The Logical Structure of Organic Chemistry and the Empirical Adequacy of the Classical Concept of the Molecule

OCHIAI Hirofumi

Abstract: Organic chemistry is based on the classical concept of the molecule, which postulates that molecules have distinct physical shapes, sizes, structures, and are composed of atoms and chemical bonds. Although this concept is not consistent in some respects with what is suggested by quantum mechanics, it reveals a novel property of molecules: molecules are designable. Thanks to this property we can synthesize chemical compounds as we desire with precise control of molecular transformations. Organic synthesis, especially the highly selective synthesis of chiral substances, demonstrates that this concept is empirically adequate. It is also shown that organic chemistry is rational and autonomous as a science with regard to the Method of Analysis and Synthesis.

Keywords: *Empirical adequacy, molecular structure, molecular design, the Method of Analysis and Synthesis, reduction of organic chemistry to quantum mechanics.*

1. Introduction

The molecules every student encounters in standard chemistry textbooks have distinct physical shapes, sizes, and structures. These molecules are composed of atoms, chemical bonds, functional groups, *etc.*, and represented by mechanical models; a typical one is the CPK model. Chemists say, for instance, that the steric hindrance of the bulky tert-butyl group hampers the backside attack of nucleophiles, as if they had witnessed what is going on in a flask. The concept that underlies this image is referred to as the classical concept of the molecule in the following sections. Although it has been the basis of chemists' reasoning about microscopic events, the adequacy of the concept is not without disputes. For instance, a quantum mechanical treatment of molecules shows that electrons in molecules are not localized in chemical bonds, but extend over the entire space. It suggests that the classical molecu-

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lar model as is described above has no physical reality and cannot be vindicated mathematically.[1] On the other hand, a great variety of chemicals are being produced in laboratories every minute all over the world. These chemicals, whether naturally occurring or not, are all designed by means of this concept. Among them are biologically active substances with dozens of chiral atoms in a single molecule. If this concept of the molecule does not represent microscopic objects we think of, and if our inference thereof is irrelevant to what is happening, to what on earth can we credit these accomplishments? In the present paper I will defend the classical concept of the molecule by showing that it represents the reality of the molecule with respect to the chemical transformations. The point of this argument is that chemical synthesis plays an important role in showing that organic chemistry based on this concept is a scientific system with regard to the Method of Analysis and Synthesis. Finally I will discuss whether or not chemistry is reducible to or supervenes on physics. Although this is a very important philosophical question in itself, it is becoming an ever more urgent issue, because it is connected with the now threatened sense of coherence and identity of chemistry. Without big questions such as 'What is life?' or 'How did the universe begin?', chemistry has suffered from scant public attention in recent years. This is apparent, for instance, from the fact that many university chemistry departments are being closed and the number of students majoring in chemistry is dwindling. Many important questions are being framed as a 'chemical' aspect of another discipline, as *Nature* has reported.[2] Is chemistry a form of engineering, or one of the applied areas of physics? In order to address to these questions, the philosophical foundations of chemistry, especially of organic chemistry, must be examined, for the latter is one of the most characteristic domains of this science.

2. Theories as a measure of the world

For anything to be perceived as existing, it must have dimensions on a certain scale. Measurement is therefore essential for perceiving the world. A scientific theory offers a kind of scale with which we measure the natural world. It provides structure as well as dimension to what seems otherwise chaotic. It is just like a perspective which makes things nearby seem big and things faraway seem small, and eventually brings depth into sight. In other words, we cannot see objects as they might exist in themselves, but see them as they are measured, for instance, by Newtonian mechanics. The apparent motion of planets is made true motion in terms of Absolute Space and Absolute Time (Friedmann 1992, pp. 137-142). The measurement in this sense is to provide the way we see, or to interpret what is there or is not there as what is to be seen from the theoretical point of view. The true motion of planets, or the interpretation of phenomena, should not only be consistent with, but better able to elucidate experiences so far accumulated, so as to make the theory regarded as empirically adequate. The meaning of 'empirical adequacy' in this paper is according to van Fraassen (1980, pp. 12, 42-69). That is, "a theory is empirically adequate exactly if what it says about the observable things and events in this world is true, exactly if it saves the phenomena". "Such a theory has at least one model that all the actual phenomena fit inside. For instance, when Newton claims empirical adequacy for his theory, he is claiming that his theory has some model such that all actual appearances, throughout the history of the universe, and whether in fact observed or not, are identifiable with motions in that model."[3] If such is the case, postulates of the theory, for instance, Absolute Space and Absolute Time or the model of the solar system, would also acquire empirical adequacy.

In the case of quantum mechanics, line spectra are explained as the transitions between quantized states of energy that derive from the solutions to the Schrödinger wave equations for the relevant systems. This interpretation was so successful at solving riddles about photo-electron phenomena that the quantum theory has become accepted as adequate. Actually it went so far as to cause wave functions or atomic orbitals to be taken as concrete entities, though they are nothing but the basis sets with which wave functions are expanded. In other words, a set of orbitals counts as a form of coordinate system, and therefore, as sometimes pointed out, assignment of electrons to specific orbitals has no physical significance (Scerri 2008, pp. 200-213). Of some interest in this regard is that we take Newtonian space and time as realistic, and do not get criticized for it, whereas they also are nothing else than a form of coordinate system against which other possibilities have been raised.[4] The truth is that we have never imagined looking at things and events through other measures than Newtonian mechanics, because the notions of Absolute Space, which is absolute in its nature, without relation to anything external, remains always similar and immovable, and of Absolute Time, which is absolute, true, and mathematical time, of itself, and from its own nature, flows equally without relation to anything, fit our feeling of daily experience.

The above argument suggests that whether or not we accept certain theoretical postulates as adequate depends on to what extent they succeed in explaining phenomena and how they appeal to our intuition. The latter depends partly on the nature of our experiences and partly on the aims of theories. The notion of space and time depends on the theoretical view of the object. So does the notion of wave function or of atomic orbital. A point I want to emphasize through these arguments is that we should focus our attention on theoretical rationality, or rationality of knowledge rather than rationality of belief, in order to evade the fruitless opposition between realism and empiricism. Such an attitude would be desirable at least to the extent that arguments are concerned with objects that belong to the world outside of our experience. They include an atom, a molecule, or a concept like chemical bond that needs to be defined theoretically to be an object of investigation at all.

Chemists understand the world through chemical phenomena that appear as a vast range of chemical species and transformations. The value of chemical theories and concepts lies in their serving as a measure for interpreting those phenomena. How they appear to us, or whether or not they exist at all in the chemical sense, depends on what purposes or interests we have, and accordingly, what kinds of theories or concepts we conceive to solve the problems formulated in terms of them. For instance, concepts like acid and base, oxidation and reduction, or electronegativity, pH, and others are among typical examples of chemical measure with which we get insight into chemical phenomena. Therefore, before we examine the empirical adequacy of the classical concept of the molecule, it will be reasonable to elucidate the logical structure of organic chemistry, for the classical concept of the molecule is among the concepts proposed for making abstract theories of organic chemistry concrete by means of more or less familiar materials.

3. The logical structure of organic chemistry

Organic chemistry is a science of molecular transformations. The recent development of synthetic chemistry has provided molecules, such as those found in naturally occurring substances, which have as many as dozens of chiral atoms in a single molecule. Although such accomplishments owe much to advanced analytical techniques as well as to the expansion of feasible reactions, a point of critical importance to be noted here is that the relation between molecular structure and chemical reactivity has been so fully set forth that it has become possible to design and control molecular events with great accuracy. In fact, since the early nineteenth century the molecule has been regarded as the object of manipulation and, by the late nineteenth century, it had become the object of design as well. As is described in the next section, this is supposed to be the consequence of radical theory first advocated by Berzelius in the 1830s. The radical theory claims that "all substances, organic and inorganic, are dualistic in nature and contain components held together by the forces of electricity" (Ramberg 2003, pp. 17-20). If molecules consist of discrete components, to determine the pieces that constitute the molecule would serve as the endpoint of chemical investigations. This mechanical view of the molecule, or in other words, the attitude of inferring microscopic objects by analogy with macroscopic ones, characterizes the logical structure of organic chemistry.[5]

In the theories of organic chemistry, and in the electronic theory in particular, chemical transformations are taken to be the mechanical displacement of atom(s) together with the accompanied transfer of electrons. In other words, the chemical reaction is the recombination of chemical bonds. The words we use to explain reaction mechanisms such as ‘addition’ or ‘elimination’, and a notation such as curved arrows to denote the transfer of paired electrons, reflect the nature of this explanatory system. The logical structure of organic chemistry can be read in standard as well as advanced chemistry textbooks which put stress on reaction mechanisms (see *e.g.* Hendrickson, Cram & Hammond 1970, Ingold 1953). No attempt was made to specify the physical nature of forces holding atoms, but the binding power has been assumed to be an intrinsic property of each chemical element. The chemical reactivity of the molecule is explained by means of the electronegativity, the valence, the electronic charge, or whatever is intrinsic to an element, rather than state functions like chemical potential. The belief that chemical properties of substances should be ascribed to the constituent elements might be traced beyond chemical atomism. Lavoisier took a substance that is not subject to further resolution by virtue of chemical analysis to be a simple substance made of a single element (Rocke 1984, pp. 4-7; Bensaude-Vincent & Simon 2012, pp. 156-161). Kekulé as well had the belief that rational formulas would derive from the elements themselves, for the number of atoms united with one atom of an element is dependent on the basicity (that is, the valency) of the element (Ramberg 2003, p. 21).

The fact that we can chemically synthesize substances according to the design of the molecule suggests that insights based on the mechanical understanding of the molecule are not irrelevant. Where do these insights come from? The clue to answer this question will be found in the practice and the habit of thought that is closely tied to the art learned in chemical laboratories. As Rocke pointed out in his famous book, cognitive activity in chemistry cannot be separated from craft skills and tacit knowledge. This is in remarkable contrast to physics, which is abstract, and firmly based on a mathematical foundation (Rocke 1993, p. 248). Inferring invisible microscopic events from macroscopic observables, sometimes referred to as ‘transdiction’, has been habitual with chemists since chemical atomism arose in the nineteenth century.[6] An excellent memory accompanied by visual imagination was a virtual necessity for understanding, and so controlling reactions as well as dealing with thousands of compounds regularly encountered in chemical laboratories. Handling mechanical models would be more favorable for most chemists, especially for organic chemists, than calculating abstract state functions by using higher mathematics.

It was fortunate for chemists that most of the chemical reactions investigated thus far are not concerted, but ionic in character, and associated with the total energy of the molecule. This implies that the localized-bond principle holds good; that is to say, such chemical reactions can be described by means of the collective properties such as bond dissociation energy, bond angles, bond lengths, *etc.*, which depend on the total energy of the molecule (Dewar 1969, pp. 135-143). This underlies the mechanical modeling of the molecule.[7] Also, this will be another answer to the question posed by Vemulapalli, and the reason why "chemists have not tried to justify the assumption of bonds between only a limited number of atom pairs in a molecule", though most of the once familiar words like 'affinity' and 'valence' were replaced by 'orbital overlap', 'sigma' and 'pi' bonds (Vemulapalli 2006, pp. 191-204).[8] On the other hand, one-electron properties such as absorption spectra are not additive of the local properties, and require true molecular orbitals.

The system of explanation in organic chemistry comprises three major theories, that is, the electronic theory, the valence bond theory, and the molecular orbital theory, of which the first has long served as a logical skeleton together with the classical concept of the molecule. Although quantum mechanics could have plunged us into a reconsideration of this viewpoint, it was instead assimilated through ingenious interpretations of abstract mathematical functions. That is to say, while quantum mechanics suggests that electrons in molecules are not localized between adjacent atoms, but extend over the entire space, the valence bond theory takes each covalent bond as a two-center-two-orbital system (or in other words, diatomic molecule fragment), assuming that overlap integrals between remote atoms are negligible. A molecule is represented as a sum of these two-center-two-orbital systems. By virtue of this method, concepts of chemical significance such as tetrahedral carbon can be represented with electron orbitals and hybridization. Although the hybridization of orbitals is a mathematical model like orbitals themselves, it is not without proper mathematical basis; in the case of degeneracy, the total energy of the molecule remains intact by displacing a basis set of wave functions with their linear combinations. Hybridization enhances the explanatory power of organic chemistry by affording empirical contents to mathematical wave functions as well as by visualizing the underlying interactions between them. Admittedly the localized bond thus generated is artificial. But every description is artificial anyway.[9] Hence, a point of critical importance is that it should be causally relevant to the fact for which an explanation is requested, though whether or not an explanation is relevant is context-dependent as is often pointed out (van Fraassen 1980, pp. 126-130).

It is often said that the phase of wave function has no physical significance, because the probabilities for measurement outcomes are the same. Actually, it has chemical significance as is amply exemplified, for instance, by orbital interactions in pericyclic reactions (Woodward & Hoffmann 1969) and in general in the frontier orbital theory discussed below. The point is not simply that what one sees depends on how one looks, but rather that one constructs what one sees in terms of one's interests and purposes of investigation. This is true even in cases where the objects of observation are given to an observer as visible phenomena or tangible physical substances. For instance, we see the pattern made with iron powders spread over a magnetic field as magnetic lines of force.

The frontier orbital theory is another illustration that the chemical implications of molecular orbitals are delineated from the viewpoint of organic chemistry. In other words, it tells us why the wave function is something more than the mathematical function. When the highest occupied molecular orbital, the HOMO, of one molecule and the lowest unoccupied molecular orbital, the LUMO, of another coincide in symmetry with each other, the reaction is allowed to proceed, and the formation of a new bond from both orbitals occurs. The frontier orbital theory directs attention to the wave functions that are relevant to the bond formation, where the symmetry of wave functions is the dominant factor to determine the reaction courses. Thus, the phase of wave functions has chemical significance. The HOMO-LUMO interaction might be taken as another picture of donor-acceptor interaction in the electronic theory (Inagaki 1975). Showing that the frontier molecular orbitals are relevant to the formation of chemical bonds, the frontier orbital theory assimilates notions of molecular orbital theory into the conceptual framework of organic chemistry.

With regard to CH_4, some binding force between atoms, whatever we call it, must be operating and four hydrogen atoms are combined equivalently with one carbon atom. Since we cannot know molecules as they are in themselves, nor observe the force operating among them, what we believe to know about them is actually what is known through models that are constructed due to our interests and purposes of investigation. Our knowledge of such entities can be at most empirically adequate. Hence theoretical entities or constructive concepts like the molecule should be linked with observable things and events. To put it the other way round, if the link between theoretical entities and the observables are established by the alleged rules of correspondence, as will be discussed in Section 5, those entities can be regarded as relevant to the objects of theoretical explanation.[10] When a chemist says CH_4 has a tetrahedral structure because of sp^3 hybridization, for instance, the empirical knowledge of chemical properties is superimposed upon the notion of orbitals. The wave function or the orbital in chemistry is something more than the physicists' orbitals, because they need nothing but mathematical functions, and because we need something with which to represent our chemical intuition.[11]

This interpretation of orbitals may be taken as the naturalistic view of chemical concepts or models. As Scerri points out, the normative view of one-electron orbitals often results in excluding chemical interpretation as it is strictly inconsistent with quantum mechanics (Scerri 2006). On the contrary, the naturalistic view connotes a paradox, which he calls a dual view of elements; that is, to regard elements as unobservable 'basic substances' on one hand and observable 'simple substances' on the other. To adopt both views simultaneously does not lead to a serious dilemma to be resolved, but can be regarded as a paradox to be embraced for what it is. Such a generous view of chemical concepts becomes possible on the recognition that "it is models, rather than high-level theories", that scientists appeal to. "No amount of nit-picking about whether or not they (orbitals) exist physically will have the slightest impact" (*ibid.*) on their use in teaching of chemistry or research.

4. The classical concept of the molecule

Woolley, in his famous paper titled 'Must a Molecule Have a Shape?', has given a clear-cut description of the conditions under which quantum mechanical or classical molecular models hold good (Woolley 1978). That is to say, an isolated atom or molecule in a true stationary state has no extension in space or time (because the configuration space used in quantum theory derives from an abstract Hilbert space and a theory of space needs to be based on the evolution in time of interacting micro-systems), so that "it makes no sense to talk about the size or shape of an atom or molecule". Such a situation seems fictitious, but it is partly realized in diluted gas or the molecular beam of a small molecule. In contrast, in time-dependent quantum states of a many-body system with Coulombic interactions, the size and shape of an individual atom or molecule (that is, molecular structure) is 'created'. In quantum chemistry, the idea of molecular structure is associated with the Born-Oppenheimer approximation in which electronic and nuclear motions are separated and molecular structure is given as a minimum of the energy surface that is a function of the nuclear positions. Hence, it is of critical importance to differentiate 'quantum structure' from 'classical molecular structure' (Woolley 1986). Then, to the extreme of a many-body system with strong interactions, in liquids and solids "the notion of structure is the essential concept that states the answer without knowing how to solve the [many-body] problem".

There have been reported a number of arguments concerning the limitations of the classical molecular model. Most of them are based on the quantum mechanical treatment of molecules and point out how it fails to depict (the electronic states of) molecules. However, those arguments do not take account of the roles the classical molecular model plays in organic chemistry. Chemistry creates its object as Berthelot wrote in 1860 (Rocke 2001, p. 254). A science of creation is based on analogies that relate molecules with macroscopic substances, because such analogies promote transdiction and make it possible to see molecules as an object of manipulation. In addition, an abstract notion like valence should be interpreted in less abstract or more familiar materials. 'Chemical bond' is an illustration of such an interpretation or model, which gives a concrete form to a theoretical idea like molecular structure (Russell 1971, pp. 90-91). It is this kind of interpretation through which theoretical ideas get correspondence with experimental facts. We say, for instance, a cyclic molecule gets opened by the cleavage of such and such chemical bonds. In fact we know by direct experience the chemical properties of substances before and after the transformation as well as the operations we must perform for the transformation to proceed. By relating such empirical contents to the postulated structures of molecules, our knowledge of microscopic entities has made progress and has been established. The theoretical character of organic chemistry is evincible in the classical concept of the molecule; it postulates that (1) the molecule has a distinct structure that is composed of atoms and chemical bonds, and (2) each part of the molecule is subject to chemical transformations rather independently of other parts of the molecule. The latter postulate reflects the empirical knowledge that most of the chemical reactions are explicable with collective properties of the molecule. It is the concept of the molecule every student encounters in standard chemistry textbooks, with which they shape their knowledge of microscopic entities. Such a molecule has a distinct physical shape and size and can be represented with mechanical models. It is constituted by the sequential connection and spatial arrangement of atoms, which are determined by virtue of valences of elements; that is, the numerical regularity related to the capacity of an element to combine with other elements, and the geometry of atomic combinations.

The historical development of the classical concept of the molecule deserves some comment here. The recognition that molecules have structures seems to have been gradually formed with the rise of the radical theory in the 1830s. Then, through the controversies about the constitution of matter between radical theorists and type theorists in the years of the 'quiet revolution', by the late 1850s Kekulé had established the conception of carbon-carbon linkage, and consequently, the 'chemical structure'. Because Kekulé was skeptical about the idea of the mechanical structure of substances, chemical structure meant for him what was expressed with reaction formulas. While he was clear concerning this point, it was left to Butlerov, a Russian chemist, to elaborate and popularize the idea. Butlerov first made a sharp epistemological distinction between the chemical and mechanical positions of atoms within a molecule, and claimed that what could be ascertained from the study of chemical properties was only the atom's chemical position. Butlerov wrote, "chemistry, which only deals with bodies in a state of transformation, is powerless to judge this mechanical structure" (Ramberg 2003, p. 25). Once the concept of structure took hold, however, the distinction between chemical and physical arrangement became blurred, especially with the introduction of the graphical notation of chemical structure, which is still used today, by Crum Brown in 1864, and above all with the introduction of the term 'bond' by Frankland in 1866. Despite the purely chemical intentions of these chemists, straight lines that depict the valences provided 'bond' with still more physical significance. Modeling practice established in the 1860s helped this trend. Although those models (for instance, Hofmann's croquet-ball models, Kekulé's tetrahedral models, *etc.*) were invented for pedagogical purposes, they went beyond the original intentions and acquired ontological significance. And finally in 1874, when van 't Hoff and Le Bell independently recognized that optical rotation could be explained by an appeal to the spatial characteristics of molecules, the mechanization of structure theory was completed. Now the molecule became an entity with a distinct physical shape and form, and could be properly expressed by mechanical models.

The molecule postulated in this concept is the synthesis of a wide range of chemical information: what types of transformations are allowed for a given molecular structure, which groups of atoms are susceptible to attacks by given reagents, *etc.* A knowledge of the shape and size of the molecule and/or substituents is essential for investigating stereo-controlled reactions. Therefore it serves as a map to show every possible site and every possible type of chemical reaction for a given molecule, whereas only one or a few of them can happen at one time. It should be as is described here for the concept to be empirically adequate.[12] As we see the world as it is measured with the scale of the map we have adopted, we see the world of microscopic entities as it is delineated on a map of the molecule. We see the molecule as composed of atoms that are linked with each other by chemical bonds. Without chemical bonds only a spatial arrangement of atoms can be recognized. The chemical bonds suggest types of reactions that atoms connected by those bonds have as well as denoting the sequences of atomic connection. For instance, 'C=C' is capable of accepting the electrophilic addition, 'C=O' the nucleophilic addition, while 'C-L', where L is a leaving group, is capable of accepting the nucleophilic substitution reactions. Chemical bonds are to the classical concept of the molecule what lines denoting roads and bridges are to a map.

The classical concept of the molecule is, as it were, a limiting concept like point mass or instantaneous velocity in mechanics. Being highly idealized, it unfolds and spells out the functional as well as the structural aspects of molecules as described above. A theoretical model need not be a miniature of what is to be represented, but it must be explanatory or suggestive of mechanism, especially when it is concerned with an object that is not given to us in direct experience. On the basis of the thus formed knowledge of the molecule we get to visualize what is going on in a flask through responses we get by adding reagents to a solution of reactants.

According to Tomasi (1999), models used in theoretical investigations in chemistry can be divided into four types; that is, (a) the material model, (b) the physical model, (c) the mathematical model, and (d) the interpretative model. A material model states the material composition of the model and corresponds to the actual portion of matter in which a given phenomenon is observed. A physical model states the physical interactions among components of the material model, or more extensively, interactions with the exterior. A mathematical model includes all aspects pertaining to the description of physical interactions in the given material model. An interpretative model interprets or describes the aspects of the phenomenon under study by using chemical concepts. The competition among interpretative models is supposed to lead, by the synthesis of the aspects of interpretation of the models, to a better understanding of the phenomenon. The classical molecular model is an illustration of the last type, and seems to meet the following criteria to judge interpretative models.

(1) Simplicity or clarity: a good model should be easily describable, understandable, and applicable.
(2) Self-consistency: the implications of a model should not be in contradiction with the basic principles of science, nor with the model itself.
(3) Stability or robustness: a model should allow the introduction of changes or complements without destroying its structure.
(4) Generality: a good model should allow one to draw new connections between observables not evident at first or not considered during the development of the model.
(5) Usefulness: a good model should provide accurate, reliable and/or useful estimates of the properties of the observables.

In addition, a good model is likely to make possible discoveries in the course of its application. The above mentioned history of the classical concept of the molecule is taken as the process by which the classical molecular model had acquired these features. The usefulness of the classical molecular model has been amply proved by the roles it plays in chemical synthesis. The classical molecular model is indispensable for chemical practitioners. Worth special notice in this regard is the advent of substances such as fullerene and carbon nanotube which still remain foreign to organic synthesis. Investigating whether or not they become amenable to structural analysis and synthesis based on the design will be a challenge for the classical concept of the molecule to remain valid in the future.[13]

5. Philosophical significance of chemical synthesis

We acknowledge that a theory is empirically adequate if the interpretations of the theory, or models, save the phenomena with respect to the purpose or interest of the theoretical investigation. It means that at least one of those models rightly represents what is going on. If a theory satisfies the above requirements, as I have already mentioned, there will be found some correspondence rule between models and observables; a rule that assigns empirical contents to the postulates embedded in the model by relating them to the concrete materials observed in experiments. Otherwise it will be a mere coincidence between the theoretical postulates and the observables, and the theory cannot be regarded as empirically adequate. Here we can tentatively distinguish two models of different character on the basis of their purposes; one which is intended for the quantitative analysis of phenomena, and the other for qualitative. The way the rules of correspondence are specified depends on the aims of the model. When a model is concerned with stoichiometry, for instance, the agreement of theoretical calculations with experimental data, such as those obtained by elemental analysis, will be of critical importance. The same is the case with quantum mechanics, whose concern is centered on the energy of interaction between particles, where the adequacy of a model is decided on how and to what extent the calculations reproduce the observed values. In such cases the rules of correspondence will be specified by means of the mathematical relationships between models and experimental data. In contrast, in cases of qualitative analysis the rules of correspondence cannot be specified from a single point of view, for approaches to be taken for representing phenomena vary with respect to the aims of investigations.

The above classification of models parallels Tomasi's three categories of theoretical studies performed with models; type (a) studies addressed to the calculation of values of properties (physical properties) of the material system; type (b) studies addressed to the interpretation of chemical or physical phenomena, where the interpretative model plays an important role; type (c) studies addressed to the development of specific research tools, in particular for the interpretative model (Tomasi 1999). While the development of tools (and models realized by the developed tools) is classified here in a distinct category from their application, actual scientific inquiries are complex enough to be reduced to either the simple application or development of tools and models. Since Tomasi's argument is based on the quantum theory of microphysics, an emphasis is placed on the quantitative aspect of phenomena with no special reference to the qualitative models which underlie organic chemistry.

In the case of the classical concept of the molecule, a point to be considered will be how informative it is in the control of molecular transformations, for it has been formulated in order to serve as a guide for inferring possible transformations. The correspondence rule in this case should therefore be such that it relates molecular structure that is not accessible to us in direct experience, *i.e.* hypothetical, to the observable behaviors or properties of palpable substances. If a molecule designed in terms of the classical concept of the molecule is created with selectivity as high as possible with the present techniques, the concept should be regarded as informative and relevant to the subjects it refers to. Chemical synthesis is a linchpin of the correspondence rule in this case.

Since molecules are inaccessible to us in direct experience, the design of a molecule corresponds to formulating a hypothesis, and chemical synthesis as verifying the hypothesis.[14] These two processes constitute the Method of Synthesis, the second stage of *the Method of Analysis and Synthesis*.[15] The Method of Analysis and Synthesis Newton advocated comprises the following two stages; the first one to formulate explanatory principles by induction is referred to as the Method of Analysis, and the second one to deduce consequences that not only conform to, but also go beyond the original inductive evidence, as the Method of Synthesis. In order for the theories to be scientific, the implications of theories, or in other words, the theoretical hypotheses, must be verified by experiments. Chemical synthesis, through the creation of various substances as they are intended, demonstrates that organic chemistry based on the classical concept of the molecule is a rational explanatory system in light of the above criterion of scientific method.

The empirical adequacy of the classical concept of the molecule is shown in the most remarkable fashion through asymmetric syntheses of chiral substances. As early as 1973 Woodward completed the total synthesis of Vitamin B12, which has more than ten asymmetric centers in a single molecule (Woodward 1973). Since then various chiral substances of complex stereochemistry have been synthesized, and many of them have been investigated for their potential usefulness as pharmaceuticals. The optical purity of those substances is sometimes of critical importance because enantiomers may have different therapeutic activities. It is also possible for enantiomers to have opposite effects. Enantiomer excess (ee) of 90%, which means a ratio of enantiomers of 95:5, is therefore not sufficient for practical use. Today's asymmetric synthesis, which produces desired stereoisomers with a selectivity of more than 99% ee, suggests that the classical concept of the molecule is relevant to the objects we think of. Otherwise it would be nothing but a miracle to produce them. In other words, if the expected substances are produced according to the design, the concept that underlies the designing should be accepted as empirically adequate and also as rational in light of the criterion of scientific method, no matter how strange it looks from other systems of explanation. The truth is that, insofar as the designing of the molecule is concerned, it represents the reality of the molecule. From an empirical point of view, chemical synthesis is the most challenging approach to the world of the molecule, because our understanding of the molecule can be verified through the production of palpable substances. Modern chemical synthesis is based on the designing of molecules and on the precise control of molecular transformations. Synthetic pathways are determined by means of a technique called retrosynthetic analysis where the structure of a target molecule is traced back along a synthetic pathway to starting materials (Corey 1989, p. 6). It is of critical importance to note here that this type of analysis works if and only if the molecule can be taken as the additive of the constituent atoms and bonds.

Another point to be noted here is that chemical synthesis reveals one of the most important properties of molecules; that is, molecules are designable. This recognition is comparable to one that the human body is not a chaotic whole, but amenable to anatomical analysis. Though it is the very basis of all the chemical processes that produce desired substances, it has not attracted the proper notice of many philosophers of science. One reason might be that chemical synthesis has not been regarded as a science, but a technology. The philosophical implications as are described above have not been widely appreciated.[16] Another reason is concerned with 'discovering' molecular properties. While it is well acknowledged that molecular properties such as bond length, bond angle, and so on, are artifacts, they have somehow been regarded as what should be discovered. It is taken vaguely that properties of matter are natural, hence to be discovered. So is the designability of molecules. This property becomes manifest through experiments based on the classical concept of the molecule. In other words, the designability of the molecule cannot stand independently of the classical concept of the molecule, and the latter depends on the former for its empirical adequacy and rationality as a scientific concept. It is chemical synthesis that has lent credit to both of these and provided order to an otherwise chaotic microscopic world.

6. The reducibility of chemistry to physics

Finally I want to argue about the reducibility of chemistry to physics.[17] Nagel states the requirements for reduction as follows; (1) the language of the reduced theory has to be linguistically connected to the language of the reducing theory, and (2) the reduced theory has to be derivable from the reducing theory (Nagel 1979, p. 354). It has been claimed that these requirements of connectibility and derivability are not strong enough to eliminate the secondary (reduced) theory by the primary (reducing) theory. In this respect, these requirements are said to be formal and non-ontological. When the reduction of one science to another is considered, it is usually recognized that the reducing and the reduced theories have structural relationships. Otherwise the above requirements will not be adaptable. Such relationships have been documented between physico-chemical theories; for instance, between the ideal gas law and the kinetic theory of gases. In an attempted reduction of chemistry to physics, however, there seems to be no straightforward relationship between the languages of both sciences, and therefore Nagelian reduction has been examined through modified models. Recently Hettema suggested that the reduction of Arrhenius' law to Eyring's absolute rate theory fits the naturalized Nagelian reduction, where reduction is taken as paraphrasing what happens when one theory explains another (Hettema 2012). In this case, a paraphrase amounts to giving a deeper mechanistic insight into Arrhenius' law.

The most important point in the conception of reduction is that the reducibility of one science to another should be decided by inspecting the logical relationships between them, rather than by inspecting whether the properties or nature of things can be deduced by another science. As Nagel claims, the conception of reduction as the deduction of properties is potentially misleading, because the properties or nature of things are not the objects of observation, but the objects of theoretical construction, and we cannot read off by simple inspection what they imply. To be noted in this regard is that chemical concepts such as valency, chemical bond, and molecular structure have been associated with the idea of molecular structure and molecular design. The molecule is not a delocalized electronic system, but a designable entity with a distinct inner structure. Theories of chemistry and those of quantum mechanics are placed on different scales, so that, if an object of one science is measured on a scale of another, what is to be seen in a proper science would be missed. Actually quantum mechanics could not find valency or chemical bond. Thus, it seems improbable that sets of concepts or notions unique to chemistry are deduced from the first principles of quantum mechanics. Among such concepts are found, for instance, acidity, basicity, chemical potential, functional group, and so on (van Brakel 2000, p. 132).

Reductionists have tried reduction of sciences whose dependency on the reducing science is easy to demonstrate, instead of examining representative ones. When the reducibility of chemistry to physics is argued, organic chemistry rather than physical chemistry should be examined, for it is one of the most characteristic domains of chemistry that distinguishes chemistry from other sciences. The reduction of organic chemistry to quantum mechanics is virtually the same as that of the electronic theory of organic chemistry to quantum mechanics, for it has long served as the logical skeleton of organic chemistry. The philosophical assumptions of this theory, of which the classical concept of the molecule is the most important, have provided order to otherwise chaotic microscopic things and events, and made them objects of chemical manipulation. It enables us to design molecules and to control molecular transformations with great precision. Thus organic chemistry has been established as a science of creation. Therefore it will be safe to settle the present issue by inspecting whether or not quantum mechanics could provide much deeper insights into molecular design and consequently realize chemical synthesis with greater precision than it is now carried out on the basis of the classical concept of the molecule.

7. Conclusion

Science, in the simplest form, consists in measuring. Hence the rationality of theories should be decided by inspecting the logical consistency between what is stated and what is conducted or achieved. This is the important point suggested by Woolley: "Every physical and chemical concept is only defined with respect to a certain class of experiments, so that it is perfectly reasonable for different sets of concepts, although mutually incompatible, to be applicable to different experimental situations" (Woolley 1978). Really problematic in this regard is the claim that "chemistry as a practice is autonomous, but it is not an autonomous science" (van Brakel 2000, p. 122). In fact organic chemistry meets the criteria of scientific explanation, and quantum mechanics cannot explain the meaning of action that is essential for organic chemistry to be rational and self-consistent. We know that molecules are designable. Chemistry discovered it. But, to tell the truth, it is a property that has been constructed according to the needs of organic chemistry, that is, to synthesize substances as they are intended. In general, scientific entities, properties, events, or processes are not simply discovered, but constructed with intentions. Hence, it is a misleading idea, as already mentioned, that a higher-level property is reducible to, or supervenes on, a lower-level property. The issue should be reconsidered from a naturalistic point of view. So should autonomy or universality of science.[18] It is said, "a science is autonomous if its laws and explanations make no appeal to the laws or categories of another science", and that "a science is universal if its laws cover the behavior of every real entity or process" (Hendry 1999). However, what is a *real entity* or a *real process*? In order for a science to be universal in the right sense of the word, it should cover actions as well as laws, the actions essential for the explanatory system to work rationally. While physicalists make a claim that quantum mechanics is causally complete or closed (because it is assumed to be autonomous and universal), that does not seem to be the case. For instance, quantum mechanical treatment of the molecule according to model Hamiltonians depends on the molecular backbone that derives from chemical theory. This means that the direction of explanation is downward – from the molecular structure to the motions of the parts (*ibid.*).[19] Taken from a naturalistic point of view, no science can be universal, though it can be autonomous. Synthetic chemistry reveals conditions organic chemistry has to meet for it to be a scientific system, and consequently it demonstrates that the classical concept of the molecule is empirically adequate.

Notes

1 Reported arguments concerning the irreducibility of classical notions such as molecular structure or chemical bond to quantum mechanics should be referred to with respect to the issue described here (see *e.g.* van Brakel 2000, pp. 119-150 and references cited therein).

2 *Nature* once featured this topic by doing interviews with many leading chemists (see Ball 2006).

3 It should be noticed that the appearances of planets would not be different if the center of gravity of the solar system were at rest or in any other state of constant absolute motion. Our confidence in the adequacy of the theory increases when theoretical predictions of previously uninvestigated phenomena are subsequently verified by experiments. Since prediction is the theoretical reasoning that goes beyond the inductive evidence from which the theory was induced, if verified, it suggests that the theory is rational as well. As to the significance of experimental verification of hypothesis, see note 15 and the relevant part in the text.

4 For instance, while Newton took space and time as things-in-themselves, Leibniz took them as relations between things-in-themselves, that is, as ideal relations between perceptions.

5 As Del Re argues, it has been admitted since the dawn of philosophy that our knowledge of a thing involves a representation made by our mind, and because our representations are still those of objects in the direct-access space, analogies play a fundamental role in representing the reality of the molecule (Del Re 1998).

6 The term 'trans-diction' was coined after pre-diction or retro-diction (Mandelbaum 1966, p. 61).

7 While Cram once pointed out from the pragmatic point of view that "mechanical models are indispensable for organic chemists because of their usefulness for exercising one's tactile proclivities" (Hargittai 2003, pp. 189-190), it must be more than that. The truth is that mechanical models represent well the reality of the molecule insofar as molecular transformations are concerned.

8 Vemulapalli, discussing the relation between physics and chemistry with a focus on chemical bond, claims that the laws of physics define a boundary within which chemical laws and theories are valid and beyond which they become meaningless. His argument serves as a good complement to the articles concerning the reduction of chemistry to physics cited in note 17.

9 From an empirical point of view, the task that science sets itself is to represent the observable phenomena, as van Fraassen put it (van Fraassen 2010, pp. 86-87). "The idea of representing phenomena need not, and if practical purposes are kept in mind, must not be restricted to copying. But more than that, [...] representation useful for particular purposes will involve selective distortion, and representation is closely involved with useful misrepresentation. Even when likeness is crucial to the purpose, we must look for likeness only in respects that serve the representation's purpose." In addition, as Schummer (1998) says, "we often ignore intermolecular interactions or Einstein-Podolsky-Rosen correlations for no other good reasons than that they do not help but prevent us from solving our current problems."

10 Nagel claims that a scientific theory consists of three components; (1) an abstract calculus, which is the logical skeleton of an explanatory system, and which implicitly defines basic notions of the system, (2) a set of rules, which assign an empirical content to the abstract calculus by relating it to the concrete materials observed in experiments, and (3) an interpretation or model for the abstract calculus, which supplies some flesh for the skeletal structure in terms of more or less familiar conceptual materials (Nagel 1979, p. 90). None of these contradicts what is discussed in this paper, though his claim concerning the aims of science may contradict empiricists' arguments. That is to say, while Nagel takes explanation as the preeminent goal of science, empiricists like van Fraassen object to this view. Scientific explanation is taken by the latter as constructing empirically adequate models that provide the correct description of what is observable. It is no more and no less than that (van Fraassen 1980, pp. 5, 92-96).

11 Scerri argues that, despite the strictures from quantum mechanics that orbitals do not truly exist, one may continue to use concepts like orbitals in chemistry, if one important change is made; that is, if we cease to pretend that the chemists' orbitals are the same as those of the theoretical physicists (Scerri 2000). He claims that we should continue to use the highly productive paradigm of orbitals and electronic configurations but only while claiming it as a distinctly chemical paradigm, not one which is strictly comparable with quantum mechanics: "Only by upholding such an independence from the quantum mechanicians' orbitals can the chemist attribute any reality to chemists' orbitals with a clear conscience."

12 Kekulé insisted that chemical formulas should be reaction formulas which convey all of a compound's chemical properties, not simply the reaction of the moment (see Ramberg 2003, pp. 22-23). Tontini claims, with Schummer, that the main import of structural formulas is that of *representing substances in certain relations with each other, i.e. substances within the chemical network* (Schummer 1998, Tontini 2004). In addition, Tontini argues, structural formulas show not only the convertibility relationships between functional groups, but how the rest of the structure

may affect the reactivity of functional groups. This seems to suggest, Tontini says, "structural formulas cannot be purely conventional signs serving as heuristic devices to pilot chemical synthesis", but they are "relatively faithful stereo-electronic replicas" of molecules, though highly stylized representations of microscopic objects they designate.

13 As Tontini claims, pursuing synthetic chemistry is not only important for practical purposes, but is also instrumental in the emergence of novel or improved chemical language (Tontini 2004). Worth special notice in this regard is that an empirically based syntax of the chemical sign system (such as valence rules) can fail, as sometimes witnessed in cases where the experimental abilities of chemists exceed the capacity of the language. For instance, it was not until the 1980s that fullerene was discovered. That is not because the synthesis of fullerene is hard to perform, but because there were no syntactic rules that would allow for the chemical equation leading to C_{60} from 60C (Jacob 2001).

14 Bensaude-Vincent & Simon claim that the logic proposed for chemistry is not the empirical hit-and-miss strategy associated with inductive reasoning, but rather the hypothetico-deductive method. Thus, if the chemist proposes a hypothesis, then "synthesis provides the means for verifying the conjecture" (Bensaude-Vincent & Simon 2012, pp. 101-116). In this sense, chemical synthesis serves as a cognitive tool as it was for Berthelot a means of arriving at a better understanding of nature.

15 As to the details of the Method of Analysis and Synthesis and the application of this method by Newton to his experiments for *Opticks*, see Losee 2001, pp. 73-74.

16 The few exceptions include, for instance: Schummer (1997), who proposes 'chemical space' (*i.e.* the space formed by 'the chemical network', and to which each chemical substances is placed in reference to the inter-convertibility of functional groups) as the chemical reference frame, points out that the most interesting feature of this reference frame is that it provides us with reference rules for chemical substances in the sense of laboratory rules to produce them. This means that chemical reactions have linguistic implications (in chemical reference frame) as well as technological usefulness. Rosenfeld & Bhushan (2000) and Bhushan (2006) delineate the ontological implication of chemical synthesis with regard to 'natural kinds'. Their arguments have much to do with my argument here in that they criticize the dichotomy between what is discovered and what is constructed. The point is clear; since there is no way to distinguish the naturally occurring from the synthesized compounds with identical chemical composition, chemistry does not offer an univocal way of classifying substances into 'natural' or 'synthesized'.

17 The reduction of chemistry to physics is still an important topic of philosophy of chemistry as is documented by the review articles (see *e.g.* van Brakel 2000, pp. 119-150 and Schummer 2006, pp. 19-39). Schummer explicates the meanings of (struggling with) reductionism for the rising discipline of the philosophy of chemistry.

18 Rowlinson claims that each science should be placed in a hierarchy of representations, and hence the conception of autonomy is untenable. Moreover, since the boundaries between sciences are always changing, it often happened that what one generation of chemists interpreted in terms of its own concepts was later reduced to a deeper physical understanding (Rowlinson 2009). A normalized molar volume called parachor, and the concept of a 'free volume' in lattice theories are listed as examples, among others. It might be the case with them, but it does not seem to be the whole story. According to Del Re (1998), for instance, "the claim that

the whole physical world is nothing but 'atoms and quanta' is as untenable as the claim that airplanes, cars, trains, *etc.*, are but the materials of which they are made. […] If a complete description of the nuclei and electrons of a molecule is not a complete description of the molecule, for the whole reality of a molecule as distinct from everything else includes 'emergent properties', then clearly a picture of the physical world only granting reality to the ultimate constituents of matter falls short of accounting for factual evidence". On the other hand, if the issue is considered from a naturalistic viewpoint, the question will be whether or not chemistry can be reduced to quantum mechanics, taking account of the present state of *ab initio* calculations. As Scerri spelled out in relation to the historical development of the periodic system, the quantum mechanical calculations are based on the aufbau principle introduced by Niels Bohr as well as calculations carried out through the Hartree-Fock method of approximation (Scerri 2000). This means that the electronic configurations of many-electron atoms cannot be strictly derived from the first principles.

[19] Hendry points out that the physicalist claim that physics is causally complete stands on feeble ground by inspecting quantum mechanical molecular models.

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OCHIAI Hirofumi:
Department of Information Culture, Nagoya Bunri University,
365 Maeda, Inazawa-cho, Inazawa, Aichi 492-8520, Japan;
ochiai.hirofumi@nagoya-bunri.ac.jp