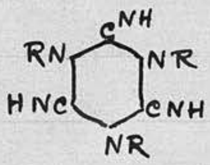
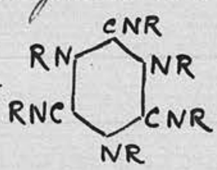


iso-melamine

Melamine is found in one form only.

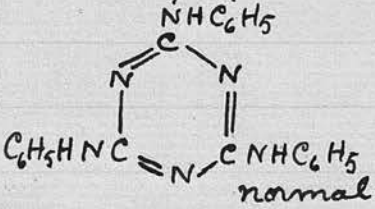
The normal ethers are obtained by heating cyanuric chloride with primary or secondary amines, there are thus obtained  or .

The iso ethers arise by polymerisation of alkyl cyanamides

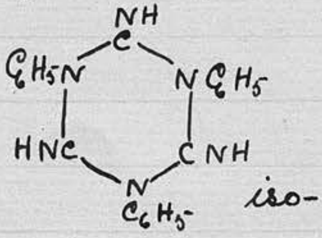
 & 

Hoffmann (Ber XVIII 3217) has also obtained phenyl derivatio which belong simultaneously to the normal & iso-melamine, i.e. the mother substance is both amido and imido.

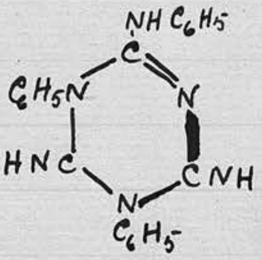
He has prepared the following.



normal-

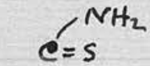
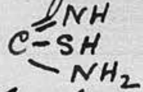


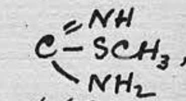
iso-

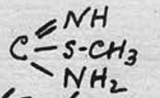


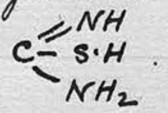
The last form is asymmetrical & is both an amido & an imido derivative.

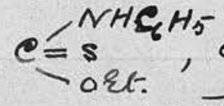
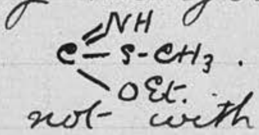
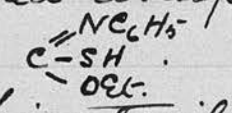
Here may also be mentioned the thiourea compounds which are related to the preceding.

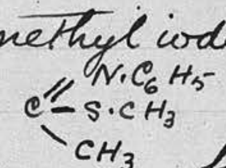
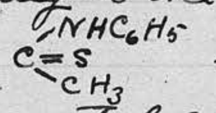
Thiourea from its modes of formation and its general likeness to urea has the formula  $\overset{\diagup \mathrm{NH_2}}{\underset{\diagdown \mathrm{NH_2}}{\mathrm{C{=}S}}}$ given to it; but alkyl compounds exist corresponding both to this formula, and to the isomeric hypothetical formula  $\overset{\diagup\!\!\!= \mathrm{NH}}{\underset{\diagdown \mathrm{NH_2}}{\mathrm{C{-}SH}}}$. The ethers of the former type, prepared by heating mustard oils with primary or secondary amines, are known to have such a constitution by their breaking up on saponifying into carbonic acid, sulphuretted hydrogen, ammonia and an amine.

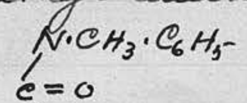
The unsymmetrical ether, on the other hand,  $\overset{\diagup\!\!\!= \mathrm{NH}}{\underset{\diagdown \mathrm{NH_2}}{\mathrm{C{-}SCH_3}}}$, breaks into carbonic acid, ammonia, & mercaptan. The ethers of this latter class are obtained by treating thiourea with halogen alkyl in presence of caustic potash.

Methyl Iodide and thiourea in alcoholic caustic potash, give imido-carbamine thiomethyl.  $\overset{\diagup\!\!\!= \mathrm{NH}}{\underset{\diagdown \mathrm{NH_2}}{\mathrm{C{-}S{-}CH_3}}}$

This reaction has been employed to prove that thio urea has the formula  $\overset{\diagup\!\!\!= \mathrm{NH}}{\underset{\diagdown \mathrm{NH_2}}{\mathrm{C{-}S{\cdot}H}}}$.

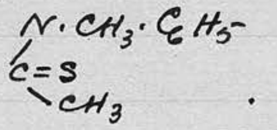
The same thing happens with some other analogous bodies. Thus phenylthiourethane with the formula  $\mathrm{C}\begin{array}{l}-NHC_6H_5\\=S\\-OEt\end{array}$, corresponding to urethane itself, when acted on by methyliodide and alcoholic potash gives this body  $\mathrm{C}\begin{array}{l}=NH\\-S-CH_3\\-OEt\end{array}$. The CH_3 unites with the sulphur and not with the nitrogen, and the ether formed corresponds to the hypothetical mother substance  $\mathrm{C}\begin{array}{l}=NC_6H_5\\-SH\\-OEt\end{array}$.

Thiacetanilide, in the same way, gives with methyl iodide and alcoholic caustic potash the compound  $\mathrm{C}\begin{array}{l}=N\cdot C_6H_5\\-S\cdot CH_3\\-CH_3\end{array}$. The ether corresponding to the normal formula of thiacetanilid  $\mathrm{C}\begin{array}{l}-NHC_6H_5\\=S\\-CH_3\end{array}$ is also known. It is prepared by acting on the acetyl compound of methyl aniline with phosphorus penta-sulphide.

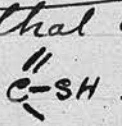


$$\mathrm{C}\begin{array}{l}-N\cdot CH_3\cdot C_6H_5\\=O\\-CH_3\end{array}$$

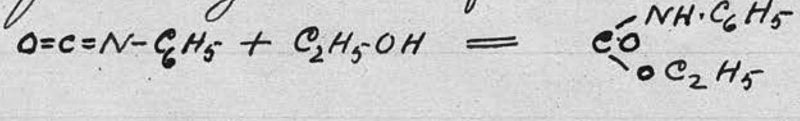
gives rise to



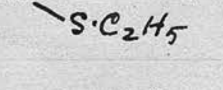
$$\mathrm{C}\begin{array}{l}-N\cdot CH_3\cdot C_6H_5\\=S\\-CH_3\end{array}.$$

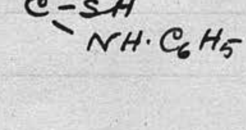
These reactions with alkyl Iodide on such sulpher bodies – thiourea, phenylurethane, etc., show how uncertain this method of finding the position of a replaceable hydrogen is. Under ordinary circumstances, from this reaction we would conclude that each of these substances contained the group  $\mathrm{C}\begin{array}{l}=\\-SH\\-\end{array}$.

When phenylisocyanate is heated with alcohols or phenols carbanilides are obtained so that this reagent forms a good test for alcoholic hydroxyl.

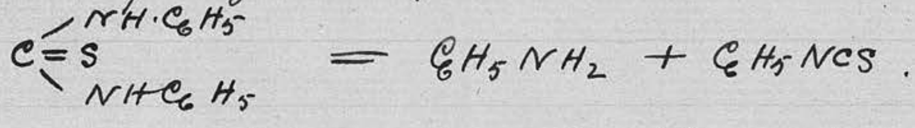


$$O=C=N-C_6H_5 + C_2H_5-OH = \mathrm{C}\begin{array}{l}-NH\cdot C_6H_5\\=O\\-OC_2H_5\end{array}$$

Goldschmidt (Ber $\overline{\underline{XXIII}}$ 253) has also shown, that it may also be used to test for the group (SH). For instance, by acting on Ethyl mercaptan with phenyl isocyanate a thiocarbanilide is obtained  $\mathrm{C}\begin{array}{l}-NH\cdot C_6H_5\\=O\\-S\cdot C_2H_5\end{array}$.

He applied this test to diphenylthiourea and failed to get any action corresponding to the formula  $\mathrm{C}\begin{array}{l}=N\cdot C_6H_5\\-SH\\-NH\cdot C_6H_5\end{array}$.

The reaction appears to have taken place in this way (1) The diphenyl theourea at 180° split up into aniline and phenyl mercaptan



$$C{\overset{NH\cdot C_6H_5}{\underset{NHC_6H_5}{=S}}} = C_6H_5NH_2 + C_6H_5NCS.$$

(2) The aniline then reacted on the phenyl isocyanate producing diphenylurea $C_6H_5NH_2 + C_6H_5NCO = CO{\overset{NHC_6H_5}{\underset{NHC_6H_5}{}}}$

It is therefore most probable that the above compounds, although by the action of alkyl Iodide they give ethers containing the group $C{\overset{=}{\underset{\backslash}{}}}S-R$, are themselves symmetrical.

In the introduction to the subject, the case of nitroso-phenols was treated, and nothing further need be said of them. Instances of this tautomerism arise with certain azo compounds and derivatives of hydrazine. By the action of phenylhydrazine hydrochloride on α naphthoquinone in acetic acid, the body formed, $C_{10}H_6{\overset{=O}{\underset{}{=N-N{\overset{H}{\underset{C_6H_5}{}}}}}}$ α naphthoquinone phenylhydrazine was found by Zincke to be identical with that prepared from α naphthol & diazobenzolchloride $C_{10}H_6{\overset{-OH}{\underset{}{-N=N-C_6H_5}}}$ phenylazo α naphthol. The substance acts both like a phenol and a base. The same holds if toluol take the place of benzol. With β.naphthol however the products are different.

Certain diazo compounds also exhibit a marked absence of isomerism. Diazoamidobenzol—p.toluidene, prepared from diazobenzol and p.toluidene, is identical with the body diazoamidotoluolbenzol

$$C_6H_5-N=N-\boxed{Cl+H}NH-C_7H_7 = C_6H_5-N=N-NH-C_7H_7 + HCl$$

$$C_6H_5-NH\boxed{H+Cl}N=N-C_7H_7 = C_6H_5-NH-N=N-C_7H_7 + HCl$$

Either of these formulae is changed into the other by the simple change in position of a hydrogen atom.

Other unsymmetrical diazoamido compounds show exactly the same thing, thus:

$C_6H_5-N=N-NH-C_6H_4Br$ Diazobenzolamidobrombenzol
and $C_6H_5-NH-N=N-C_6H_4Br$ Diazobrombenzolamidobenzol
are identical, and a variety of others that might be mentioned. It has not been found possible from the reactions of these bodies to assign to them any one of the two formulae in particular. Thus, when the diazoamidobenzol-p.toluidene mentioned above is boiled with dilute sulphuric acid, the decomposition takes place according to both formulae, for, phenol & p.toluidene, and at the same time, p.cresol $C_6H_4{<}^{OH}_{CH_3}$ and aniline are produced.

It would be interesting to compare the bodies, corresponding to these unsymmetrical diazo bodies, prepared from secondary instead of primary amines. In them the moveable hydrogen would be replaced by alkyl. Diazobenzol and methyl p.toluidene might yield $C_6H_5-N=N-N{<}^{C_7H_7}_{CH_3}$, while diazotoluidene and methylaniline might give the body $C_6H_5-\underset{CH_3}{N}-N=N-C_7H_7$. No attempt seems to have been made to prepare bodies of this description. It is true that the introduction of a side chain makes them more unstable, but it is possible that they are capable of existence. Such a mixed diazoamido body is known in the case of diazobenzol-dimethylamin.

The next class of bodies to be considered contains a great many examples of this so called tautomerism. There are a number of ring formations which like oxypyridins & pyridons contain either a hydroxyl and a nitrogen, or an imide group and a ketone oxygen, thus,

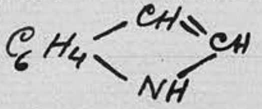
or

oxypyridine pyridon.

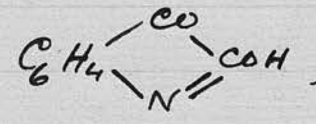
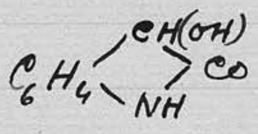
In some cases this difference is apparent in the formation of actual isomers, but usually only in the formation of two classes of ethers.

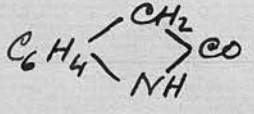
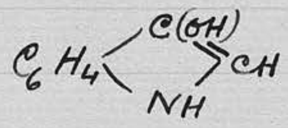
Among the bodies to be mentioned in this class, are certain belonging to the indol group, oxyderivatives of pyridine and quinoline, pyrazolons and acridine derivatives.

Most of our knowledge of the Indol group is due to Baeyer. Indol is represented by the formula

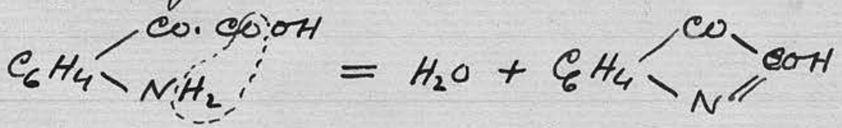


& derived from it there are the following bodies.

Isatin  ; Dioxindole 

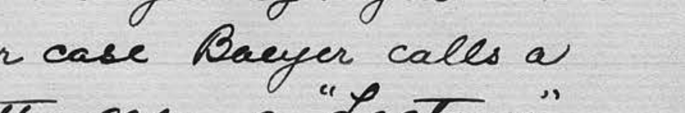
Oxindole  ; Indoxyl 

When o. nitrobenzoyl formic acid is reduced, the o. amido derivative isatic acid is obtained as a white powder. This latter body is unstable and loses water on warming, giving isatin.



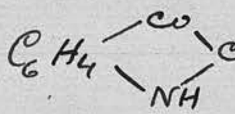
isatin.

This is the formula given by Baeyer to isatin. It is a common occurrence for these o. amido acids to lose water forming intramolecular anhydrides. They may lose water in two ways; both amidogen hydrogens and the oxygen of carboxyl may go out, or the hydroxyl and one amidogen hydrogen. The product in the former case Baeyer calls a "Lactime", in the latter case a "Lactame". Isatine as above represented is therefore a lactime. Oxindole, on the other hand, which is the intramolecular anhydride of o. amidophenylacetic acid, is a lactame.



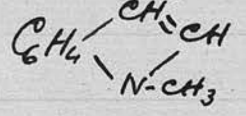
Isatin has two classes of ethers corresponding to the lactime and lactame forms.

Baeyer, according to the view already mentioned, supposed the lactame ethers to be derivatives of a hypothetical "pseudo" isatin.

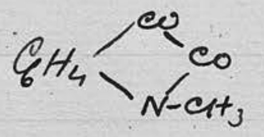


$C_6H_4\left<\begin{matrix}CO\\NH\end{matrix}\right>CO$ pseudo isatin (lactame)

There is no doubt regarding the constitution of these ethers. The lactime methyl Ether is prepared from silver isatin, which is quite a stable body, by the action of methyl iodide. Caustic potash splits it into potassium isatate and methyl alcohol.
The lactime ether—methyl pseudo isatin, is prepared from normal methyl indol by oxidation with sodium hypobromite.

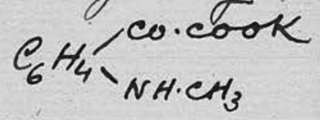


$C_6H_4\left<\begin{matrix}CH=CH\\N\text{-}CH_3\end{matrix}\right.$ gives



$C_6H_4\left<\begin{matrix}CO\\N\text{-}CH_3\end{matrix}\right>CO$

This ether dissolves at once in caustic potash giving the potassium salt of methyl isatic acid

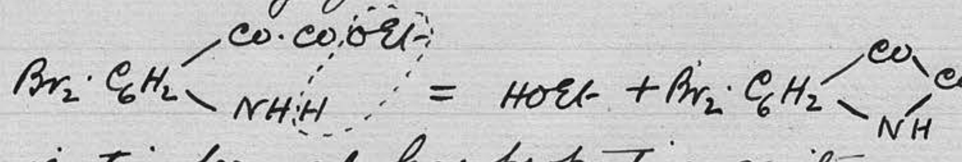


$C_6H_4\left<\begin{matrix}CO\cdot COOK\\NH\cdot CH_3\end{matrix}\right.$

Hence its constitution is that given.

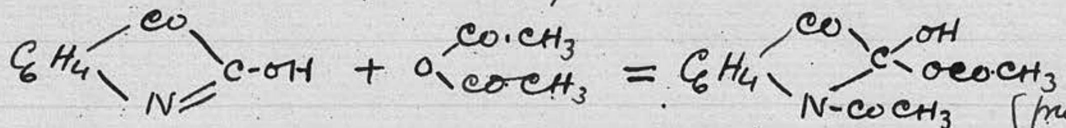
On the other hand we are not so certain of the constitution of isatin itself. Baeyer's chief argument for this formulae was the formation of the lactim ethers from the salts of isatin, by the action of alkyl iodides. He supposed simple substitution to take place, but, as it has already been seen in the case of certain thio compounds, a simple substitution does not always occur.
There are not a few weighty facts which point to the other constitution as being the correct one.

According to Baeyer, the ethyl ether of dibrom-isatic acid on heating, gives alcohol and brom-isatin.

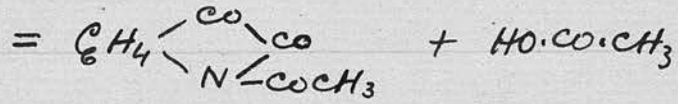


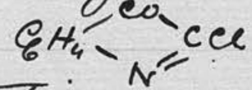
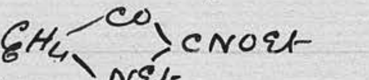
$$Br_2\cdot C_6H_2\left<\begin{matrix}CO\cdot CO\cdot OEt\\NH\cdot H\end{matrix}\right. = HOEt + Br_2\cdot C_6H_2\left<\begin{matrix}CO\\NH\end{matrix}\right>CO$$

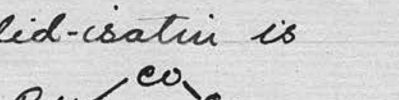
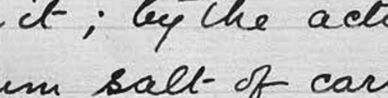
The brom isatin formed has properties quite analogous to those of isatin itself, and from its mode of formation it appears to be of the lactame form. Again acetic anhydride gives with isatin an acetyl derivative of the lactame form. To account for this discrepancy, Baeyer had to suppose that an addition product first was formed, & that the reaction proceeded thus:



[product hypothetical addition

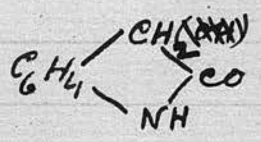


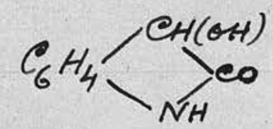
It seems that only lactame derivatives give indigo by reduction, Isatinchloride  and lactimethers give indigo by reduction, and ethyl pseudoisatin ethyl oxim  gives ethyl indigo; yet isatin itself does not yield indigo by reduction.

Goldschmidt in a recent paper Ber XXIII 253 confirms Gumpert's statement about the action of phenyl isocyanate on Isatin (Jour. f. Prakt Chem. [2] 32. 283) It is this, when isatin is heated with phenyl isocyanate, a carbanilid-isatin is formed having the constitution , as is proved by the action of alkalies on it; by the action of caustic potash the potassium salt of carbanilid isatic acid is formed 

The formation of this carbanilid-isatin cannot be explained in the same way as Baeyer accounted for the formation of the acetylbody; but it is at once explained if we suppose isatin to be a lactame.

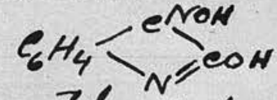
The formulae given for oxindole and dioxindole agree well with their observed properties.

 oxindole the lactame of o. amido acetic acid.



dioxindole the lactame of an unstable o·amido mandelic acid.

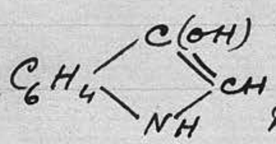
When oxindole is treated with nitrous acid isatoxime is produced, which Baeyer represents as



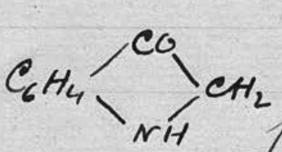
here we must suppose a wandering of the Hydrogen atom from the lactame to the lactime position, unless isatin be lactame. The same is the case with dioxindole. When ~~diox~~ isatin is reduced dioxindole is formed, isatin being readily produced again by oxidation.

It would seem from all these considerations that isatine had the lactame constitution, or that it formed an actual case of tautomerism. ~~H~~, Deductions made concerning the constitution of such bodies, from the behaviour of their metallic salts, must be of doubtful value, since it is uncertain whether the metal occupies the same place as the hydrogen or not. The general question of the constitution of metallic derivatives will be spoken of later.

Indoxyl reacts according to both its normal and pseudo constitution, and derivatives are known of both.

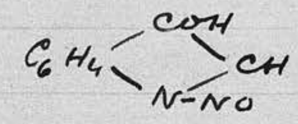


normal

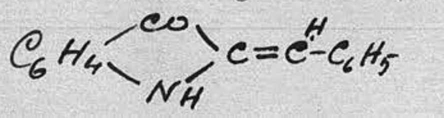


pseudo.

It forms a nitrosamine with nitrous acid,



which proves the presence of an imide group. The action of potassium pyrosulphate towards it in giving potassium indoxyl sulphate, also shows that there is a hydroxyl group present. But indoxyl also reacts as if it had the pseudo constitution; thus, it condenses with benzaldehyde and pyruvic acid to form indogenides of these bodies.



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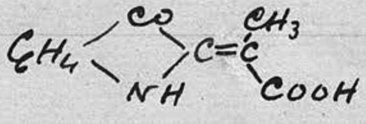
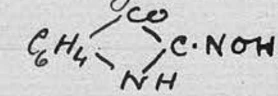
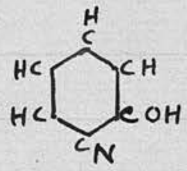
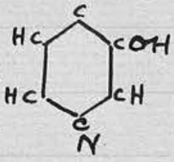


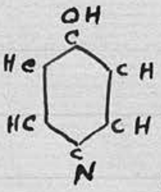
There is also a isonitroso derivative of pseudoindoxyl which is identical with pseudoisatoxim 

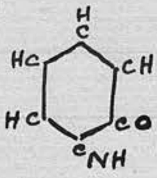
$C_6H_4\left<\begin{matrix}CO\\NH\end{matrix}\right>C\cdot NOH$

The derivatives of oxypyridine furnish a good number of examples of bodies showing this twofold behaviour. Oxypyridines have the forms

α. 

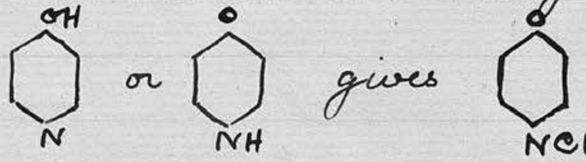
β. 

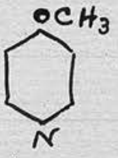
γ. 

Or they may have an imido group thus:  pyridon

Oxypyridines themselves behave at the same time like acids & bases; they form salts with acids and alkalies. Their constitution has not been settled.

They yield as a rule both classes of ethers, which may be obtained directly from the mother substance.

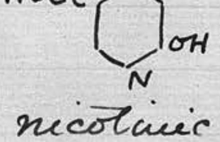
Thus γ. oxypyridine when heated with methyl iodide gives methyl pyridon. 

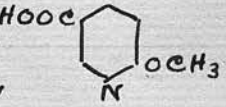
γ. chlorpyridine, prepared from γ oxypyridine by the action of Phosphorus pentachloride, when treated with sodium methylate gives the isomeric methoxypyridine 

The same is true of the α and β compounds.

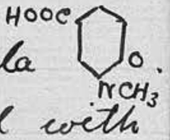
Pechmann (Ber XVII 2384, XVIII 318) describes a very interesting case which, if anything, seems to point to the pyridon form as being that of the original bodies.

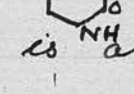
When cumalic acid  is treated with ammonia in the cold, oxynicotinic acid is produced, which is usually considered to be an oxypyridine derivative.

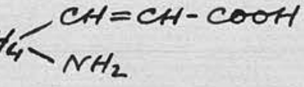


By the action of methyl iodide on this in presence of caustic potash, methoxynicotinic acid was supposed to arise, 

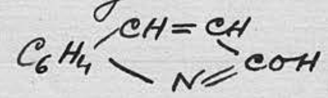
Exactly the same body is obtained when cumalic acid is treated with methylamine.

This mode of formation points to the lactame formula . When oxynicotinic acid in hot alkali solution is treated with sodium amalgam, ammonia is evolved. By a similar treatment oxynicotinic ether yields methylamine and not ammonia, proving that the ether has the lactame form.

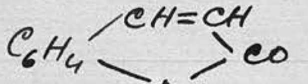
It is probable, therefore, that when ammonia acts on cumalic acid the hydrogen remains attached to the nitrogen as does the alkyl. The substance formed would then be α pyridon β' carboxyl . By supposing this the action of methyl iodide is at once explained.

Among the oxyquinoline derivatives, we may say that carbostyril holds the same place as isatin does among the indole derivatives. It is the intramolecular anhydride of o-amidocinnamic acid, and according to Baeyer is a lactame. 

$C_6H_4\begin{matrix}\diagup CH=CH-COOH\\ \diagdown NH_2\end{matrix}$

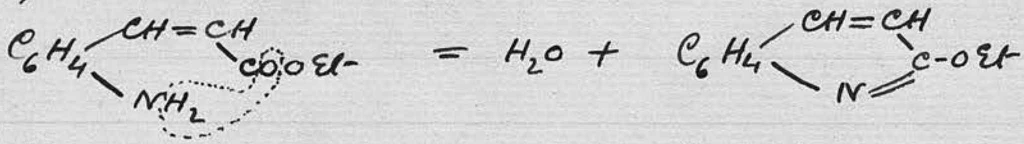
gives 

$C_6H_4\begin{matrix}\diagup CH=CH\diagdown\\ \diagdown N= COH\end{matrix}$

Pseudocarbostyril is then .

$C_6H_4\begin{matrix}\diagup CH=CH\diagdown\\ \diagdown NH\diagup\end{matrix}CO$

<u>Lactime</u> ethers are formed by the action of alkyl iodide on the sodium or silver salt of carbostyril, while the <u>lactame</u> ethers arise by the action of alkyl iodide on <u>free</u> carbostyril. The lactame ethers are the more stable of the two. The lactime ethers arise also from o-amidocinnamic ethers, by heating with zinc chloride and alcohol, water is removed thus:



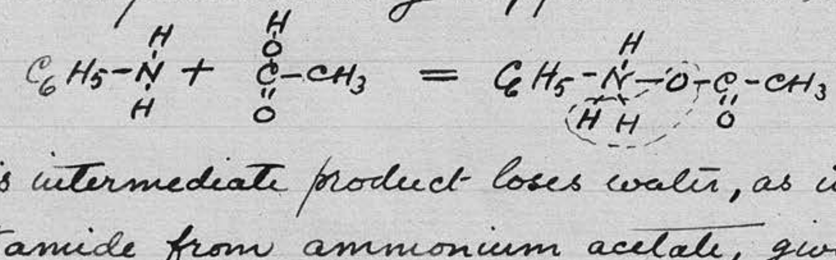
$$C_6H_4\begin{matrix}\diagup CH=CH\diagdown\\ \diagdown NH_2\end{matrix}COOEt = H_2O + C_6H_4\begin{matrix}\diagup CH=CH\diagdown\\ \diagdown N= \end{matrix}C-OEt$$

This was Baeyer's chief proof for the lactime constitution of carbostyril. He concluded that carbostyril would arise from free o-amidocinnamic acid in the same way as the ether arises from the ethyl ether of the acid, namely, according to the lactame mode of formation.

Now according to the way in which the lactime ether was produced from the ether of the acid, namely, by heating with zinc chloride and alcohol, the reaction could hardly go otherwise. In the presence of excess of alcohol there was little to induce alcohol to leave the molecule, and in the presence of such a powerful dehydrating agent as zinc chloride — which does not abstract alcohol — it was only to be expected that water should be removed. Compare for instance the difficulty with which water is split off here, and the ease with which alcohol goes off in the case of dibromisatinic ether.

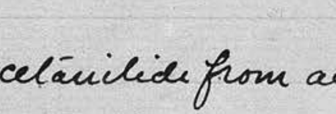
It may be noticed in those cases where normal and pseudo ethers exist, that the pseudo ether is the more stable of the two. In the cases to which reference could be made the melting or boiling points of the pseudo ethers were invariably higher than those of the normal ethers, and in not a few cases, by simply heating, the normal ether passes into the pseudo form. Thus γ methoxypyridine on heating changes into methylpyridon, and methoxylepidine into methyl lepidon. We should expect a similar state of matters with the hydrogen derivatives, the lactame formulas should be the more stable one. On heating isatin or carbostyril there is no sign of an isomeric change taking place. In the amidoacids there is an acid part and a secondary amine part. It is natural to suppose that these should act on one another as acids generally do on secondary amines, i.e. where water is split off. For example, in the case of acetanilide the reaction takes place we may suppose in two stages, thus:

(1)



$$C_6H_5-\overset{H}{\underset{H}{N}} + \overset{HO}{\underset{O}{C}}-CH_3 = C_6H_5-\overset{H}{\underset{H\,H}{N}}-O-\underset{O}{C}-CH_3$$

(2) This intermediate product loses water, as in the formation of acetamide from ammonium acetate, giving acetanilide

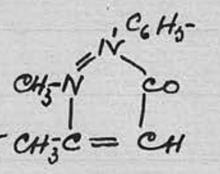


$$C_6H_5-\overset{H}{N}-\underset{O}{C}-CH_3$$

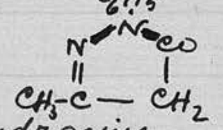
The formation of acetanilide from acetyl chloride and aniline, confirms this formula for acetanilide.
From such a reaction it would seem that the hydroxyl is

more easily removed than the carbonyl oxygen. The ready splitting off of alcohol from bromisatic acid points to the same thing. Both experiment and analogy point, on the whole, to the lactame constitution for these intramolecular anhydrides of o.amido acids.

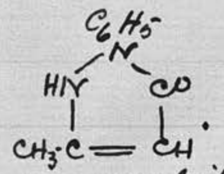
Antepyrine (1,2,3,) phenyl dimethyl pyrazalon



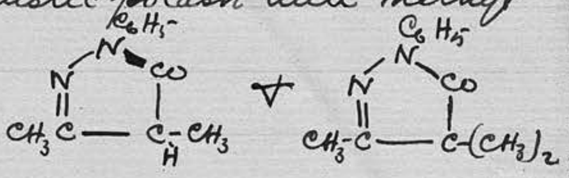
has this formula assigned to it on account of its formation from acetoacetic ether and sym. phenyl methyl hydrazine.



1 phenyl 3 methyl 5 pyrazolon is prepared from acetoacetic ether and phenylhydrazine. Antepyrine may therefore be regarded as a derivative of "pseudo" 1 phenyl 3 methyl 5 pyrazalon



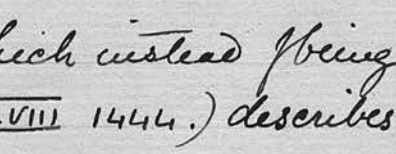
If this (1,3.5) phenyl methyl pyrazalon be treated in the cold with caustic potash and methyl iodide there are produced



But if the reaction is carried out with methyl alcohol & methyl iodide at 100°C, antepyrine is produced, corresponding to the hypothetical mother substance. This case is very similar to that of methoxylepidine in changing into methyl lepidon. The (CH_3) instead of replacing the hydrogen crosses over to the nitrogen. We can either suppose that original substance exists in two tautomeric forms, or that the methyl actually leaves the Carbon & joins itself to the N. Knorr supposed that the methyl iodide first gave an addition product, and then hydriodic acid split off.

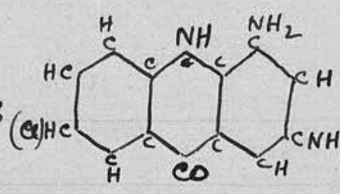
Acridine has two derivatives which instead of being tautomeric are isomeric. Jourdan (Ber XVIII 1444.) describes two bodies prepared in the following ways.

I Dinitro-diphenylamine ortho carboxyl acid

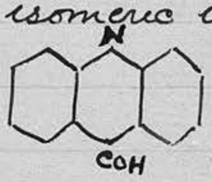


$\underset{COOH}{C_6H_4}-NH-\underset{H}{C_6}H_2(NO_2)_2$,

when reduced with tin and hydrochloric acid, has the nitro groups changed into amido groups, and at the same time water is lost. The body produced is diamidohydroacridine. It was a chlorine derivative which was actually prepared.



II If however the above mentioned acid be treated with sulphuric acid, water goes out and on reducing now with tin and hydrochloric acid the substance produced is not the same as the above, but is isomeric with it, and reacts according to the constitution It is an oxyacridine derivative. The former body is unacted on by hot alkali while the latter readily dissolves.



There are still to be considered a class of bodies which sometimes appear to act as if they had hydroxyl, at other times as if they had ketone oxygen. In this class there are β diketones, phloroglucin, and succinic succinic Ether.

β. diketones are bodies which contain the group $-CO-CH_2-CO-$, like acetoacetic ether $CH_3-CO-CH_2-CO-OEt$ and benzoyl acetone $C_6H_5-CO-CH_2-CO-CH_3$, etc.

One of their most characteristic properties is, that the hydrogens of the methylene may be replaced by metals, one of them at least. They in fact behave like acids.

The two possible formulae for acetoacetic ether are

(1) $CH_3-CO-CH_2-CO-OEt$ (2) $CH_3-COH=CH-COOEt$ {β. oxycrotonic Ether}

Acetoacetic ether is produced as its sodium salt by the action of sodium on acetic ether. Various theories have been proposed to account for the reaction.

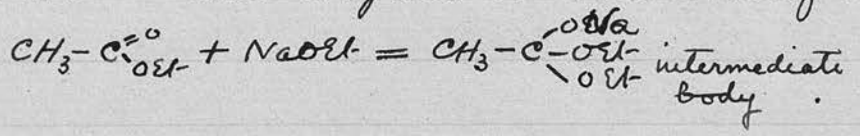
Two of these Geuther's and Michael's need not be given here; they both supposed the formation of doubtful intermediate products.

Frankland and Duppa supposed the sodium first to replace a hydrogen in the methyl group, $CH_3-COOEt + Na = CH_2Na-COOEt + H$. and that the intermediate body then reacted with another molecule of acetic ether,

$$CH_3-COOEt + CH_2Na-COOEt = CH_3-CO-CH_2-CO-OEt + NaOEt$$

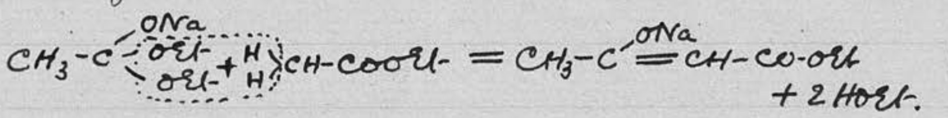
$$CH_3-CO-CH_2-COOEt + NaOEt = CH_3-CO-CHNa-COOEt + HOEt.$$

According to Claisen's theory, first a small quantity of sodium ethylate is formed, by the action of sodium on the trace of alcohol invariably present in the acetic ether. $Na + HOEt = NaOEt + H$. This ethylate then adds itself to the acetic ether.



$CH_3-C\begin{array}{l}=O\\ \diagdown OEt\end{array} + NaOEt = CH_3-C\begin{array}{l}\diagup ONa\\ -OEt\\ \diagdown OEt\end{array}$ intermediate body.

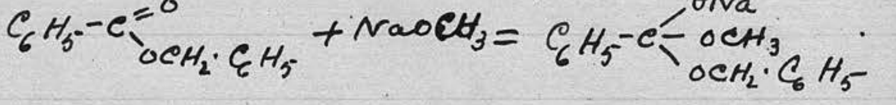
This intermediate body then reacts with another molecule of acetic ether



$$CH_3-C\begin{array}{l}\diagup ONa\\ -OEt\\ \diagdown OEt\end{array} + \begin{array}{l}H\\ H\end{array}\rangle CH-COOEt = CH_3-\overset{ONa}{C}=CH-CO-OEt + 2HOEt.$$

The alcohol ~~thus~~ liberated then reacts on more sodium giving more ethylate, and the reaction goes on faster.

Of all the theories proposed that of Claisen's finds most experimental support. Wislicenus showed that if the acetic ether employed were perfectly pure, & contained no trace of alcohol, the sodium acted on it with extreme slowness, even on boiling. Besides, sodium does not act on the hydrogen of methyl directly. This argues against the theories of Geuther, Michael, & Frankland & Duppa. Claisen's theory also accounts for the gradual increase in the velocity of the reaction. He has also shown that bodies like the above mentioned intermediate product actually exist. Thus by the action of sodium methylate on benzyl ether, such a body is formed



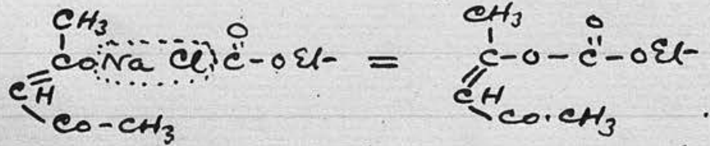
$C_6H_5-C\begin{array}{l}=O\\ \diagdown OCH_2\cdot C_6H_5\end{array} + NaOCH_3 = C_6H_5-C\begin{array}{l}\diagup ONa\\ -OCH_3\\ \diagdown OCH_2\cdot C_6H_5\end{array}.$

The same substance is obtained from benzoic methyl ether and sodium benzylate, or from benzaldehyde and sodium methylate. The formation of benzoylacetic ether, from benzoic ether and acetic ether (Ber XX 653), appears to proceed according to Claisen's theory. An addition product is first obtained by heating benzoic ether with sodium ethylate, and on adding acetic ether the benzoyl-acetic ether is formed.

Wislicenus has shown (Ber XX 3394), that when normal acid ethers — acetic ether, propyl ether, & n. butyric ether — are made to act on oxalic ether in presence of sodium ethylate, in each case a β diketone is obtained. It is the CH_2 next the carboxyl of the acid ether that is attacked. With isobutyric acid, on the other hand, no such reaction occurs.

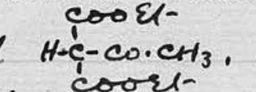
All these facts are quite in agreement with Claisen's theory. The question of the actual constitution of these metallic salts of β diketones is a difficult one. According to Claisen's theory of their formation, the metal is united to the oxygen.

Most of the chemical reactions certainly favour the other view that the metal is united to the methylene carbon. When alkyl iodides react on them, the alkyl is always found united to the carbon, and the same is generally true of the action of aci-chlorides. There are one or two cases where it would appear that the derivatives of the other formula are obtained. Zedel has prepared, from sodium acetylacetone and Chlorcarbonic ether, such a body.

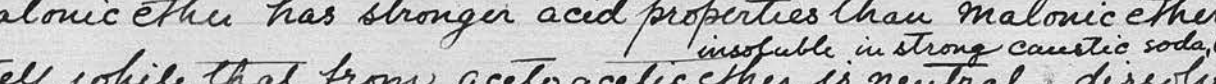


$$CH_3\text{-}C(ONa)\text{=}CH\text{-}CO\text{-}CH_3 + Cl\text{-}\overset{O}{C}\text{-}OEt = CH_3\text{-}C(\text{-}O\text{-}\overset{O}{C}\text{-}OEt)\text{=}CH\text{-}CO\cdot CH_3$$

which behaves in every way like an anhydride.

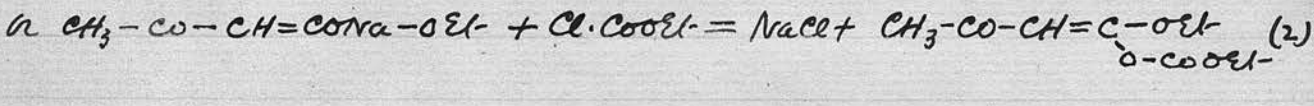
When acetyl chloride reacts on sodium malonic ether, acetyl malonic ether is obtained  $H\text{-}\underset{COOEt}{\overset{COOEt}{C}}\text{-}CO\cdot CH_3$. Conrad and Genthzeit (Ann 214·31) by the action of chlorcarbonic ether on aceto-acetic ether, obtained a body which they described as identical with acetyl malonic ether. But Michael (Jour. f. Prakt. Chem. 37·473) combats this. He finds the two bodies prepared by the above methods to be different. The one from malonic ether has stronger acid properties than malonic ether itself, while that from aceto acetic ether is neutral, insoluble in strong caustic soda, but dissolves **slowly** in dilute caustic soda splitting into carbonic acid, acetone and alcohol. The sodium salt of the other body is stable.

Michael considers that with the aceto-acetic ether & chlorcarbonic ether two reactions are possible.



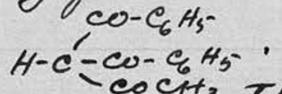
$$CH_3\text{-}CONa\text{=}CH\text{-}COOEt + Cl\cdot COOEt = NaCl + CH_3\text{-}\underset{O\text{-}COOEt}{C}\text{=}CH\text{-}COOEt \quad (1)$$

or



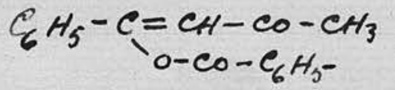
$$CH_3\text{-}CO\text{-}CH\text{=}CONa\text{-}OEt + Cl\cdot COOEt = NaCl + CH_3\text{-}CO\text{-}CH\text{=}\underset{O\text{-}COOEt}{C}\text{-}OEt \quad (2)$$

and that formula (1) or (2) must represent the body.
This question requires to be further investigated.
In these β. diketones it is usually supposed that the hydrogen of the methylene is rendered replaceable under the influence of the adjacent negative carbonyl groups $-CO-CH_2-CO-$. When therefore a third carbonyl group is introduced $-CO-\overset{CO-}{C}H-CO-$ the substance ought to show still stronger acid properties; this is generally found to be the case. Fischer & Bülow (Ber XVIII 2133) prepared a substance from benzoylaceton and benzoyl chloride, which they supposed to be dibenzoylacetone,



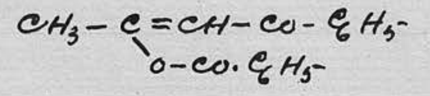
$$H-C\begin{cases}CO-C_6H_5\\CO-C_6H_5\\COCH_3\end{cases}$$

, but this constitution did not agree with the properties of the body, which showed no acid properties whatever. Claisen concluded (Ber XXI 1153) that the body had either of the constitutions



$$C_6H_5-\underset{\diagdown O-CO-C_6H_5-}{C}=CH-CO-CH_3$$

or



$$CH_3-\underset{\diagdown O-CO.C_6H_5-}{C}=CH-CO-C_6H_5-$$

Dr Smith (Inaug. Diss. Munich 1889) found by the same method which Fischer employed, a mixture of dibenzoylacetone and an isomeric substance which was not a β. diketone. It did not show any of the acid properties of dibenzoylacetone and none of the properties of Zedels anhydride. It may be that this second substance and the one which Michael obtained are analogous; but practically nothing is known regarding their nature.

In the formation of pyrons from β diketone copper salts, the copper appears to be attached to the carbon and not to the oxygen. Although several cases are thus known of derivatives of β diketones where the radicle introduced is joined to the oxygen, yet from the general chemical behaviour of the salts, they would seem to have the metal united to the carbon. Theoretical reasons have been advanced, however, for the other arrangement.

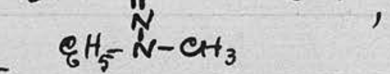
In favour of a definite constitution for the β diketones themselves the evidence is conflicting.

Many bodies containing the group $=C=CH-OH$

do not appear capable of existence in this form, but this grouping passes into the form $=\underset{H}{C}-\underset{H}{C}=O$. This is most noticable among the lower members of the series. If an attempt be made to prepare vinyl alcohol from vinyl sulphuric acid, acetaldehyde is obtained instead, $CH_2=CH\cdot OH$ changes to $CH_3-\underset{H}{C}=O$. In the same way the grouping $:C-COH=CH_2$ tends to go into $:C-CO-CH_3$.

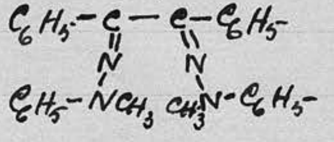
B. diketones, on the other hand, react as if sometimes the one form sometimes the other existed. In agreement with the form $-CO-CH_2-CO-$ we have the action of nitrous acid, which gives rise to isonitrosobodies, e.g. $CH_3-CO-\underset{NOH}{C}-COOEt$ B isonitroso acetoacetic ether. ~~Also~~ acetyl chloride acts not on the free B diketones but on their sodium salts only.
On the other hand there are reasons for supposing the other constitution $-CO-CH=C(OH)-$. When dimethyl phenyl hydrazine reacts on double ketones we should expect two condensation products to be formed. With α diketones and γ. diketones this is the case, but with β diketones only one is obtained (Ann. 253. 15).

With benzil there are obtained by the action of one molecule methylphenylhydrazine the body



$$C_6H_5-\underset{\underset{C_6H_5-N-CH_3}{\overset{\|}{N}}}{C}-CO-C_6H_5,$$

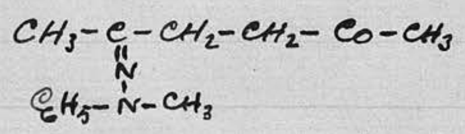
and with two molecules



$$C_6H_5-\underset{\underset{C_6H_5-NCH_3}{\overset{\|}{N}}}{C}-\underset{\underset{CH_3N-C_6H_5}{\overset{\|}{N}}}{C}-C_6H_5.$$

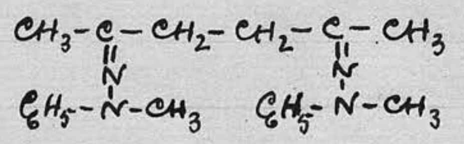
Similarly, two such derivatives are obtained from acetonyl acetone $CH_3-CO-CH_2-CH_2-CO-CH_3$,

viz,



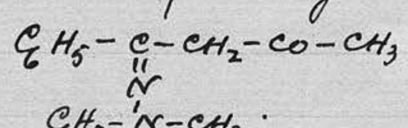
$$CH_3-\underset{\underset{C_6H_5-N-CH_3}{\overset{\|}{N}}}{C}-CH_2-CH_2-CO-CH_3$$

and



$$CH_3-\underset{\underset{C_6H_5-N-CH_3}{\overset{\|}{N}}}{C}-CH_2-CH_2-\underset{\underset{C_6H_5-N-CH_3}{\overset{\|}{N}}}{C}-CH_3.$$

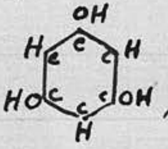
But with benzoyl acetone for example only one hydrazide has been obtained viz



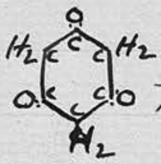
$$C_6H_5-\underset{\underset{C_6H_5-N-CH_3}{\overset{\|}{N}}}{C}-CH_2-CO-CH_3.$$

By the action of two molecules no further addition takes place, the mono derivative only results. We may account for this, by supposing the methylene hydrogen to have moved over to the oxygen. By supposing this the explanation of the formation of a great many condensation products of these β diketones becomes very simple.

Phloroglucin usually reacts as if it were trioxybenzol, but sometimes as if it were triketohexamethylene.



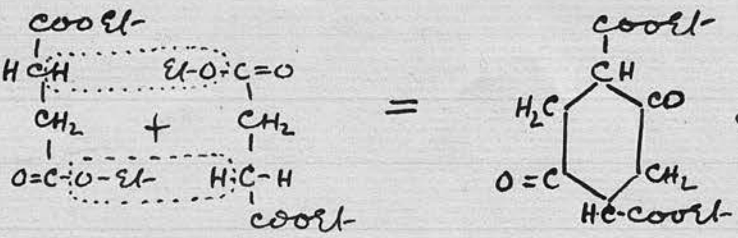
trioxybenzol



triketohexamethylene.

It reacts according to the first of these constitutions in that it is soluble in alkalies; it also forms a triacetyl derivative and a tricarbanilid compound with phenylisocyanate (Ber $\overline{\text{XXIII}}$ 253). But it reacts as a hexamethylene body towards hydroxylamine since a trioxime is formed.

When sodium acts on succinic ether succino-succinic ether is produced

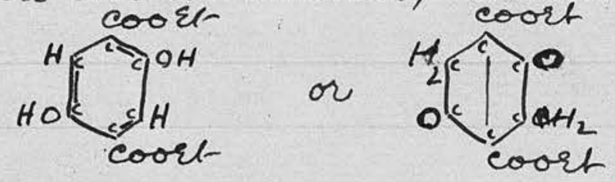


succino-succinic ether

Over the derivatives of this substance a considerable amount of discussion has taken place. As it is written in the above formula it is a derivative of hexamethylene, viz, diketohexamethylene p.dicarboxyl ether. But it may also be represented as an oxybenzene compound,

hydroquinone hydro p.dicarboxyl ether.

It behaves sometimes according to one representation sometimes according to the other. It dissolves readily in alkalies, and the sodium salt with acetyl chloride gives a diacetyl derivative. On the other hand the free ether acts more usually like a quinone derivative. It gives a diphenylhydrazine and a dioxime with hydroxylamine. Baeyer regarded it on this account as a quinone (Ber $\overline{\text{XIX}}$ 428), but from the action of acetyl chloride on the sodium salt he considered the sodium to be united to the oxygen. If succinosuccinic ether be treated with Bromine, a substance containing two atoms of hydrogen less is obtained, which may be written in two ways



The substance behaves generally as if it had the hydroxyl constitution, and Baeyer assigned the first formula to it. But it also shows the same twofold behaviour. It gives no reaction with phenylhydrazine, hydroxylamine or ammonia; but on the other hand it does not react with phenylisocyanate.

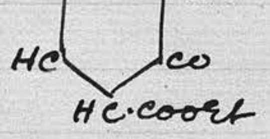
Many of the derivatives of succinosuccinic ether can exist in two or three different crystalline modifications. Only one of these however is usually stable; the others passing readily on disturbance into the more stable ordinary modification. Hantzsch and Herrmann at once connected this di- and tri-morphism with the apparent tautomeric behaviour of the bodies.

They proposed to use the word "Tautomerism", to designate that property of certain substances to show a double ~~properties~~ behaviour, as Laar had employed it. But in order to designate the actual occurrence of a change of position of the hydrogen atom, they proposed to use the word of V. Meyer's, "Desmotropy". When the two different arrangements of the atoms manifested themselves in two distinct varieties of the substance, these two varieties they called the "Desmotropic states" of the body. (Ber XX 2801.) Hantzsch and Herrmann therefore concluded, that these different crystalline forms of the succinosuccinic ether derivatives represented the different "desmotropic states" of the substances.

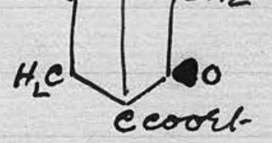
There is usually a difference in colour between the varieties obtained. For instance, O. Lehmann found that Hydroquinone p. dicarboxyl Ether, the body obtained by the reduction of succinosuccinic ether, crystallises at the ordinary temperature in green rhombic prisms, but from hot aniline solution it crystallises in dichroic (pale green & colourless) asymmetric plates. This variety, on cooling, changes into green asymmetric plates, which on coming in contact with the rhombic, green crystals, changes into that form. The green rhombic crystals are the stable variety. The colourless variety may also be obtained by subliming the green rhombic crystals between watch glasses. Other derivatives of succinosuccinic ether, by similar treatment, give usually a second "mobile" variety. One of these varieties is usually coloured the other colourless.

Graebe and Liebermann first pointed out that as a rule quinones were characterised by being coloured, while simple benzol derivatives were colourless.

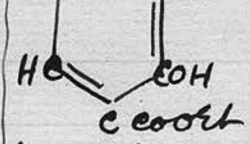
Hantzsch and Herrmann making use of this generalisation, laid it down as a rule, that when a tautomeric body existed in two modifications differing in their physical characteristics, these different physical states corresponded to the desmotropic states of the body. Further in the case of the derivatives of succinosuccinic ether they concluded, from Graebe and Liebermann's generalisation, that the coloured variety of the tautomer always represented the quinone derivative, while the colourless variety represented the hydroxy-derivative. Thus, for the three varieties described above, they give the following constitutions



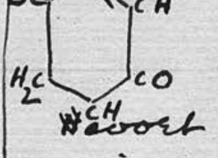
stable (green)



"mobile" (green)



"mobile" (colourless)

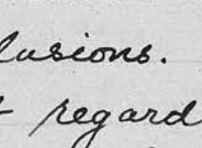


variety not yet discovered

The assumption which these chemists make, that all p-hydroxybenzenes are colourless, while quinones are coloured is quite unwarranted, and the principle they thus establish in assigning constitutions to bodies is a dangerous one. Much more is necessary than the knowledge of a physical property in settling the constitution of bodies. In many cases it is difficult to prove the contrary of what Hantzsch and Herrmann state, but exceptions have been found which throw doubt on their conclusions.

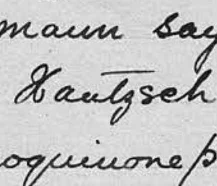
First of all there seems to be doubt regarding the true colour of some of these bodies. Hantzsch describes succinosuccinic ether as existing in two forms, colourless and pale green. Lehmann says it is quite colourless, as do most chemists. Hantzsch has always described the unstable form of hydroquinone p-dicarboxyl ether as colourless; Lehmann, who discovered them, says it is dichroic — pale green and colourless, & Muthmann adds that it is more intensely coloured than succinosuccinic ether.

Dichlorhydroquinone dicarboxyl ether



at ordinary temperatures is colourless.

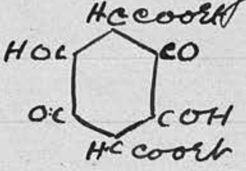
When melted or dissolved in benzol it becomes green, Hantzsch and Herrmann therefore concluded that the green variety was a quinone



.

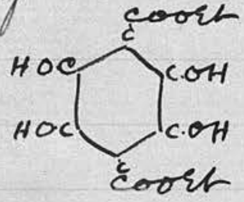
Goldschmidt (Ber XXIII 253) has shown that there is no ground for such a conclusion. If what Hantzsch says regarding this compound be true, then phenyl-isocyanate should only act on the colourless variety and not on the green. When the substance is dissolved in a little benzol and heated to 150°C with phenylisocyanate two molecules of the latter unite with one molecule of the chloro body, and this substance is produced, $C_6Cl_2(COOEt)_2(O{\cdot}CO{\cdot}NHC_6H_5)_2$; showing that even in the green variety hydroxyl and not Ketone exists. The same is true of the bromine derivative.

Again tetraoxyterephthalic acid diethyl ether is a yellow substance, and according to Hantzsch had therefore the constitution



.

When it is heated with phenylisocyanate four molecules are taken up, giving $C_6(COOEt)_2(OCO \cdot NHC_6H_5)_4$. This was formed when even a small quantity of phenylisocyanate was used. Consequently the above is not the true formula but the substance contains four hydroxyls

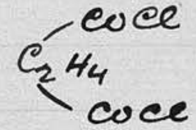


and ~~the substance~~ is a true benzol derivative. Other experiments point to the same conclusion.

A great many substances show polymorphism similar to that of succinosuccinic ether derivatives. Ammonium nitrate crystallises in four different forms dependent on the temperature. The temperatures of transformation of the crystals being 35°C 85°C + 123°C. Anthracene, Benzophenone, chlorodinitrobenzene and others exhibit similar polymorphism.

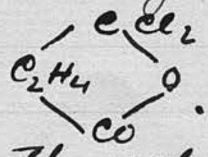
It is highly improbable that the change in the crystalline form of these bodies is in anyway conditioned by a change in their chemical constitution. It would seem that these are simply physical isomers, and that there is not such a close connection between the chemical composition and the physical appearance as would at first seem likely. The phenomenon is rather to be classed along with that of allotropy. In both the change of one form into the other is dependent chiefly on the temperature; and heat is absorbed or evolved in both cases. The molecules which condition the crystalline structure of a body are according to the theory of allotropy, not simple but compound molecules. So that the changes which are seen in the above compounds, depend on ~~the~~ a change in the size or arrangement of the physical molecules

We may now ask if there are any other bodies which behave as tautomers but have some other element than hydrogen conditioning the two states? If there are any cases they are rare. Chlorine, in one or two compounds appears to act in this way e.g. Succinyl and phthalyl chlorides. Succinyl chloride acts apparently according to the two formulae



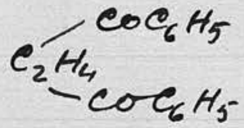
$C_2H_4(COCl)_2$

and



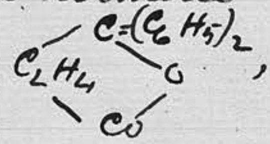
$C_2H_4{<}^{CCl_2}_{CO}{>}O$

. Augers (Bull. Soc. Chem 49 [1] 323·345) by the action of aluminium chloride and benzol on succinyl chloride obtained two isomeric bodies. apparently



$C_2H_4(COC_6H_5)_2$

and



$C_2H_4{<}^{C=(C_6H_5)_2}_{CO}{>}O$,

and concluded that the chloride was a mixture of the two isomers. Emery (Ber. Dec 1889) finds that on fractionating succinyl chloride, prepared from succinic anhydride and phosphorus pentachloride, two different bodies are obtained containing the same percentage of chlorine; but these bodies have not been further examined.

Having now given an account of the more important cases of this phenomenon of a twofold behaviour, we come to consider more closely what may be its true explanation. In tautomerism proper, there ought to be a continual passing to and fro of the hydrogen atom, so that both forms of the substance would then exist together. In some cases this may be but it is not likely that, in general, such a delicate balance of equilibrium should exist in the molecule. Instances in which both kinds of derivatives are obtained in the same reaction are rare, although in many cases, both kinds of derivatives are about equally stable. We may consider each of these compounds to have a definite constitution under given conditions. If these conditions are changed, as perhaps under the influence of another reagent and the ordinary conditions of an experiment, the substance may pass into the "pseudo" form as a preliminary step in the reaction, or as part of the reaction itself. This is one way of regarding it; but we may, especially in cases of so-called double decompositions, do away to a large extent with the idea of a direct substitution.

When a reagent acts on one of these tautomeric bodies a hydrogen is removed, and some other monovalent element or radicle is introduced into the residue, not necessarily where the hydrogen was, but where there is the strongest affinity between the residue and the new element or radicle. This does not express the whole state of matters, for we have to consider the transporting of the new radicle to the position of greatest affinity. If the new residue is "mobile", the position of greatest affinity will be assumed at once; but if the new residue is characterised by an "immobility", that is if it is difficult to move about, then it may be drawn into a position where the affinity is strong enough to hold it, but the arrangement is not the most stable possible. In some of these cases then by the action of heat, when the mobility of the radicle is increased, we should expect the compounds to pass over into its most stable form. It has been mentioned how notably in thioxypyridine derivatives this is the case; the less stable form passes into the more stable.

The mobility of hydrogen and metals is in marked contrast with the immobility of hydrocarbon radicles.

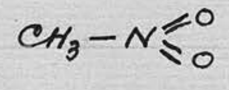
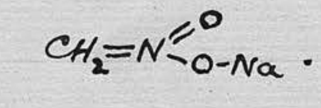
This is seen well in electrolysis, while hydrogen and metallic salts are electrolytes, "alkyl" is not an ion.

Isomers capable of existing with alkyl usually desappear when the alkyl is replaced by metal or hydrogen.

If now both metals and hydrogen show this great mobility, in these tautomeric bodies does the metal occupy the same place as the hydrogen?

It has been usual in most cases to suppose that it does. Baeyer, in deciding the constitution of Isatin, supposed hydrogen and the metal to occupy the same position. But more recently several chemists notably Michael and Goldschmidt have combated this view. Michael considers (Jour. f. Prakt. Chem 37. 507) in all those cases of tautomerism, that the metal is in a different position to the hydrogen. He considers that metals are very seldom united to carbon directly, but to it through an oxygen or a sulphur, when this is possible. The corresponding hydrogen on the other hand remains attached to the carbon. Thus for acetylacetone he gives $CH_3-CO-CH_2-CO-CH_3$, but for its sodium salt

$CH_3-CO-CH=CONa-CH_3$;

& Nitromethane  $CH_3-N\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}$ gives  $CH_2=N\begin{smallmatrix}\nearrow O\\ \searrow O-Na\end{smallmatrix}$.

He comes to these conclusions from considerations regarding the electro condition of the atoms. In acetylaceton for instance, the strong electro-negative oxygen of carbonyl causes the strong electropositive sodium to wander from the carbon to the oxygen, the oxygen being more negative than the carbon. The less positive hydrogen however does not pass over, since the negative influence of the oxygen is extended to it through the carbons, & it is made too negative to pass over like the sodium.

Goldschmidt, on the other hand, imagines the reagent to be split into its ions, and each ion attacks that part of the compound for which it has most affinity. For instance the formation of the sodium salt of thiacetanilide is usually expressed thus $C_6H_5-NH-CS\cdot CH_3 + NaOH = C_6H_5-NNa-CS\cdot CH_3 + H_2O$

We have seen how the sodium salt gives rise to ethers of the form $C\begin{array}{l} {=}N\cdot C_6H_5 \\ {-}S\cdot R \\ {-}CH_3 \end{array}$ by the action of alkyl iodide.

We must suppose the sodium to be attached to the sulphur, otherwise this ether can only arise by a wandering of the alkyl from the nitrogen to the sulphur, that is from the more stable position to the less stable as regards alkyl, — for the ethers with alkyl united to sulphur are less stable than those in which alkyl is united to nitrogen eg. methylthioacetanilide

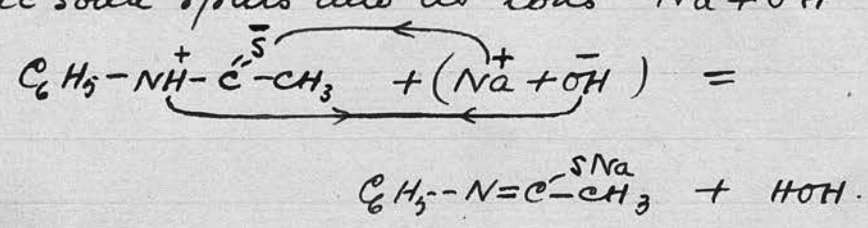
$C_6H_5N\cdot CH_3-CS\cdot CH_3$ solid, melting point 58°–59°, Boiling point 290°

Isothioacetanilide $C_6H_5N{=}C\begin{array}{l} -SCH_3 \\ -CH_3 \end{array}$ liquid, boiling point 245°.

Goldschmidt therefore represents the action of caustic soda on thioacetanilide thus.

Caustic soda splits into its ions $Na + OH$

Then



$$C_6H_5-\overset{+}{N}H-\overset{\overset{-}{S}}{C}-CH_3 + (\overset{+}{Na} + \overset{-}{O}H) =$$

$$C_6H_5-N{=}\overset{SNa}{C}-CH_3 + HOH.$$

This is very similar to the idea expressed at first, namely, that the element introduced goes where there is the greatest attraction. Before we can be certain of the above mode of representation, we would require to know the state of the second body as regards ions.

Michael's method of reasoning is also uncertain and cannot be carried so far as he would go. Perhaps in simple cases the true state of matters is arrived at by such reasoning. Only in certain instances can we be sure of the relative states of electrification of the atoms in a compound, and we can know very little about the influence which the charge of one atom has over that of another.

With the strong affinity which we know the more basic metals have for oxygen and sulphur, it is not unlikely that in those cases of metallic compounds in question, the metal is actually united to them instead of to the carbon. In speaking of B. diketones it was seen that their chemical relations taken in the ordinary acceptance pointed generally to the formula $-CO-CHNa-CO-$ for the sodium salt, and this formula has usually been considered the correct one. But the reactions which decided this, do not contradict this supposition of the metal being united to oxygen. There are general experimental grounds for supposing, that in many cases, the metal is not united directly to carbon.

As a rule, organic compounds which have metal united directly to carbon, as in the metallic salts of nitrob[illegible] alkyls, and alcohol radicles, show a distinct behaviour from those in which the metal takes the place of a hydrogen of alcoholic hydroxyl. In the former class the metal is replaceable by bromine, but not by acetyl or methyl. In the latter class the reverse is true. Also, many of the metallic salts of the first class are stable in acids. It is not difficult to see to which class the metallic salts of these tautomeric bodies belong.

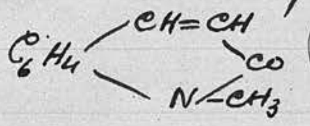
By supposing the metal to be united to oxygen or sulphur, we would have, with the B. diketones especially, to imagine in general a wandering of the new radicle back to the carbon; but on the other hand there would be explained the difficulties in connection with the thio-compounds, with Isatin, the anhydride derivatives of B. diketones, and others.

It may be noticed that with pyridine and quinoline derivatives, and some others, when methyl iodide acts on the sodium salt, the less stable <u>methoxy</u>

derivative is obtained, while by acting on the *free* substance the more stable *methyl* derivative is obtained.

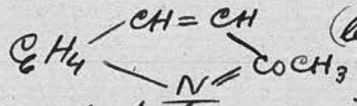
Carbostyril furnishes a good example of this.

Free carbostyril with methyliodide gives



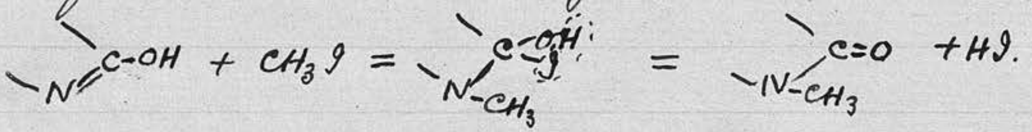
(more stable)

While the sodium salt gives



(less stable)

The action of methyliodide on the free substance, in giving a defferent ether from the sodium salt, has been sometimes explained by supposing an addition product to be formed, and then hydriodic acid to be split-off.



Such an explanation is not satisfactory since there is supposed the formation of a doubtful intermediate product; also there is just as much reason for supposing such an addition with the sodium salt.

It is questionable whether methyl iodide is so easily split into methyl and Iodine, for the alkyl iodides are not electrolytes.

The different behaviour of the metallic and the hydrogen derivatives rather indicates, that the two have different constitutions; and also that the pyridines and quinolines are constituted according to the lactame form. It is certainly more satisfactory to deduce the constitution of a body from the behaviour of reagents on itself than on its derivatives.

If in a reaction then, the element or radicle introduced into the compound seeks for the position where there is the greatest affinity, then, the arrangement of atoms in the residue will have as much to do with the nature of the resulting compound as the constitution of the reagent. The investigation of V. Meyer, on the nitrites and nitrobodies, shows this.

When alkyl iodides are treated with silver nitrite

nitrites and nitrobodies are obtained. With methyl iodide nitromethane alone results $CH_3-N{=O \atop =O}$.
With ethyl iodide about equal proportions of ethyl nitrite and nitroethane are obtained; $C_2H_5-O-N=O$, and $C_2H_5-N{=O \atop =O}$. As we ascend the series the quantity of nitrobody formed gradually decreases, while the quantity of nitrite increases, until finally only nitrite is obtained. Such a reaction then gives little indication of the true constitution of silver nitrite. The motive of the reaction is the formation of silver iodide $Ag + I = AgI$; the two residues alkyl and NO_2 unite, but whether the NO_2 enters as $-O-N=O$, or $-N{=O \atop =O}$, depends on the nature of the alkyl radicle.

Other instances might be given of changes in one part of a molecule influencing the arrangement at another part, so that not only has the relation of neighbouring atoms to be taken into account but also the relation of the more distant atoms.

Widmann's research on cymol (Ber XIX 251) shows this in a marked manner. Cymol is p. methyl-normal propyl benzol $CH_3-C_6H_4-CH_2-CH_2-CH_3$.
If the methyl be exchanged for certain other groups eg. $(COOH)$, $(CH_2{\cdot}OH)$, (CH_2Cl), the normal propyl, changes into isopropyl. Cumic alcohol has the formula $CH_2{\cdot}OH-C_6H_4-\underline{CH}{CH_3 \atop CH_3}$. By simply replacing a hydrogen of the methyl in cymol by (OH) or (Cl) etc., the normal propyl becomes isopropyl.

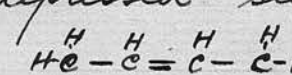
We thus see, that when one element or radicle is taken from a compound and another introduced instead, the change in the distribution of the affinities may be such as to cause rearrangements in the whole molecule. This may perhaps mean changes in distant parts of the molecule, or a change in the point of attachment of the new radicle.

If in tautomeric bodies then, reactions proceed according to this principle, Baeyer's view of a "normal" and a hypothetical "pseudo" compound is a correct one, but such a view does not preclude the occurrence of actual cases of tautomerism, although it reduces the number of tautomeric phenomena. Cases like those of the unsymmetrical diazoamido derivatives can hardly be explained, except by supposing a continuous movement of the hydrogen between the two positions.

There are many examples in this paper of substances which although they do not show simultaneously a double behaviour, that is under the action of one reagent and with particular conditions, yet they show different behaviours with different reagents.

It is most likely, that in these bodies the hydrogen assumes one or other of the positions, as part of the reaction.

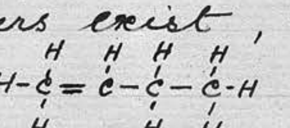
As to why some hydrogen compounds show isomerism and others not, it may be noticed that, where there is a comparatively large proportion of carbon in the vicinity of the hydrogen, isomers exist. The unsaturated hydrocarbons furnish an example of this, in them the mobility of the hydrogen seems to be depressed since isomers exist, thus:



$H_3C-CH=CH-CH_3$

(pseudobutylene)

and



$H_2C=CH-CH_2-CH_3$

(butylene).

are isomeric.

In the case of isomerism of an acridine derivative, quoted in the foregoing, nitrogen and oxygen are certainly present, but the number of carbon atoms influencing the hydrogen atom is very large.

From what has been said in this paper, it is evident that the settling of the chemical constitution of these tautomeric bodies, by purely chemical means, is a very difficult matter. Whether this will be arrived at with any more certainty by the application of physical means, is a question which time will decide.