SPACE REPRESENTATION OF ORGANIC NITROGEN COMPOUNDS.

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It appears highly desirable to discuss the present state of our knowledge relating to the constitution of ammonium compounds and especially of asymmetric pentavalent nitrogen compounds. Quite a large number of space formulas of organic ammonium compounds have been proposed with a view to explain their isomerism and especially their stereoisomeric modifications, and it appears to the author that the time has arrived to select the most appropriate one from among them in the light of recent experiments.

It will be more convenient to discuss the constitution of pentavalent nitrogen compounds first and trivalent compounds afterwards.

Van't Hoff[1] was the first to assign a space formula to pentavalent nitrogen compounds and represented such nitrogen by a cube, of which the nitrogen atom is at its center and the 5 bonds are directed to 5 of the corners of the cube. Willgerodt[2] represented the nitrogen atom as at the center of two superimposed tetrahedra, the valence directions being stretched towards the 5 corners. Bischoff,[3] on the other hand, suggested a third arrangement in which the nitrogen atom was represented to be at the center of a 4-sided pyramid, the 5 bonds being directed towards the 5 solid angles. The last arrangement, being the most symmetrical and giving the smallest number of isomers, is generally accepted as a true representation of pentavalent nitrogen, and H. O. Jones[4] has been at considerable pains to show, though without success, that it satisfactorily explains the passage of trivalent to pentavalent nitrogen. It is the purpose of this paper to show that none of the above hypotheses is adequate to explain recent experimental results relating to the isomerism of organic ammonium compounds and that some other space representation of pentavalent nitrogen is necessary

Ever since Werner's classical conception of the idea of primary and secondary spheres of chemical action and the formation of coördinated groups, the desirability of representing ammonium compounds by means of a single tetrahedron is increasingly being recognized. Werner[5] originally represented ammonium salts as $(NH_3 \cdots H)X$, or $\left(\begin{smallmatrix} H \\ H \end{smallmatrix}\!\!>\!N\!<\!\!\begin{smallmatrix} H \\ H \end{smallmatrix}\right)X$, in

[1] Ansichten über die Org. Chem., 1, 80 (1878).

[2] J. prakt. Chem., 41, 291 (1890).

[3] Ber., 23, 1197 (1908).

[4] Trans. Chem. Soc., 87, 1728 (1905).

[5] Ber., 36, 152 (1902).

which the subsidiary valence, even when inside the coördination group, was represented as different from the other three valences of nitrogen, in consequence of which H. O. Jones[1] in 1905 discarded the tetrahedral representation of ammonium compounds as suggested by Werner's hypothesis, with the observation that "the number of isomerides predicted on this view is practically the same as that on the 'cubic' configuration of van't Hoff and the 'double tetrahedron' configuration of Willgerodt. These isomerides do not exist, so that this hypothesis must be modified and the association of acidic radical with one particular alkyl radical eliminated before it can be considered." This objection is no longer tenable as Werner has modified his views and held that there is practically no difference between a subsidiary and a principal valence inside the coördination group. On this view ammonium compounds will have a tetrahedral configuration with the acid radical in the subsidiary sphere of action and without any connection with nitrogen. With similar octahedral representation of coördinated cobalt,[2] chromium and other complex metalloammine compounds Werner has explained the isomerism and optical isomerism of these compounds.

After Werner, Wedekind as early as in 1904 held that "it is certain that in the tetratoionic radical N*abcd*, in active ammonium compounds the center of activity must possess *tetrahedric* grouping."[3]

Aschan, also in 1903, while accepting van't Hoff's diagram, for the sake of simplification, represented pentavalent nitrogen at the center of a tetrahedron, the fifth bond being directed to the center of gravity of one of the tetrahedron faces.[4] Meisenheimer after his discovery of the amine oxides in 1909 while accepting Werner's main contention about the coördinated ammonium groupings proposed a modification of the tetrahedral configuration in which, while the 4 positive groups are arranged at the corners of the tetrahedron, the negative group takes up a position on one of the faces.[5] Jones and Dunlop,[6] following Werner tentatively, suppose that the "four alkyl groups arrange themselves symmetrically around the nitrogen atom to form a group (Na_4) having enough residual valency to unite with an electronegative radicle."

Werner's ideas about the constitution of ammonium compounds are open to the serious objection that as a matter of fact he has postulated the existence of as many as three kinds of valence, *viz.*, (1) principal valence of nitrogen, (2) subsidiary valence of nitrogen and (3) residual valence of the ammonium group by means of which the acid radical is

[1] *Trans. Chem. Soc.*, **87**, 1728 (1905).

[2] Werner, *Ber.*, **44**, 1887, 2445, 3231, 3272, 3279 (1911).

[3] *British Association Report*, **1904**, p. 521.

[4] *Z. physik. Chem.*, **46**, 293 (1903).

[5] Meisenheimer, *Ber.*, **41**, 3966 (1909).

[6] *Trans. Chem. Soc.*, **101**, 1751 (1912).

combined with it. But it is not necessary at all to complicate matters by the assumption of all these three kinds of valence in the case of ammonium compounds at any rate, as the explanation of their isomerism is perfectly feasible with the assumption of one kind of valence only. As there is no escape from acknowledging the pentavalence of nitrogen as in the amine-oxides $O: Nabc$ it is necessary, as is done by Meisenheimer,[1] to acknowledge the pentavalence of nitrogen in ammonium compounds generally in which all 5 bonds are attached to it by principal valences, though 4 of them are in the inner zone and the fifth in the outer zone as supposed by Werner. The essential idea underlying this view is that the negative radical being in the outer zone or secondary sphere, though attached to the nitrogen atom, has no influence on the asymmetry of the ammonium group, except when, as 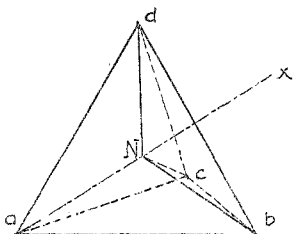in the amine oxides, it acts inside the primary sphere. Moore and Winmill[2] partly accepted Werner's and partly Meisenheimer's ideas. A modification of Meisenheimer's configuration is proposed here. Meisenheimer, like Werner, denied any combination of the fifth group with the nitrogen atoms. Instead of making the position of the fifth group on one of the faces it would be consistent with its position in the outer sphere to keep it outside the tetrahedron and have it linked to the nitrogen atom with one bond through one face. For the sake of convenience and symmetry the line denoting the fifth bond is made equal to the lines representing the other 4 bonds.

Fig. 1.—Proposed form of single tetrahedron formula of pentavalent nitrogen.

We would now proceed to show that the proposed tetrahedral configuration of nitrogen explains more satisfactorily a much larger number of facts regarding the isomerism and constitution of organic nitrogen compounds than does van't Hoff's, Willgerodt's or Bischoff's formula. As late as 1915 Cohen, Marshall and Woodman[3] have written, "the choice of space formulas for nitrogen at present lies between the double tetrahedron arrangement of Willgerodt and the pyramid formula of Bischoff," and Singh[4] attempts to deduce the constitution of two directly linked nitrogen atoms from the pyramid formula. A systematic survey and explanation of experimental results bearing on this subject with the help of the tetrahedral representation of nitrogen has been wanting and it is the purpose of this paper to undertake it with a view to demonstrate that the tetrahedral configuration deserves recognition as perhaps the truest space representation of nitrogen.

[1] *Ann.*, **397**, 273 (1913).
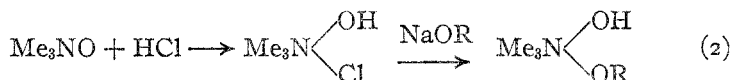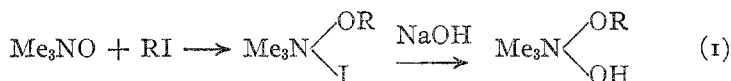[2] *Trans. Chem. Soc.*, **101**, 1672 (1912).
[3] *Ibid.*, **107**, 887 (1915).
[4] *Ibid.*, **109**, 780 (1916).

Now there are three things principally to be considered while discussing the suitability of the tetrahedral formula as distinguished from the other formulas hitherto recognized: (1) the non-equivalence of the fifth bond to the remaining 4 bonds; (2) the number of isomers to which Na_3bx, Na_2bcx and $Nabcdx$ may give rise; (3) the passage of trivalent nitrogen to penta-valence. We would discuss these one by one and show that the tetra-hedral configuration best conforms to experimental results.

Non-Equivalence of the Fifth Bond.

The non-equivalence of the fifth bond is generally recognized so far as it concerns the fact that it is always connected with an acid radical in ammonium compounds. That it acts in the secondary sphere as shown in the formula and thus would be capable of giving rise to isomers has recently been experimentally proved by Meisenheimer.[1] He combined alkyl iodides and hydrochloric acid respectively with trimethylamine oxide. The resultant substance of the first reaction was treated with caustic soda and that of the second reaction with sodium alcoholates when two *isomeric* substances were obtained. He represented the reactions as follows:

$$Me_3NO + RI \longrightarrow Me_3N\big\langle{}^{OR}_{I} \xrightarrow{NaOH} Me_3N\big\langle{}^{OR}_{OH} \qquad (1)$$

$$Me_3NO + HCl \longrightarrow Me_3N\big\langle{}^{OH}_{Cl} \xrightarrow{NaOR} Me_3N\big\langle{}^{OH}_{OR} \qquad (2)$$

The substances were not actually isolated, but their solutions, when heated, yielded different products. The first substance decomposed yielding quantitatively trimethylamine, an aldehyde and water, while the second substance yielded trimethylamine oxide and the alcohol R.OH. Several such isomeric substances have been prepared and shown to behave differently when heated. Isomerides of the types $Me_3N\big\langle{}^{OR}_{OR_1}$ and $Me_3N\big\langle{}^{OR_1}_{OR}$ have also been prepared. Their different behaviors led Meisenheimer to represent them as $[Me_3N.OR]OR'$ and $[Me_3.N.OR']OR$ in which the difference of properties is due to the non-equivalence of the fifth bond which acts in the secondary sphere. Fromm[2] has given a different interpretation to Meisenheimer's results by supposing that the alkyl iodide and hydrochloric acid attach themselves differently to the amine oxide. Fromm supposed that by the action of alkyl iodides oxon-

[1] *Ann.,* **397,** 273 (1913).

[2] *Ibid.,* **399,** 366 (1913).

ium compounds would be produced of the type $Me_3N:O{<}^{Me}_{I}$ which

when acted upon by Ag_2O would yield $Me_3N:O{<}^{Me}_{OH}$.   This substance,

on heating, would produce the amine, formaldehyde and water as found
experimentally.   He further contended that if the fourth and fifth va-
lences of nitrogen are different two isomeric compounds would be formed
by the interaction of hydrochloric acid and the amine oxide and also that
the proposed formula for the two isomerides discovered by Meisenheimer
show them to be alcoholates of a very feeble base $NMe_3(OH)_2$ and would
therefore both be hydrolyzed by water yielding MeOH and $NMe_3(OH)_2$.
Meisenheimer,[1] in reply to Fromm's criticisms, reiterates his objections to
the oxonium formula and contends that of the two isomerides only that
in which the methoxy group is attached to the fifth positive valence of
nitrogen would alone be dissociated by water, but the other in which the
methoxy group is attached by the fourth negative bond would not be
hydrolyzed, as methoxylamine $MeONH_2$ is not.   As regards Fromm's
contention that two isomerides would be produced by the action of hydro-
chloric acid on the amine oxide if the fourth and fifth valences are different,
Meisenheimer points out that of the five valences of nitrogen four are
negative and the fifth positive and it is to the latter alone that the nega-
tive chlorine will be attached, thus producing one additive compound only.
In a subsequent paper[2] Fromm accepts Meisenheimer's contention that in
ammonium compounds there is a fifth positive valence different from the
four negative valences, but believes that in amine oxides there are two
positive and three negative valences, a contention which is easily met
when it is seen that the oxygen atom is held to the nitrogen atom by one
positive and one negative bond.

   Now let us see how far the non-equivalence of the fifth bond has been
recognized in the existing solid representation of nitrogen.   It is not suffi-
cient that the direction of the fifth bond would be different from the rest
but it must be shown to act outside the primary sphere or inner zone.
*It is to be noted that in the optically isomeric complex metallo-ammine com-
pounds of cobalt and chromium discovered by Werner the acid radical has
also no influence on the asymmetry of the molecule and does not affect the isom-
erism of the compound* and hence Werner has successfully explained
their isomerism by keeping the ionizable acid radical in the outer zone.
It therefore stands to reason to suppose that the fifth bond should be
represented to act in the outer zone.   Now this supposition would find
no representation except in the proposed tetrahedral figure for nitrogen.

[1] *Ann.*, 399, 371 (1913).
[2] *Ibid.*, 399, 377 (1913).

In the double tetrahedron and the cube formulas the fourth and the fifth bonds are in the same straight line though pointing in opposite directions. In the cube formula, however, the angles which bonds 1, 2, and 3 make with the bond 4 are smaller than with the fifth bond. In the pyramid formula, however, the fifth bond being directed towards the apex of the pyramid is non-equivalent to the other four which are all directed towards the four angles of the base. But in the single tetrahedron formula not only is the fifth bond shown as directed differently from the remaining four bonds, but it is shown to act outside the primary sphere, a consideration which is not observed in any of the existing formulas and which conforms to the observed fact that the fifth bond makes no difference in the asymmetry of the molecule.

Number of Isomers of Organic Ammonium Compounds.

The next thing to consider is the number of isomers possible according to the existing and proposed formulas of nitrogen compounds and those obtained by experiment. It will be found that experiment invariably conforms to the number of isomers possible according to the single tetrahedron formula only. . We will proceed to consider one by one the possible isomers of the types Na_3bx, Na_2bcx and $Nabcdx$ when x is the negative radical and a, b, c, and d are organic radicals.

(a) Na_3bx.—According to the cube and double tetrahedron formulas two isomers would be possible, neither of them, however, being divisible into enantiomorphs. The pyramidal and the single tetrahedron formulas demand that no isomers be formed. Experiments also show that no isomers of this type are actually formed. V. Meyer and Lecco[1] prepared trimethylethyl-ammonium iodide by two methods, viz., by the interaction of trimethylamine and ethyl iodide and of dimethylamine and methyl iodide, but obtained the same compound. Le Bel[2] obtained two different crystalline trimethyl-isobutyl-ammonium chlorides and chloroplatinates, but the difference was simply due, as was pointed out by Le Bel himself,[3] to dimorphism which is frequently found in the chlorides and chloroplatinates of the amines and quaternary bases. Schryver and Collie[4] prepared the chlorides and chloroplatinates of benzyl-trimethyl-ammonium, trimethyl-propyl-ammonium, trimethylethyl-ammonium and other organic ammonium compounds by combining the radicals in different ways but found that only one substance was produced. Their experiments conclusively show that no isomers of this type are actually formed by combining the radicals in different ways.

(b) Na_2bcx.—The cube and double tetrahedron formulas would require

[1] Ber., **7**, 1747 (1874); **8**, 233, 936 (1875).

[2] Compt. rend., **110**, 145 (1890); **112**, 725 (1891); Bull. soc. chim., [3] **4**, 104 (1890).

[3] J. chim. phys., **2**, 340 (1904).

[4] Proc. Chem. Soc., **7**, 39 (1891).

three isomers of this type of which one would be asymmetric and should therefore be capable of being resolved into optical isomers. According to the pyramid formula, two isomers would be possible, one being asymmetric and therefore divisible into optical enantiomorphs. The tetrahedral formula, however, suggests that no isomers would be formed—a conclusion which is borne out by numerous experiments on this subject. Though Schryver and Collie[1] obtained two crystalline modifications of dimethylethyl-isoamyl-ammonium chloroplatinate, the difference was due to dimorphism. H. O. Jones[2] made a systematic study of compounds of this type and found that one and the same compound was invariably formed even when the combination of the radicals was effected in the cold. Menschutkin,[3] Evans[4] and Wedekind[5] were equally unsuccessful in their attempts to prepare isomers of this type. *These experiments conclusively show that the negative radical has no influence in disturbing the symmetry of the ammonium molecule*, for in these compounds, though there were four different radicals of which the negative radical is one, no isomers were obtained. As regards Aschan's compounds,[6] their isomerism may readily be explained on any hypothesis of the constitution of ammonium compounds, as it is due to the absence of rotation of the two nitrogen atoms in the two rings, the rotation being prevented by the formation of the middle ring.[7]

(c) *Nabcdx*.—We now come to the consideration of compounds in which all the four radicals exclusive of the negative radical are different. The cube and the double tetrahedron formulas would yield as many as four and the pyramid formula three asymmetric isomers, each of which would be capable of being resolved into optical varieties. The single tetrahedron formula, on the other hand, would require only one compound, which being asymmetric would be capable of re-solution. Experiments fully confirm the anticipations of the single tetrahedron formula *and of no others*. As regards ordinary isomers the experiments of Jones, Pope and Harvey, B. K. Singh and others show that only one compound is produced in whichever order the alkyl groups are introduced. Then regarding optical isomers, from the time Le Bel who in 1891 was the first to resolve methylethyl-propyl-isobutyl-ammonium chloride into optical varieties down to our present day not more than two optical isomers of compounds of this type have been prepared, while the cube and double tetrahedron formulas would require as many as 8 and the pyramid formula 6 such varieties.

[1] *Proc. Chem. Soc.*, **7**, 39 (1891).
[2] *Trans. Chem. Soc.*, **83**, 1400 (1903).
[3] *Z. phys. Chem.*, **17**, 226 (1895).
[4] *Trans. Chem. Soc.*, **71**, 522 (1897).
[5] *Ber.*, **32**, 527 (1899).
[6] *Z. phys. Chem.*, **46**, 293 (1903).
[7] See *British Association Report*, **1904**, 192.

It will thus be seen that experiments have amply shown that so long as the four positive radicals in the ammonium group are not different, no isomers are actually formed and that when they are different, only two optical isomers are obtained. These experimental results are supported by none of the current configurations of nitrogen but only by the proposed single tetrahedron formula.

The difference between the existing and the proposed formulas as judged by the number of isomers of various classes of ammonium compounds predicted by them and actually obtained by experiment would be brought home more clearly by a perusal of the following table in which the number of such isomers is shown:

TABLE I.—ISOMERS ALLOWED BY SPACE FORMULAS.

	$Na_3x.$	$Na_2cx.$	$Nabcdx.$
Double tetrahedron	2	3^1	4^2
Cube	2	3^1	4^2
Pyramid	nil	2^1	3^2
{ Single tetrahedron	nil	nil	1^2
{ Experiment	nil	nil	1^2

It will be seen at once that of the four formulas the single tetrahedron alone conforms *invariably* to experimental results.

Trivalent Nitrogen.

The next problem that arises is to determine whether trivalent nitrogen has a plane or a space configuration and to examine how the passage from trivalence to pentavalence is effected. Evidences exist indicative of both kinds of configurations for trivalent nitrogen and so far as existing work is concerned it is difficult to choose definitely between them.

If the three bonds lie in one plane with nitrogen no isomerism is possible, but if they are bent along the edges of a tetrahedron, stereoisomeric compounds would be formed when the three radicals are different. So far as substituted amines are concerned, all previous attempts have hitherto failed to produce stereoisomeric derivatives. Le Bel[3] was the first to attempt the re-solution of these compounds but was unsuccessful. Kraft[4] attempted to resolve benzyl-ethylamine and p-tolyl-hydrazine by the fractional crystallization of their hydrogen tartrates, and Behrend and König[5] repeated Kraft's experiments and also attempted to resolve β-benzyl-hydroxylamine but were equally unsuccessful. Nor did Ladenburg[6] succeed in his experiments to resolve methylaniline, tetrahydro-

[1] One divisible into optical isomers.
[2] Each divisible into optical isomers.
[3] *Compt. rend.*, **112**, 11 (1891).
[4] *Ber.*, **23**, 2780 (1890).
[5] *Ann.*, **263**, 184 (1891); *Ber.*, **24**, 447c (1891).
[6] *Ber.*, **26**, 864 (1893).

quinoline and tetrahydro-pyridine. Kipping and Salway[1] combined active acid chlorides with various kinds of substituted amines, both inactive and active owing to the prior existence of an asymmetric carbon atom, but failed to get the calculated number of isomers which would correspond to the nitrogen atom if it had a space configuration. Reychler[2] and Jones and Millington[3] crystallized the salts of substituted hydrazines of the type

$$\genfrac{}{}{0pt}{}{a}{b}\!\!\diagdown\!\!N.NH_2$$ from non-hydroxylic solvents in order to avoid hydrolytic dissociation but failed to resolve them.

On the other hand, isomers of compounds containing nitrogen as a part of a ring have been successfully prepared. Ladenburg[4] obtained an isomer of coniine differing in rotatory power and some other properties, the difference being due to the two different positions of the hydrogen atom joined to nitrogen with respect to the propyl group. Ladenburg[5] offered a similar explanation for l-isostilbazoline which he obtained by heating artificial l-stilbazoline. The constitution of the two isomeric tropines and tropylamines discovered by Willstätter and Müller[6] has also been explained on the hypothesis of a space formula of trivalent nitrogen.

Hantzsch and Werner's well-known theory[7] for the explanation of the isomeric aldoximes and ketoximes which has been successfully adopted to explain the isomerism of diazo compounds, hydrazones and osazones, postulates a tetrahedron configuration of trivalent nitrogen in these compounds. The success with which this theory has explained the isomerism of these nitrogen compounds has been steadily maintained for the last quarter of a century and were it not for the fact that the re-solution of the simple tertiary amines containing different radicals has not been successfully accomplished, the space formula of trivalent nitrogen would have been universally applied.

Lastly the discovery of optical isomers of the amine oxides, which may be prepared by the *direct oxidation* of the amines, points almost unmistakably to a space configuration of the simple amines. Though in the amine oxides, the nitrogen is pentavalent, their isomerism appears to be *primarily due to the amine itself*, as divalent oxygen does not possess a space configuration. Even if it is contended that the amines have a plane configuration, owing to the fact that all attempts to resolve them have invariably failed, it must be conceded that during their oxidation

[1] *Trans. Chem. Soc.*, **85**, 438 (1904).

[2] *Bull. soc. chim.*, [3] **27**, 979 (1902).

[3] *Proc. Camb. Phil. Soc.*, **2**, 489 (1904).

[4] *Ber.*, **26**, 854 (1893).

[5] *Ibid.*, **37**, 3688 (1904).

[6] *Ibid.*, **29**, 936, 1636, 2228 (1896); **31**, 1212, 1655 (1898).

[7] *Ibid.*, **23**, 11 (1890).

the bonds of trivalent nitrogen are bent along the edges of a tetrahedron, *as otherwise no isomers of amine oxides would be possible.*

From a perusal of the existing work on the configuration of trivalent nitrogen, the author has come to the following conclusion: that in the amines nitrogen has a plane configuration, but in certain classes of organic compounds where nitrogen is directly linked to carbon (as enumerated by Hantzsch and Werner) and when trivalent nitrogen passes to pentavalence the three bonds of trivalent nitrogen become bent along the edges of a tetrahedron.

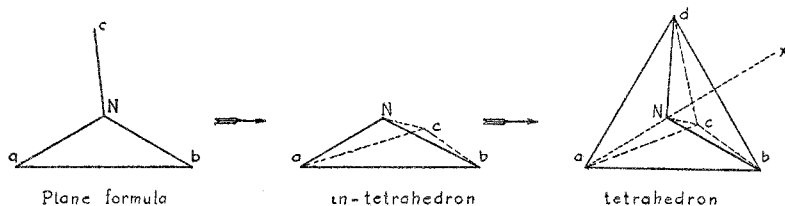Plane formula   in-tetrahedron   tetrahedron

Fig. 2.—Passage of nitrogen from trivalence to pentavalence.

In this connection an innovation in nomenclature is desirable. Hantzsch and Werner gave a tetrahedron constitution to trivalent nitrogen and supposed that it occupies its apex. Pentavalent nitrogen is also given here a tetrahedron configuration in which nitrogen forms the center. If the configurations of both the trivalent and pentavalent nitrogen be denoted by complete tetrahedra, the passage of trivalent to pentavalent nitrogen becomes difficult to understand. The author suggests that the configuration of trivalent nitrogen be represented by the inner tetrahedron while pentavalent nitrogen by the complete tetrahedron, the former being abbreviated as "*in*-tetrahedron" (see Fig. 2).

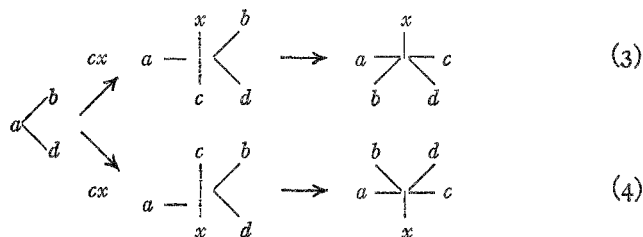### Passage of Trivalent to Pentavalent Nitrogen.

In the several existing configurations for pentavalent nitrogen the three valences of trivalent nitrogen are, in some, in the same plane with nitrogen, and in others bent at different angles. In the double tetrahedron formula the three original bonds lie in the same plane with nitrogen, but in both the cube and the pyramid formulas they are bent towards the different angles of the solid figure. In the case of the proposed single tetrahedron formula for pentavalent nitrogen, if the three valences of trivalent nitrogen are supposed originally to lie in the same plane with nitrogen, they become bent along the edges of the inner tetrahedron while passing from trivalence to pentavalence as explained above. If, on the other hand, trivalent nitrogen is supposed to have originally an inner tetrahedron configuration then during the passage of trivalence to pentavalence the three bonds retain their original positions.

It is necessary to mention here a paper by H. O. Jones,[1] who has attempted by an ingenious method to show that the pyramid configuration is capable of explanation of the existence of only two optical isomers of the compounds of the type $Nabcdx$ and the non-existence of any isomer of the compounds of the type Na_2bcx. The method by means of which he accomplished this has been ostensibly called "valence isomerism," which, as a matter of fact, appears to be nothing but an arbitrary shifting of radicals from one position to another. It is to be remembered that in the pyramid configuration the radical X, which occupies the apex, is in the same plane with two pairs of radicals, passing respectively through the opposite angles of the base of the pyramid. The four radicals at the four corners of the base are *symmetrically situated* with respect to X and there is no reason why there would be any want of equilibrium and why they should be arbitrarily shifted in order to establish equilibrium. It is therefore difficult to understand, as Jones believes, that there must be one arrangement more stable than the others, seeing that the positions of the four radicals are perfectly symmetrical.
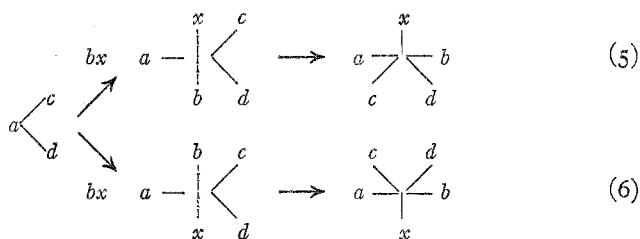
The way in which Jones seeks to show that there will be only two optical isomers of the type $Nabcdx$ and not 6 is open to serious objection. He represents the passage of trivalent to pentavalent nitrogen with dissimilar groups as follows:
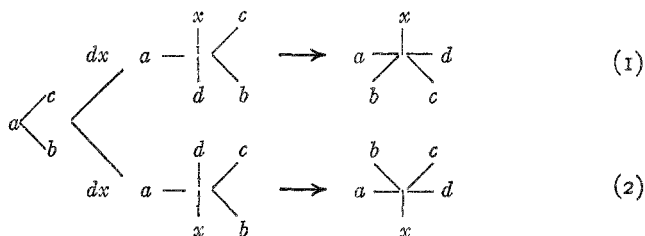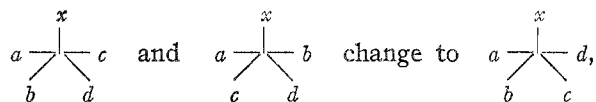

The relative positions of b and c are not altered and those of a and d alone are altered. Bearing this in mind, a, b, d with cx and a, c, d with bx would yield another two pairs of optical isomers, and not as Jones would have it the same pair of isomers as in the case of a, b, c and dx.

[1] *Trans. Chem. Soc.*, 87, 1728 (1905).

$$bx \quad a - \Big|\Big\langle \begin{smallmatrix} x & c \\ \\ b & d \end{smallmatrix} \quad \longrightarrow \quad a \overset{x}{\underset{c}{\diagup}}\overset{}{\underset{d}{\diagdown}} b \qquad (5)$$

$$bx \quad a - \Big|\Big\langle \begin{smallmatrix} b & c \\ \\ x & d \end{smallmatrix} \quad \longrightarrow \quad a \overset{c}{\diagdown}\underset{x}{\Big|}\overset{d}{\diagup} b \qquad (6)$$

The Figs. 1, 2, 3, 4, 5, and 6 are solid figures in plane projections. When once the groups a, b, c, d have found their respective places, as the case may be, they can never be supposed to shift from one position to another, *as owing to their symmetrical situation no force is acting upon them to disturb the equilibrium.* But Jones has given a further twist to the radicals and would suppose that both

$$a \overset{x}{\underset{b}{\diagup}}\overset{}{\underset{d}{\diagdown}} c \quad \text{and} \quad a \overset{x}{\underset{c}{\diagup}}\overset{}{\underset{d}{\diagdown}} b \quad \text{change to} \quad a \overset{x}{\underset{b}{\diagup}}\overset{}{\underset{c}{\diagdown}} d,$$

a supposition for which there is absolutely no justification. Similarly there is no justification to dispense with the isomers of the Na_2bcx, as has been done by Jones, by shifting the positions of the groups. It would appear that Jones himself might have been aware later on of the absurdity of his own earlier arguments, though he has not acknowledged it, as in 1912 Jones and Dunlop[1] tentatively suggested some sort of tetrahedric grouping of ammonium compounds.[2]

The Amine Oxides.

The discovery by Meisenheimer that the amine oxides exist in two optical isomers is an important factor in determining the configuration of the nitrogen atom. *None of the existing configurations give any symmetrical representation of the isomeric amine oxides.* The amine oxides have been obtained by the direct oxidation of the amines by hydrogen peroxide or Caro's acid[3] and therefore the oxygen atom is combined with nitrogen by the fifth and one of the four remaining bonds, possibly the fourth bond, as in the amines the three bonds are already engaged. Now in the double tetrahedron formula, the bonds 1, 2, 3 being in the same plane, the double bond formed by 4 and 5 would make the configuration of the amine oxides a plane one which will not yield optical isomers. If, however, the bond 5 and one of the three bonds 1, 2, 3 from the double bond for oxygen, the configuration would be a space representation but a highly unsymmetrical one. In the cube formula, whether the fifth bond

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[1] *Trans. Chem. Soc.*, **101**, 1751 (1912).

[2] It is curious that J. B. Cohen, without examining the soundness of Jones' arguments, has incorporated them in his well-known text-book on organic chemistry (Vol. I).

[3] Meisenheimer, *Ann.*, **385**, 117 (1911).

makes a double bond with any of the remaining four bonds, the resultant figure would be unsymmetrical. In the pyramid formula if the fifth bond makes the double bond with any of the remaining four, the resultant figure would still be somewhat unsymmetrical as there would be a double bond at one corner of the square bases, but *a graver objection would arise, viz., that the resultant configuration would require three asymmetric isomers, each capable of being resolved into enantiomorphs*, while as a matter of fact only two optically isomeric amine oxides have ever been prepared. Even if the double bond be at the apex of the pyramid, as Jones suggested, the resulting figure would be an unsymmetrical one. The isomerism as well as the method of preparation of the amine oxides are, however, very satisfactorily explained by the tetrahedron formula as shown in Fig. 3. In fact the isomerism of the amine oxides as well as their preparation by the direct oxidation of the amines are crucial proofs of the validity of the tetrahedron configuration of nitrogen.
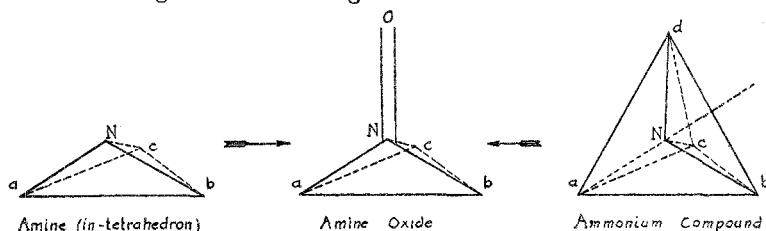

Fig. 3.

Combination of Asymmetric Nitrogen with Asymmetric Carbon and Nitrogen Atoms.

We would now proceed to discuss the existence of isomers obtained by the combination of one asymmetric nitrogen and one such carbon atom, and also of two such nitrogen atoms.

Asymmetric Carbon and Nitrogen Atoms.

According to the proposed form of the single tetrahedron formula the combination of one asymmetric carbon with one such nitrogen atom would yield different isomers according as the combination takes place either through the fifth or one of the remaining four bonds. If the combination takes place through the fifth bond, as in the case of combination with active acids such as camphorsulfuric acid, four isomers would be obtained which, however, would all be optically active, DBDA, IBIA, IBDA, DBIA, two of them being dextro-rotatory and two levo-rotatory. A complete series of these four kinds of isomers has been actually obtained by Harvey,[1] who has successfully resolved benzyl-phenyl-allyl-methyl-ammonium camphorsulfonates into two pairs of dextro and levo varieties.

If, however the combination takes place through one of the four negative

[1] *Trans. Chem. Soc.*, **87**, 1481 (1905).

bonds of nitrogen, as in the case of ammonium compounds containing both an asymmetric nitrogen as well as an asymmetric carbon atom, compounds will be produced of the following configurations,

$$N + C + \qquad N - C - \qquad N - C + \qquad N + C -,$$
$$(1) \qquad\qquad (2) \qquad\qquad (3) \qquad\qquad (4)$$

plus and minus signs representing dextro and levo, respectively. The first two compounds will be dextro and levo respectively and if the dextro or levo rotation due to the asymmetric carbon atom is not equal respectively to the levo or dextro rotation due to the asymmetric nitrogen atom, then two more varieties will be produced (3 and 4), one of which will be dextro and the other levo.

So far as experimental work is concerned, not much work has been done on this subject and satisfactory results are wanting. Kipping and his co-workers[1] obtained four isomers of the compounds of the type NRH X in which both R and X contain one asymmetric carbon atom each. Kipping[2] at first sought to explain the isomerism of these compounds with reference to the pentavalent nitrogen atoms, but his explanation was on the face of it wrong, as nitrogen compounds with three hydrogen atoms combined with the nitrogen atom cannot yield any isomers due to the presence of the nitrogen atom itself. Kipping rectified his earlier mistake in a subsequent paper,[3] in which he showed that the isomerism noticed by him was due to the isomerides of the acid constituent of the salts examined. Jones[4] has studied the isomerism produced by the combination of methyl-*l*-amylamine with alkyl iodides, and though his experiments are not conclusive, he found that in the formation of an asymmetric nitrogen atom in a compound containing an asymmetric carbon atom, two compounds are formed which differ in melting point, solubility and in rotatory power and which are readily transformed one into the other. Scholtz[5] obtained two isomers of coniinium derivatives, when the nitrogen atom in *d*-coniine was made asymmetric. Wedekind and Ney[6] obtained two stereoisomers by the interaction of 2-propyl-tetrahedro-isoquinoline with *l*-menthyl-iodo-acetate, one containing a dextro and the other a levo ammonium complex respectively. It is to be remembered that the single tetrahedron formula yields the *smallest* number of these isomers, while the existing configurations of pentavalent nitrogen would require a much larger number of isomers, which, being non-existent in the case of the simple ammonium derivatives containing one asymmetric nitrogen atom,

[1] *Trans. Chem. Soc.*, **77**, 861 (1900); **79**, 430 (1901); **83**, 918, 937 (1903).

[2] *Ibid.*, **77**, 867 (1900); **79**, 430 (1901); **83**, 948 (1903).

[3] *Trans. Chem. Soc.*, **87**, 628 (1905).

[4] *Ibid.*, **87**, 139 (1905).

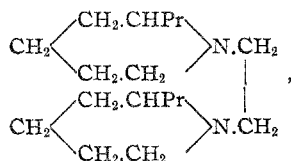[5] *Ber.*, **37**, 3627 (1904).

[6] *Ibid.*, **42**, 2138 (1909).

cannot certainly exist in the case of compounds containing asymmetric carbon and nitrogen atoms. Further work on this subject has been done by Wedekind and Ney[1] and Wedekind and Bandau[2] when the number of isomers obtained corresponds to two optical isomers for one pentavalent asymmetric nitrogen atom when combined with asymmetric carbon atoms.

Two Asymmetric Nitrogen Atoms.

When two asymmetric nitrogen atoms would combine, two active and two inactive isomers (one dextro, one levo, one inactive by external compensation, and one inactive by internal compensation) should be produced as in the case of tartaric acid. It is to be remembered that according to the double tetrahedron and cube formulas of nitrogen as many as 8 optically active isomers and according to the pyramid configuration 6 such isomers are obtained with one asymmetric nitrogen atom only, and therefore in the case of two such nitrogen atoms, the number of probable optically active isomers would be, according to the existing formulas of nitrogen, absurdly large. So far as experimental evidence goes, no simple cases of this type of di-ammonium compounds have been studied, as compounds containing two pentavalent nitrogen atoms joined together are not stable. Wedekind,[3] however, has obtained two isomers of ethyl-2-ethylene-bistetrahydro-isoquinolinium-2-acetate iodide,

$$C_2H_4\left[NI(CH_2.COOEt)\diagdown\begin{matrix}CH_2.C_6H_4\\ |\\ CH_2.CH_2\end{matrix}\right]_2,$$

but the compounds obtained were not resolved into optical isomers. In 1910 Wedekind[4] obtained two isomers of trimethylene-bis-(phenyl-methyl-ethyl-ammonium iodide), $CH_2(CH_2.NMeEtPhI)_2$, but failed to resolve either into optically active forms. Recently Wedekind and Ney[5] have attempted to obtain the possible isomers of ethylene-bis-d-coniine,

$$CH_2\diagdown\begin{matrix}CH_2.CHPr\\ CH_2.CH_2\end{matrix}\diagup N.CH_2$$
$$CH_2\diagdown\begin{matrix}CH_2.CHPr\\ CH_2.CH_2\end{matrix}\diagup N.CH_2$$

which contain in addition to two nitrogen atoms two asymmetric carbon atoms. When the nitrogen atoms were made pentavalent and asymmetric by combination with benzyl iodide, two isomers were obtained. The more abundant α-isomeride decomposed at 130° and had $[\alpha]_D +$ 40.42°, while the β-isomeride decomposed at 214° and had $[\alpha]_D + 15.42°$
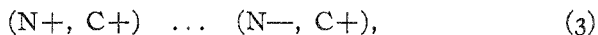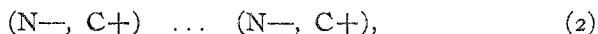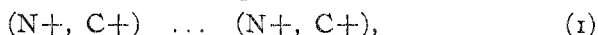
[1] *Ber.*, **45**, 1289 (1912).

[2] *Ann.*, **401**, 326 (1913); **404**, 322 (1914).

[3] *Ber.*, **36**, 1163 (1903).

[4] *Ibid.*, **43**, 2707 (1910).

[5] *Ibid.*, **46**, 1895 (1913).

in methyl alcohol solutions. From theoretical considerations three isom-
erides would be possible with d-coniine represented below,

$$(N+, C+) \quad \ldots \quad (N+, C+), \qquad\qquad (1)$$
$$(N-, C+) \quad \ldots \quad (N-, C+), \qquad\qquad (2)$$
$$(N+, C+) \quad \ldots \quad (N-, C+), \qquad\qquad (3)$$

plus and minus sign denoting dextro and levo respectively. The α- and
β-isomerides are supposed to have the first two structures, while Wedekind
and Ney supposed that the third isomeride represented by the last constitu-
tion being too unstable passed into the first variety, which, as a matter
of fact, formed the bulk of the crystals obtained. This work fully con-
firms the capacity of a di-quaternary ammonium compound to exist in
different optical isomers.

It will be necessary to refer here to a paper by Singh,[1] in which he
points out that (1) when substituted hydrazines, $\overset{a}{\underset{b}{>}}N.N\overset{a}{\underset{b}{<}}$, are con-
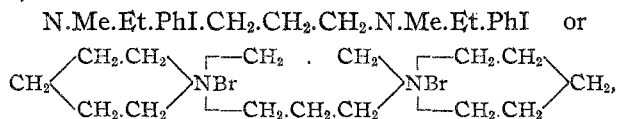verted into quaternary compounds, monoquaternary and not diquater-
nary azonium compounds are formed and only one nitrogen atom is
made pentavalent, the other remaining trivalent, but (2) when a carbon
chain such as one or more CH_2 groups intervene between the two tri-
valent nitrogen atoms, both of them become pentavalent. He ascribes
this phenomenon to steric hindrance and attempts to deduce his conclu-
sions from the pyramid formula for pentavalent nitrogen.

This phenomenon is, however, easily explained by the very natural
supposition that the combination $N\!\!=\!\!N$ is much more stable than
$N\!\!\equiv\!\!N$, owing to the much simpler constitution of trivalent nitrogen,
so that when the two nitrogen atoms in $N\!\!=\!\!N$ pass on to pentavalence
the group passes on $N\!\!\equiv\!\!N =$ and not so far as $N\!\!\equiv\!\!N$, especially when
heavy radicals are attached. The ability of forming chains of two or
more atoms joined together is peculiar to carbon and is *not shared to any
great extent by any other element*. In fact it is owing to this unique prop-
erty of carbon, as Kekulé pointed out, that the existence of a separate
chemistry of carbon compounds in the shape of organic chemistry has
been possible. To ascribe to steric hindrance the inability of pentavalent
nitrogen to form chains of two or more atoms joined together, as supposed
by Singh, is to misunderstand the very basis of combination of elements,
as his conclusion, if applied to all known elements excepting carbon, would
lead us to the absurd conclusion that their inability to form chains of
atoms is due to steric hindrance consequent on the pyramid structures of
their atoms.

As regards the second point, Singh fails to interpret correctly the mean-
ing of the intervention of carbon chains between two pentavalent nitrogen

[1] *Trans. Chem. Soc.*, **109**, 780 (1916).

atoms. There is absolutely no necessity for supposing that "the steric hindrance due to the disposition of the bonds which is present in the case of two directly linked nitrogen atoms is absent here," for in such cases as, for example,

$$N.Me.Et.PhI.CH_2.CH_2.CH_2.N.Me.Et.PhI \quad or$$

$$CH_2 \Big\langle {CH_2.CH_2 \atop CH_2.CH_2} \Big\rangle NBr {\lceil -CH_2 \atop \lfloor -CH_2.CH_2.CH_2} \cdot {CH_2 \atop } \Big\langle {\lceil -CH_2.CH_2 \atop \lfloor -CH_2.CH_2} \Big\rangle CH_2,$$

we have to deal with two *single and separate* pentavalent nitrogen atoms and not to a chain of nitrogen atoms joined together so that no question of steric hindrance or its negative ever arises here. *Chains* of two or more pentavalent nitrogen atoms are difficult of formation[1] but there is obviously no bar to the existence of *single* pentavalent nitrogen atoms joined to carbon or any other element.

Cyclic Ammonium Compounds.

Jones,[2] and Buckney and Jones[3] have studied the isomerism of substituted and pyridinium (I) and (II), quinolinium (III) and tetrahydroquinolium compounds (IV) which they thought "according to current views of the
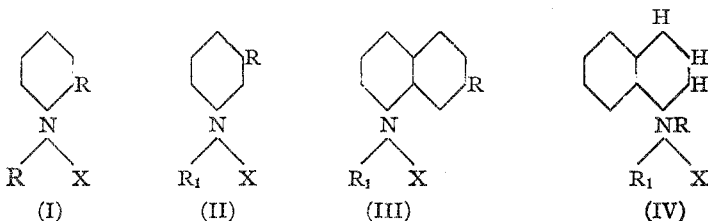
configuration of the nitrogen atom should all exist in optically active forms." But as a result of their experiments it has been found that pyridinium and quinolinium compounds could not by any means be resolved into active isomers while tetrahydro-quinolinium derivatives yield such isomers. Jones[2] admitted that "the absence of activity in these compounds is inexplicable on the current views as to their constitution," which, however, may very readily be explained if the tetrahedron con-

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[1] It must not, however, be understood that compounds containing two pentavalent nitrogen atoms joined together do not exist at all. Instances of such compounds are not only the dihydrochlorides of hydrazine, methylhydrazine, ethylhydrazine and As-dimethylhydrazine mentioned by Singh but also the dihydrochloride of a hydrazine derivative containing large-sized radicals such as the dihydrochloride of diphenyldibenzylhydrazine ($C_7H_7.NPh.NPh.C_7H_7$) (Franzen and Zimmermann, *Ber.*, 39, 2566–9 (1906)) which crystallizes in white needles and melts at 215.5°. Such compounds are, of course, not very stable owing to the weakness of the combination of two pentavalent nitrogen atoms.

[2] *Trans. Chem. Soc.*, 83, 1405 (1903).

[3] *Ibid.*, 91, 1821 (1907).

figuration of nitrogen be accepted. In the tetrahedron formula, if the double bond is created by the fifth and one of the four remaining bonds as in the amine oxides, the tetrahedron remains intact, but in the pyridinium and quinolinium compounds the fifth bond is occupied by a negative radical and the double bond between the carbon and nitrogen is necessarily occasioned by two of the remaining four bonds, and the tetrahedron formula ceases to exist in a symmetrical form. In the case of the tetrahydro-quinolinium compounds such as alkyl carolinium salts the double bond between the carbon and nitrogen has vanished and hence the existence of optical isomers of these compounds. The tetrahedron formula suggests that when a pentavalent nitrogen is joined with carbon by a double bond of which the fifth positive bond is not one, isomers would not be possible, but if in any compound the fifth bond constitutes one of the double bonds, as in the amine oxides, isomers would exist. As a matter of fact no compounds containing a double bond between carbon and pentavalent nitrogen with a negative radical have as yet been resolved.

Conclusion.

It would appear that the following facts, *viz.*,

(1) The discovery of isomers of the type [$Me_3N.OR$]OR_1 and [$Me_3N.-OR_1$]OR showing that the fifth bond is non-equivalent to the other four bonds of nitrogen;

(2) The non-existence of any isomers of the type Na_2bcx (in which there are four different radicals of which x is one) showing that the negative radical has no influence in the formation of isomers and therefore acts in the secondary sphere;

(3) The non-existence of any isomers of the type Na_3bx and Na_2bcx and the existence of *only two* optical isomers of the type $Nabcdx$;

(4) The existence of only four optical isomers of compounds containing one asymmetric carbon and one such nitrogen atom or two such nitrogen atoms and the non-existence of the absurdly large number of isomers predicted by the current formulas;

(5) The non-existence of pyridinium and quinolinium compounds and the existence of isomers of tetrahydro-quinolinium compounds are explained on no other hypothesis so satisfactorily as on that of the single tetrahedral representation of pentavalent nitrogen. The passage of trivalent to pentavalent nitrogen is also satisfactorily explained. The single tetrahedron formula therefore is the most appropriate space representation of pentavalent nitrogen and the "*in*-tetrahedron" formula of trivalent nitrogen.

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