Better Realism Through Chemistry

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ABSTRACT

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The practise and history of the science of synthetic chemistry, that of preparing new substances, is examined in relation to the issue of atomic/molecular realism, the status of the literal existence of atoms and molecules. The discussion is situated by a brief examination of leading contemporary work considering scientific realism in general. On the basis of past criticism of scientific realism and general metaphysical principles regarding existence and observability, it is argued that a good case can be made for the existence of causal entities bearing sufficiently close analogical resemblance to familiar, everyday objects. Numerous considerations from the current practise of synthetic chemistry and its history are argued to support a position of realism concerning atoms and molecules. This conclusion is drawn because hypothesised molecules and their shapes have numerous causally efficacious properties resembling those of macroscopic bodies, and because these properties only expand their coherence through technological and intellectual innovation independent of the molecular hypothesis.

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CHAPTER 1: INTRODUCTION

Section 1: The Pertinence of Chemistry for Scientific Realism

As a sort of meeting-ground between the manifest appearances and fundamental theory, chemistry is well placed to help us understand the place of their interplay in a scientific realist account. This thesis explores the science of synthetic chemistry – the science of making new substances – with a view to locating criteria for the real. I will argue that an examination of this science and its history supports a realist construal of atoms and molecules. A more general account in support of scientific realism will not be attempted, but it is to be hoped that the strategy adopted here may be of use for future studies in this direction.

Traditionally, scientific realism has been defended by reasoning to the truth or verisimilitude of scientific theories: mature accounts of such a position are provided by W. H. Newton-Smith [1981] and by Richard Boyd [1983]. Numerous critics have vigorously opposed such views. Some, such as Bas van Fraassen [1980] and Arthur Fine [1984], question the usefulness of looking for truth, as such, in scientific theories. Others, such as Larry Lauden [1981], criticise scientific realism more directly by attacking the possibility of a successful correspondence theory of truth, and by use of the infamous 'pessimistic induction': since so many scientific theories have come and gone, successfully employed and then abandoned as somehow wrong, the same is to be expected of any particular theory now in use.

More recent literature concerning scientific realism seems to indicate that the critics, if not derailing the possibility of a realist construal of science, have forced its advocates to offer new accounts of realism that answer their objections. Of particular note are Ian Hacking [1983] and Nancy Cartwright [1983], who argue that reality is not to be seen in the formalism of scientific theory, but instead in causally efficacious entities. While I am inclined to accept this view, I also admit Stathis Psillos' [1999] view that entities to which science may refer are partly known through confirmation of relations, some of which might be partially formalised.

There clearly is a tension here, between the pragmatic sort of immediate acquaintance seen as realism's exemplar by Hacking, and the need to see things in their systematic relations, crucial to the views of Psillos and the traditional scientific realists. The tension manifest in this comparison expresses in a concise form two related aspects of the recent scientific realism debate, neither of which is anything new to this work. Firstly, it is not always clear where the disagreement lies: for what is there, and for what is there not, consensus as to 'reality'? This in turn seems to be a symptom of a still more contentious issue, that of the proper *criteria* for determination of the real. Secondly, this debate with its claims and counter-claims is deeply analogous of the longer-lasting *general* realism debate (i.e., concerning not only theoretical entities of science but also more pedestrian entities such as tables).

I could not responsibly claim to resolve this tension in the present work, but to return to our object of study: the practise of synthetic chemistry (preparative chemistry, chemical synthesis) lives with it, and has done so for a long time. Informed both by a rich heritage of empirical observation, and more recently by the concepts of quantum physics, this science provides data of relevance to scientific realism. Most notable for this purpose is the variety of inferential techniques exhibited in its practise. Sometimes, synthesis stays 'close to the surface' of common-sense spatial concepts in inferences; at other times, it makes heavy use of the formal apparatus of quantum theory. Happily, its practise exhibits a range between those extremes in numerous ways.

Thus there is a motivation for the study of chemical synthesis as a case study for realism. Even a cursory look at the inferential techniques of synthesis reveals a wealth of distinctions that are of interest to the present topic. We will be well served to take this look at some actual syntheses rather than only at generalisations. Therefore, this thesis presents details of some experiments in which I myself participated, and which tended to bias me towards the realist account I seek. There is nothing uniquely interesting about these particular studies except that the present work is facilitated by my having been there. A brief examination of the goals and culture of synthesis as a science necessarily prefaces such a discussion.

More wisdom might possibly be gained by examining selected episodes in the history of chemistry, not least because nineteenth century chemists themselves engaged in a fierce debate between realist atomism and the doctrine now called 'operationalism' [Brock 1967: viii]. Therefore, the present work includes also a discussion of the historical evolution of chemical synthesis, with the emphasis on lessons for atomic/molecular realism. The main features of interest are the retention of classical methods of synthesis and surrogates for the same, and what that implies for the assumptions of chemistry as a science. Of great pertinence, too, is the contemporary development of a new offshoot of chemical synthesis known as *combinatorial chemistry*, in which literally tens of thousands of new substances may be prepared at once.

In brief, then, the thesis argues for a form of scientific realism concerning atoms and molecules through a study of synthetic practise and its history. It should be clear from the above that the thesis is to be developed simultaneously with being argued. I aim to show that in some particular cases, scientific realism is no more problematic than is general realism, and that they should be judged by similar standards. As to chemistry, certain of its inferential methods the same as those used in everyday discerning, particularly in classical chemistry. The persistence of some of these methods through theory-change, and the attempt by chemists to link new ones to them, is argued to be evidence of atomic and molecular realism.

Hence molecules, resembling 'normal' things (i.e. the manifest, the obvious) in relevantly analogical ways, are properly viewed in the same way. Practises in synthetic chemistry resemble the detail of our machinations with normal things; the coherence of its methods interpreted in a context that is only very weakly theory-dependent displays a genuine pay-off given a realist interpretation. Molecules are, I argue, "entities believed to exist because of analogical and logical evidence similar in nature to that by which a judge may condemn a man as the author of a crime" [Del Re 1998: A.1]. Beyond a point the burden returns to the skeptic: it is the contention of this thesis that synthetic practise meets this point.

The argumentative strategy relies on coherence, offering a formulation of what Cartwright calls an 'inference to the best cause' [1981] (discussed below). The thesis argues that the only reasonable construal of synthetic practise leads to atomic/molecular realism. Briefly, molecules do many of the things that existents are supposed to do, and we can do with them many of the things we expect to be able to do with existents. The most notable and accessible example of such is that inferences concerning molecules often *do not rely on the syntax of theories but instead on the humblest sort of reasoning concerning positions in space*. To name but a few examples, molecular fragments with similar drawn representations are held to have the similar literal shapes, large fragments are held to have a greater ability to physically block processes than do small ones, and certain bulk properties of substances can be read straight off drawings of molecules without mathematical calculation.

The argument assumes on the basis of elementary reflections on the metaphysics of ontology (developed in chapter 2) that where such available operations on objects of science are sufficiently analogous to those used unproblematically with normal things, we have reason to believe that inferential procedures concerning objects of science should be viewed as reflecting the same attitude towards those objects as our attitude concerning normal things. These 'objects' about which inferences are made are characterised by a web of concepts that combines their pragmatic appearance to us and systematic relations in the formalism – the same as for normal things.

The account is recognisably a version of Hacking's [1983] celebrated 'entity realism'. In the present work, the entities in question are of course atoms and molecules. I will not attempt to defend scientific realism more generally. To do so would in fact be contrary to the general aims of the thesis in that it proposes to apply an argument to best explanations on a case-by-case basis, and not to theories. Hence there is no intended 'package deal' here.

It would not be unfair for a reader to view the argument as a cheat, in the sense that the conditions for 'objecthood' are presented in a way that entails realism. However, the conditions are not arbitrary ones, but are ones that are required for normal things also.

As argued in chapter 2, there is no coherent way to represent *any* objects as coming ready-made with 'object' tags. There is always a degree of convention in defining them too.

The thesis is not intended to despise theories. I retain the view, necessary for a distinctively scientific realist position, that mature theories of natural science are best viewed as approximately true, at least some of the time. Their formalism captures certain features of objects whose existence reasonably can be affirmed (on the basis of independent pragmatic reasons). At the same time, the adoption of a realist position tied to entities rather than theories allows the question of verisimilitude to be put to one side for the present work.

The positive argument, which begins in chapter 2, follows a very brief survey of recent work concerning scientific realism.

Section 2: Recent Approaches to Scientific Realism, For and Against

There is neither need nor call for a detailed discussion of the various positions in the scientific realism debate, as Psillos' monograph [1999] includes long analyses along with technical details. Moreover, an excellent brief typology of available positions is presented by Kukla [1998]. Therefore, the review here considers these positions at the generic, outline level.

It is simplest for dialectical purposes (and, incidentally, historically accurate) to start by considering instrumentalism and its cousins. With roots deep in the forest of Western metaphysics, while usually denying the same, instrumentalism (along with operationalism, logical empiricism, and phenominalist positivism) relies on a distinction between the observable and the unobservable, or the manifest and the scientific. Cups of water (or, water-cup qualia) are observable; water molecules are not. It is held that in some way or another, terms referring to the unobservable can be definitionally eliminated from theories. Historically, the forms of instrumentalism arising in the early part of this century represented a culmination of English empiricism's struggle with the problem of knowledge. The essential attraction of this sort of position is that speculation is minimised; reference stays as close as possible to experienced reality.

That the versions of instrumentalism that arose at this time focused on terms in theories was a manifestation of the (philosophical) theorists' interest in formal reasoning and admiration for instrumentalist programs that had arose in the context of relativity and quantum theory. Physicists had achieved success by positing that only objects of direct measurement are definable in scientific theories [Feynman 1965: v. III. 2-8]: "The basis of a science is its ability to *predict* [2-9]." Philosophically. it was hoped that the combination of the logical impeccability and retention only of the manifest would secure knowledge.

Psillos' monograph explores the technical details of numerous variants of instrumentalism and related views [1999: 1-69], and finds them all lacking in the ability to maintain a logically impeccable, meaningful distinction between terms referring to the observable and those referring to the unobservable. Vocabularies for the two cannot be kept separate, and there is no plausible way to reduce the unobservable to the observable [24]. The contemporary discussion of scientific realism has been motivated to a large degree by responding to instrumentalism, most notably, its alleged lack of *explanatory power*: there is no way to explain theories' novel predictions on an instrumentalist construal [35]. However, I do not discuss the details of instrumentalist positions because they are no longer advanced by scientific realism's most vocal critics.

Contemporary scientific realism is also motivated by opposition to certain "non-rationalist" views of scientific progress, often motivated by sociology of knowledge [Newton-Smith 1981: 7]. Such views impute change in science to factors outside its range of study, such as the prestige of individual scientists, and have become popularised in the wake of Thomas Kuhn's seminal work [Kuhn 1996] on theory-change through paradigm shifts. On some such views, the traditional epistemological concepts of truth and explanation become largely irrelevant.

Whatever challenges to realism the work of Kuhn and his followers pose, it has also given contemporary realists a datum on which to hang their realism. For realists starting from the sixties on, the datum to be explained is the *success of science* [Psillos 1999: 70]. On an anti-realist view, it is held, the success of science is a brute miracle [Putnam 1975: 73]; an instrumentalist view cannot motivate successful, novel predictions and an anti-rationalist view lacks resources for explaining how scientific manipulation can be effective at all [Newton-Smith 1981: 7]. Thus, a realist view is required to explain its success. Most are likely to agree with Psillos that this is the "central argument in defence of scientific realism" [1999: 70]. Newton-Smith [1981] and Boyd [1983] provide representative versions of such an argument, both licensing their conclusions with the 'best explanation' argument-form, which can be formulated in the its general form as:

> (i) Science exhibits progressively increasing success in prediction
> and control.
> (ii) Scientific realism explains this success.
> Therefore, we have good reason to believe in scientific realism.

Newton-Smith attempts to defend scientific realism by appealing to verisimilitude, the increasing truth-likeness of theories. For Newton-Smith, scientific realism consists in the theses [1981: 13-14]

> (i) theories are true or false according to how they correspond with reality, and
> (ii) the goal of science is the discovery of explanatory truths about the world.

In defending these theses, and presenting a detailed technical account of the conditions for a satisfactory theory of verisimilitude [183-207], Newton-Smith intends to present not only a plausible realist view but also a plausible account of scientific progress. Scientific realism explains verisimilitude increase and therefore progress. As such, his argument is intended to be supported by its ability to account for the intuitions of 'anti-rationalist' views while retaining realism.

Boyd presents a similar conception of scientific realism [1983: 195]:

> (i) 'Theoretical terms' literally refer.
> (ii) "Scientific theories, interpreted realistically, are confirmable...with ordinary methodological standards."
> (iii) The success of science is due to the ever-increasing conformity of its findings with the truth.
> (iv) Reality as described by science is independent of us.

Boyd tells us that the best evidence for this view comes from scientific practise. "...realism provides the only acceptable explanation for the current instrumental reliability of scientific methodology in mature sciences" [221]. Boyd is concerned with the success of practises; he seems to say that the inference to scientific realism from the manifest growth in ability to predict and control is a mirror of a sort of inference used in science itself [207-209].

As noted earlier, instrumentalism no longer sports prominent defenders, but a sophisticated variant, 'constructive empiricism', is proposed by Bas van Fraassen [1980].

He wishes to retain that point of plausibility in favour of instrumentalism, that of sticking to the phenomena. His key innovation is to take a pragmatic view as to the unobservable/observable distinction. While the account takes a "literal" view of the objects of scientific discourse, treating them as truth-conditioned in the usual way [9-11], there are in-principle limitations to the human ability of observing. The limitations to observation are "our limitations, *qua* human beings" [17]. However, we do not need to worry about the status of the unobservable. Scientific theories, to be acceptable, need not be true, but only empirically adequate: to be true about observable phenomena [12]. We can note for later interest that van Fraassen regards the opposing view, scientific realism, as requiring that acceptance of a scientific theory implies a proposal that it is true [8]. This view is perhaps unfair since a scientific realist can be a pure instrumentalist about only some theories and not others; in any case I argue that the theories as such do not get us to the most plausible construal of realism.

A somewhat different tack against scientific realism is taken by Arthur Fine [1984]. His 'natural ontological attitude' applies a deflationary concept of truth to scientific theory. He suggests that we understand scientific posits as defined by their place in scientific practise, according to "standard rules of usage" [1984: 274]. Fine is reacting to the failure to reach the successful correspondence theory of truth, historically connected to the scientific realists' position (see Newton-Smith 1981: 28-29). He does not quarrel with a scientific vocabulary that seems to imply realism, asserting only that the very implication of realism is an optional extra for philosophy of science as it is for science itself [Fine 1984: 271]. Fine suggests that realism is dead in science [260, 268-269]. Notably, too, Fine claims that there is no way to understand 'truths' in scientific discourse like those of simple observation [270]. It is not clear to me how to understand this position given working chemists' seeming penchant for realism.

Some recent works defending scientific realism concede that theories cannot be supported as true or false as a whole, instead looking at the role of particular judgements in scientific practise. Of these, one of the clearest and most important is Ian Hacking's *Representing and Intervening*, published in 1983. Hacking looks closely at entities *qua* experimentally manipulatable beings. It is this feature, and not their place in theories, that convinces Hacking of their real being [1983: 22-29]. His general attitude is such as to "...count as real what we can use to intervene in the world to affect something else, or what the world can use to affect us" [1983: 146].

We should note that 'affect' in this usage seems more clear in the context of 'affecting something else'. Hacking feels no need to clarify the usage too much in that there is usually no problem in understanding it in particular cases. Those that might arise would not be in the purview of studies specifically of realism – they would be in the domain of philosophy of language (see Hacking 1983: 85). But the usage of 'affect' in the context of 'being affected by the world' is readily confusable with an analytic definition: what else could be real? The point is that we can (partially) define 'affecting the world' through our actions, by describing them, but seem to have fewer options as to delineate what is affecting us exactly. What, we might ask, *doesn't* affect us?

A position closely allied to Hacking's is advanced by Nancy Cartwright [1983]. In *How the Laws of Physics Lie*, Cartwright calls herself an 'anti-realist' but she is an anti-realist about theories, not about all objects of scientific discourse. I shall draw on hers and Hacking's insights in the sequel; their work marks a turn in the realism conversation that affects all discussion since. They provide the needed turning point for the claims of the present work.

The next chapter will conclude among other things that scientific theories as such, at least in their present formulations, cannot provide any particularly unproblematic basis for construing scientific realism, in agreement with Hacking, Cartwright, and critics of realism. Less abstractly, we also will see that chemical practise embodies assumptions about the real that cannot plausibly be viewed as strongly theory-dependent. Moreover, a realist interpretation of this practise will have to focus on the entities. Ultimately, it is the resemblance of these entities to the ones manipulated in the kitchen that convinces me of their reality. In this my motivations resemble those of Hacking's when he advances the ability to spray electrons as his reason for believing in them [1983: 22].

But I also am convinced that this attitude needs to be supplemented with an account of the role of logical connections in establishing findings. The ability to spray electrons, in itself, may incline us to believe in them, but an inability to connect this with other propensities related to spraying would incline us to think that our seeming spraying ability is a misrepresentation of the process. We need to know something about electrons' other propensities in order to understand the workings of the spraying device, for instance, and to distinguish it from a device that sprays the superficially similar particles Γ, say. A realist position can be convincing only if it deals with some of the ways we distinguish those types of particles. We are lead to a deeper conversation. While successful practise is the best kind of confirming evidence, it must be connected to the context in which it is interpreted in order to serve as a basis for particular existence claims.

We return then, to the above-mentioned tension between emphasis on particular observations and theoretical formalism. Numerous works published subsequent to the Hacking and Cartwright works have attempted to deal with this tension in several ways. For example, Aronson, Harré, and Way in the provocatively entitled *Realism Rescued* [1995] attempt to extend the idea of correspondence to a more general one involving non-classical logic and ontological rather than propositional 'fit'.

While I have some sympathy for this sort of project, the one intended here is more modest. The argument is not general; the aspects of chemical practise here analysed are taken on a case-by-case basis, and compared to ordinary existence judgements. It is the use of theories selectively, sometimes respecting and sometimes ignoring their syntax, that places chemical practise on a similar level with such judgements.

Cartwright, in her [1981], compares her position to that of theory realists. Her earlier-mentioned 'inference to the best cause' is intended as an alternative to the best explanation argument. The difference she notes is that the best cause inference is got by following the causal sequence of experimental result back to the likely cause. The inferences drawn in this thesis are intended to follow formulations of this argument-form. However, it would be tendentious not to acknowledge the notorious problems in formulating the terms 'explanation' and 'cause'. Moreover, as we saw above, the distinction between entity and theory realism is not as clear as would be ideal. Therefore, there is no attempt to hang anything essential on any of these terms.

The strategy to be followed represents an effort to spell out some of the "specific, concrete causal processes" [Cartwright 1981: 385] that implicate molecules in synthetic practise, in current and historical perspective.

Section 3: Organisation of the Following

In chapter 2, I start by considering realism in general, emphasising certain of its features related to the limits of epistemic access and consequences for the syntactical encoding of phenomena. I turn to scientific realism, examining the relationships of its problematic features with those of the general variety. The appearance of disanalogy between these varieties partakes of the observable/unobservable distinction, and realist arguments must examine the dimensions of this distinction in order to meet the challenges of sophisticated anti-realist positions such as those of van Fraassen and of Fine. Much of this work has been done in Psillos' recent monograph [1999], which is very helpful for locating the difference in intuitions motivating realist versus anti-realist positions and in particular for prescribing the resources that a convincing realist account needs.

Looking generally at the nature of scientific discourse, and more specifically at that of chemistry, I conclude that the real in science resides in objects describable only in *interpretations* of theories, interpretations that must be relatively theory-independent, employing categories proper to normal things (like spatial extent). Therefore, it is a necessary condition for the existence of real entities of science that they be consistently and coherently known through a variety of observation processes, partially systematised by formal structures, but such that they provide the means to successful inference independent of those formal structures. I would project no possibility of narrowing this to a sufficient condition, because such a stipulation must remain vague in practise. However, we do have a natural yardstick – our experience with normal things. The chapter concludes with assertions concerning the ways in which molecules match this experience.

In chapter 3 an analysis of current practise in synthetic chemistry is carried out. The overlapping commitments implied by the various operations in the synthesis laboratory illustrate the points nicely. By noting the coherence of various laboratory methods and the freewheeling sort of attitude to theory successfully used in practise, I reach a realist position for atoms and molecules. As mentioned earlier, if we confine our attention to the limited domain of chemical synthesis, the coherences between various chemical inferences, obtaining in numerous (relatively) theory-independent ways, lead to either realism or gross cosmic coincidence.

In chapter 4, a similar strategy is followed, focusing on the evolution of synthetic practise and the history of atomic/molecular realism within chemistry itself. A brief visit of the historical events leading to the consensus of molecular realism by chemists provides a historical case study of interest and paramount salience. This is explored in the first two sections. The third section briefly comments upon how the molecular hypothesis seems to provide a quite clear-cut understanding of the evolution of chemical practises from 1800 to the present. Finally, the fourth section describes the emergence of the new science of *combinatorial chemistry*, the science of producing thousands of new substances simultaneously. It provides a living example of an emerging science with all its links to previous practise. Though a new science, its practise continues to rely on chemists' realist construal of molecules.

Chapter 5 concludes the thesis. I shall conclude that the plausible construal of synthetic practise and its history is a realist one, and that the new practises of combinatorial chemistry only strengthen this conviction. The first three sections present the thesis claim and argument in standardised form, along with discussion of their formulation in relation to Hacking and Cartwright, and contrast with the role of realism in the practise of other sciences. Section 4 briefly fields objections, and section 5 concludes.

CHAPTER 2: IN SEARCH OF A CRITERION FOR THE REAL

Section 1: Realism: General, Scientific, Atomic/Molecular

General realism is defined generically in the *Stanford Encyclopedia of Philosophy*, here paraphrased:

> Objects *a*, *b*, and *c*, and so on, exist, and that they exist and possess properties *F*, *G*, and *H* is independent of all observers and observers' propensities [Miller 2002].

There is much to be gained by briefly considering the problems that accompany attempts to define objects as unambiguously real. Proposed definitions of *scientific* realism are surveyed in the previous chapter so there is no need to go over them again.

Each account of realism requires a metaphysical analysis; one must determine the content of a realist position simultaneously with an attempt to defend one. When I say that experience of normal things is a natural yardstick to apply to purportedly real scientific entities, this is not meant to imply that they are unproblematic. But their problems do not touch scientific realism because experience with normal things is the final arbiter; scientific entities, it is clear, are always as least as problematic as normal things.

I take for granted that the leading positions in the current scientific realism conversation assume general realism for everyday objects of life, as opposed to positions such as idealism. The general issue is largely orthogonal to that of the scientific one, as approaches to scientific realism can do nothing to address metaphysical issues of general realism. Not only that, even if we are unable to accept a metaphysical realist position, a proxy of the scientific realist position can nonetheless be accepted. For example, standard interpretations of Kant's transcendental idealism distinguish a transcendental ideality from empirical reality for normal things: therein, the *Transcendental Aesthetic* asserts that determinations of objects must be *conformable* to the forms of our intuition rather than independent of us, but *the Refutation of Idealism* asserts that normal things are not properly thought of as *caused by* our intuitions.

The arguments, therefore, are addressed to finding the real in scientific discourse specifically. Nonetheless, problems of general metaphysics recur in interpretation of scientific discourse. This is not to suggest, necessarily, that there is no difference in kind between scientific and non-scientific discourse. What is suggested is that we need some examination of the criteria of the real for the macroscopic, to guide the search for a rationale for atomic/molecular realism. If there are identifiable differences between normal things and the objects named by science, we need tools thereby sharpened in order to express those differences.

Let us propose this. Suppose we can obtain a scientific realist position that is not an assignable degree more problematic than standard interpretations of general realism. Then we should believe that position. Let us briefly consider the metaphysics of ordinary existence judgements. This leads, very quickly, to considerations of what scientific theory is supposed to do for us.

Take a look at macroscopic objects. Suppose that we have as good a grip on them as we please. Consider now a table, as all philosophers do. How can it be given a *comprehensive* definition? Its boundaries are not sharp. Little bits of dust are constantly dissolving in the table's paint. It is not possible sharply to distinguish bits of dust on the table from those which are 'part of' the table. Nonetheless, I assume that tables exist.

Consider storms. These consist of disturbances of air owing their driving force, according to science, to variations in solar radiation. They grow and shrink in size; they move over different areas. Even pretheoretically, they do not maintain the same composition of clouds over time. Moreover, clouds can pretheoretically be known to have unclear boundaries through experience with mountain clouds; we can see the variations in cloud density, but cannot know where the cloud ends. Nonetheless, I assume that storms and clouds, even stormclouds, exist.

A consequence of these examples is that our perception of the reality of normal things cannot require a definition which is 'total': logically impeccable and expressing all possible outcomes for those things. Therefore, a realist position cannot require such definitions in determination of the extension of 'real'. For syntactical representations, we can also see that no formalism will allow for extensional substitution, for a token representing an everyday physical object, with the *totality* of its constituents. As well, we have unlimited choices as to the possible ways of dividing a physical object, in naming parts, so extensional definition cannot be unique. There can be no unproblematic tokens for objects.

These logical problems are not necessarily of interest for normal things, but become interesting in the consideration of scientific realism. Broadly speaking, the reference of our terms for normal things must be established by practise; no syntactic criterion of referenda is available. This given, it is difficult to give any general criteria for existence and availability for reference.

Ultimately I appeal to modest, everyday observation as a prototype; existence judgements of atoms and molecules are similar to existence judgements of normal things.

In addition to being representable in simple logical systems, normal things such as rocks and tables exhibit properties that we utilise without the use of argument as such:

> (i) We can determine expected behaviour in many situations by considering only their spatial extent.
> (ii) We can mill them to numerous shapes for various purposes.
> (iii) We are aware of their presence without the use of any particular theory.

Section 2: Unsuitability of Syntactic Views of Realism

The living heir to high church metaphysics, through the medium of enlightenment-era reductionism, is the search for fundamental theory in science. The picture of reality that emerges is simple and compelling: we hope to escape the problematic features of the changing and ambiguous world by positing logically and metaphysically unproblematic entities as underlying the world. For modern science (especially) this has taken the form of layers of *composition*; the macroscopic is made of microscopic bits, particles, with well-defined properties. While this notion seems unobjectionable in principle, efforts to define the fundamental particles such that wholes are *syntactically reducible* to parts have not been successful.

It is widely held, for example, that chemistry has been reduced to quantum mechanics, since the behaviour of molecules can be computed, in principle, from their equations of motion. In practise, though, approximate theories are employed whose mathematical constructs do not correspond to any syntactically definable entity in quantum theory. What is more, the posits that appear to correspond to entities in those 'approximate theories' actually *violate* the requirements of the quantum equations of motion [Scerri 1994: 160-170]. The natural thing to imagine is that states of molecules can be built up from states of individual particles (i.e. electrons). But there are no syntactical constructions in the equations, plausibly assignable to individual particles, to which the formalism can be reduced.

Common practise in the theoretical computation of electronic states in molecules indeed assumes, as a starting point in a calculation, that the overall electronic state can be represented in terms of individual electron motions. A mathematical procedure adds terms to the equations of motion that perturb independent particle states, such that the calculated states will be closer to those required by the unapproximated formalism. To the extent that this is done, intuitive understanding of the motion in terms of individual particles becomes less and less accurate.

As far as the practise of modern science is concerned, the traditional reductionist program has failed. It has failed because we must add conditions, *ad hoc* from the point of view of fundamental theory, in order to investigate large-scale phenomena. For example, in obtaining approximate wavefunctions for molecules, we impose conditions derived from general chemical knowledge not inhering in the equations of motion [Del Re 1998: B.1]. Numerous similar examples from outside chemistry can easily be imagined once this is grasped. More generally, as argued by Nancy Cartwright, it is in the nature of physical law to be usable only in this way [1983]. Even if Cartwright is wrong in this general thesis, her book provides ample evidence that in practise, the laws actually are used in this way.

At a minimum the burden of proof is shifted to the claim that physical law, within its formalism, can provide a full account of phenomena observed in science. There is some ambiguity in 'account' here, since we cannot expect an 'account' of literally all relations between things. What is desired is a basic set of elements that comprise any physical phenomenon that we might see. The problem is that while the objects of science are perhaps less logically problematic than those of everyday life, they are phenomenologically fuzzier. For example, for the hydrogen atom, the electron in all states has a finite probability of being an arbitrary distance from the nucleus. It is everywhere and nowhere. There is no possibility of experimental verification of this position distribution. What is more, as discussed above, the isolation of the atom must be assumed; formally, this move corresponds to assuming that the atomic motion is separable from all others. That is a boundary condition that must be added 'by hand' i.e. from the *head* of the scientist.

It is necessary to be clear on another point concerning tokens that appear in the equations of physical theory: they need not be unambiguously assignable to the objects that we think are assignable to parts of those theories' syntax. The fact is that quantum theory, for example, has no particles in it at all. Quantum theory is mathematical, and contains no tokens for them. The tokens that 'represent' them are *parameters*, for example electron mass and charge. And there are no springs or boxes in classical mechanics! Whatever logical reduction from one theory to another is available involves the identification of mathematical constructs with others, not constructs to objects.

This would not be a consideration if the reductionist program could work. But the program will not work, and so we cannot use those fundamental parameters as defining features of reality, if the theories are interpreted syntactically. Suppose we represent an electron in a potential field as satisfying the Schrödinger equation:

$$H(q, m; \mathbf{r})\, \psi = e^{-iH(q, m; \mathbf{r})t}\, \psi$$

The electron is identified as the thing that has the charge q and mass m that parameterises the Hamiltonian H. The electron is not in the equation! It appears on an *interpretative* level. The logical system in which the equation is expressed can be satisfied by models in which the bearers of these properties *also* have properties consistent with others attributable to electrons. It can be satisfied also by 'electrons' that do not. For reasons similar to those mentioned above concerning normal things (section 1), there are no syntactical criteria for characterising electronhood.

Section 3: Scientific Realism: in Search of a Criterion

Theories, considered as syntactical constructions, lack the ability to express our ontological constructions, for the manifest and the microscopic alike. This should not be surprising if we reject the logical constructivism that characterises early neo-positivism, whereby the objects of scientific knowledge are constructions from sense data. In the absence of a successful theory of experience along these lines, it is to be expected that any syntactical representation of experience is necessarily incomplete. There just is not room there, in the syntax, for our many levels of attitudes and meta-attitudes.

This is clearly seen in science textbooks and monographs. Figures and equations do not appear without captions. If they did, they could not be understood. There will be those inclined to think that the captions are in principle dispensable, and act as elliptical inscriptions of syntactically impeccable assertions. That is not so. We can write a Hamiltonian for a 'hydrogen atom', but as Cartwright notes [1983: 137], the isolated hydrogen atom does not occur in nature; an isolated atom is a mental construct. The only 'real' Hamiltonian, if there is one, is for the universe. And it does no good to say that in treating the hydrogen atom in isolation, we are approximating its real condition for an atom far away from others. For to do so is to admit that we need interpretation if theories are to be applied.

Scientific reality, wherever it is, is in what is said about those equations and figures. "We cannot scientifically investigate reality as such...[it] is so complex that global scientific representations of too big or too complex portions of it are elusive" [Tontini 1999: I.1]. Talk of real things must inhere in interpretations. We cannot rely on our theories to provide us with descriptions of the universe's raw material. Thus, what Hacking calls 'realism about theories' [1983: 27] is refuted, unless interpretations are admitted as integral parts of theories. The latter move would give away the strongly foundational role of equations that is, as far as I can tell, the most attractive motivation for theory realism. The mathematical formulations of theories cannot provide criteria for the reality of specific things in a more specific and unproblematic way than can our talk of normal things.

As well, theories come and go with time. When theories evolve into others, some features always disappear. Yet much of the interpretation survives and can still be comprehended by newer theories; for example, while the modern view of atoms is very different from that of the nineteenth century, references to atoms in nineteenth-century chemical research can still be applied to their proxies, modern atoms, without change. The history of science convinces many philosophers that we can anticipate for any particular theory that it will eventually turn out to be false in some detail. Whether or not this is the case, the motivation for realism requires a meeting-ground for those nineteenth-century and modern atoms. A plausible and historically informed construal requires a way to understand their relationship.

At the same time, it seems that being manipulable in some logical system must be part of a common-sensical construal of the empirically real. For example, common household items can be combined using ordinary arithmetic without fail. As a minimum, real individuals must somehow be distinguishable from others. Syntactic encoding will not do for defining the real, but that which cannot be seen in basic logical relations with something else must be, in Kant's (translated) phrase, "nothing to us". Whatever is not subject to some sort of syntactic encoding must be a noumenon.

What is more, the ability to define relations between things is symptomatic of their existence. A posit that is successfully formulated in terms of other, more easily understood things, may be a candidate, so to speak, for objecthood. Those relations that can be established with other things serve as evidence of its presence. This applies even in the case of the macroscopic; consider Del Re's example of a mountain. We do not know it 'directly'; we perceive "either a remote, intangible image, or parts...from which we reconstruct the whole" [1998: B.4]. He argues that similarly, we have no direct experience of the planet itself.

In general metaphysics, then, we cannot obtain a convincing account of 'direct' experience with objects (again assuming the lack of a plausible logical constructivist position). Moreover, empirically, we literally see through a lens. Our sense experience is selective; it is adapted to certain kinds of detection. I look to successful macroscopic inferences as exemplars of the real.

I want to avoid the horrible complexities, here, of separating observer-dependent from observer-independent components of true judgements, and will only note that the limits of epistemic access for the macroscopic place a ceiling on reasonable requirements for a convincing scientific realist position. Exactly where those limits are to be drawn is a perplexing metaphysical problem. Van Fraassen, in establishing his anti-realist position, admits as much [1980: 16]. He seems to favour a construal of 'observation' that privileges unaided perception, saying that the moons of Jupiter, though requiring a telescope to be seen, could nonetheless be seen unaided for those close enough. The discussion above leads to the conclusion that this will not do because 'observation' of anything of sufficient complexity to warrant scientific study always involves extrapolations.

Section 4: How to Reconcile Apparently Conflicting Commitments for Scientific Realism: Common Sense Realism

I shall follow Hacking and Cartwright in ducking the issue of a characterisation of requirements for a *general* scientific realist position. I hope only that my discussion of chemical practise will be sufficiently convincing that such might be possible. Again it is worthwhile to note that a theme of this thesis is an emphasis on small-scale judgements in chemistry as opposed to theories.

The obvious move seems to be the one taken by Hacking: to look at entities rather than at theories as such to find the real. He finds the manipulability of entities, if not identical to their reality, the only reliable symptom of their reality [1984: 258-259]. We must be careful, though, in what we think 'manipulability' consists in: as with 'observation', this sort of word is unclear enough to lead to difficulties in assessing the relative merits of realist and anti-realist positions. Also, this distinction, between believing in theories and believing in entities, is not entirely clear. Psillos insists that we know entities, if at all, through their relations.

> What makes electrons different from, say, neutrinos is that they have different properties, and obey different laws. One should rely on these theoretical descriptions in order to manipulate these entities effectively and exploit their causal powers [1999: 256].

This extends the point made earlier concerning 'direct access' to observables. There is no understanding of any entity *entirely* divorced from its relations to other things.

We are left with a vexed question here. Seemingly, we are saddled with theories in our explication of existence claims, but we cannot prime the reality pump that reductionism initially seems to promise us. I suggest that we need to look to interpretations used in scientific practise in order to understand the correct place of theory here. We can look for relative coherence of inferences from theory applied at numerous levels, with much reasoning done *outside* the formal systems proper to science. Realism requires an account of theory's role in managing these inferences. Psillos tells us:

> ...scientific realism is not an all-or-nothing doctrine, in the sense that one must either believe to an equal degree everything a scientific theory predicates of the world or else believe in nothing but (perhaps) observable phenomena [Psillos 1999: 161].

Our commitments to various aspects of theories must differ, Psillos urges, but evidence got for parts of those theories may point us to reasonable belief in phenomena whose features agree with entailments of those parts. And those parts sometimes persist through theory-change.

We need to extend Hacking's account of what ought to incline belief in entities. We have got some clues by considering general realism and normal things. Commitment to the existence of entities requires acceptance of a systematic web of relations in which they lie. Let us admit that arguments for realism will not be elegant on the present view. As suggested earlier, it seems that the correct approach lies with the features of our encounters with normal things which are not immediately manifest. As earlier noted, I have no intention of doubting the existence of normal things. And there are common-sense lines of reasoning concerning unseen normal things strikingly similar (though far less detailed and nuanced) to lines of reasoning concerning atoms and molecules, actually used in synthetic chemistry.

Not all realists will necessarily be sympathetic to considering scientific realism from the point of view I take here. Norton-Smith opines

> ...there is no reason *a priori* to assume that the items needed in an explanatory theory will be like the entities of which we have experience. Consequently, we ought not to build any analogical requirement into the specification of a viable form of realism [1981: 38].

Newton-Smith defends theory-realism, which is rejected above. Nonetheless, the discussion here is not necessarily incompatible with these particular remarks. Attempts for general criterion of realism are foresworn. It might be that in some cases, better evidence for entities contained in some interpretations of *parts* of theories is got by considering formalisms and their empirical consequences than individual entities. Indeed, it might be that the basic formalism, with differences in interpretative references, survives theory-change better than do the entities. For the present work, though, the most solid evidence for atoms and molecules comes not from interpretations of theories, but in their resemblances to normal things in causal sequences that lead to macroscopic observations. The present thesis is that this evidence is solid enough for that conclusion alone. The possibility is left open for a more general realist account that subsumes the argumentative strategy used here whilst accepting Newton-Smith's claims.

The position taken here bears some resemblance to the 'structural realism' proposed by John Worrall [1989]. Worrall's article looks in detail at studies in diffraction before and after the introduction of Maxwell's equations and the ensuing crisis of interpretation faced by the physicists of the time (1860's). Worrall claims we should be realists about mathematical formalism retained through theory-change. This resembles the present argumentative strategy in that the arguments refer to findings retained through theory-change and subsumed in new formalisms. Crucially, though, the arguments differ in that the present account relies upon our ability to manipulate symbols *without* use of mathematical formalism, guided by judgements proper to normal things.

Among prominent critics of realism, Arthur Fine's work in particular is in very sharp contrast to the present one. For Fine, we have an essentially unanalysable concept of truth: we should understand scientific posits as defined by their place in scientific practise, according to "standard rules of usage" [1984: 274]. Essentially, Fine's 'natural ontological attitude' tells us not to analyse scientific knowing. This really forswears the enterprise of philosophy of science. It creates an artificial barrier between realms of knowledge. Suppose a new field of study, chemical education, creates new faculties in universities with trained chemists cooperating with philosophers. What if they produce a document like this one; should we believe the claims in that document? I fail to see the point of claims made by Fine and others concerning autonomy of various intellectual practises. They seem to be about academic turf, not science or philosophy.

In fact, the analogical resemblances of molecules to normal things are strengthened in their power of conviction by accessibility to common sense and by actual historical chapters in chemistry. These resemblances, I repeat, are amply understood in numerous contexts that never invoke a formalised, mathematical theory. The following are discussed in detail in the next chapter but a considerably longer list could be generated without much effort.

I. Molecules resemble normal things in numerous spatial aspects. Operations on molecules routinely are done assuming regular spatial intuition. Moreover, many classifications of molecules and their chemical properties rely essentially on those intuitions. Some of these are explored in the next chapter.

II. The success of formal drawings of molecules as a tool in chemistry is well motivated by molecular realism; it has no motivation from fundamental theory.

III. The near-total coherence between determinations of compound identification from classical methods and those from atomic/molecular spectra (as opposed to the *contents* of spectra) is also unmotivated by theory and thus is a sheer coincidence without asserting atomic and molecular realism. Moreover, spatial intuition can be used successfully to interpret spectra on unknown materials, using drawings as a tool.

These contentions will be supported by the following two chapters. I ask with Del Re, if there is no robust sense in which molecules and their structures are real,

> why do all experiments give results in agreement with the claim that molecules have a structure corresponding to that model, in the analogical sense discussed above? [1998: C.1]

Again, those experiments are often motivated by humble spatial intuition, not theory. The sort of reasoning here investigated is that giving evidence for "entities believed to exist because of analogical and logical evidence similar in nature to that by which a judge may condemn a man as the author of a crime" [1998: A.1]. As a consequence of the numerous analogical resemblances I present in current practise and history of chemistry, continued doubt would lead to doubt as to the utility of similar lines of reasoning to reach conclusions regarding normal things. And that doubt is axiomatically ruled out here.

CHAPTER 3: COHERENCE OF CHEMICAL METHODS OF INFERENCE IN PRACTISE

This chapter supplies the detail of current practises in chemistry which exemplify the features I claim properly lead to a realist conclusion for atoms and molecules. For those unfamiliar with current philosophy of chemistry (a small fraction of total philosophy of science) some of the features of synthetic chemistry might seem surprising. A cursory look at this science is necessary in order to look at the implications for realism in chemistry.

At this point it is useful to make a distinction between three forms of synthetic chemistry. The contemporary practise of 'neo-classical synthesis' is to be understood as the synthesis chiefly of one target substance at a time, through manipulations involving mixing and change of environment in substances already available. These are often similar to the methods of chemists working before the beginnings of modern physics; this sort of practise is termed 'classical synthesis'. Finally, 'combinatorial chemistry' denotes the recent practise of preparing very large numbers of distinct substances simultaneously.

Luckily for our present endeavour, even a cursory look at synthetic chemistry reveals much about the interplay of theory and experiment that is its practise. The discussion will be confined to what is known as *synthetic organic chemistry* – chemistry chiefly of molecules involving chains of carbon atoms[1]. For details, I draw on a series of syntheses in which I personally participated, using neo-classical methods of chemical synthesis [Merrin *et. al.* 1992]. The connections to the claims that conclude the previous chapter are made following details of technique.

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[1] The overall aims and methods of the other major branch, synthetic inorganic chemistry, are very similar.

Section 1: Synthetic Chemistry: Grand Counterexample to Received Views in Philosophy of Science

The science of chemistry is popularly known for the production of new substances: chemical synthesis. Indeed this activity comprises the bulk of institutional chemistry research [Schummer 1997: I.2.]. It is the royal counterexample to the oft-uttered claim that science is a search for new and better theories; numerous features of the practise are highly distorted if seen as a search specifically for theories. Rather, the synthetic chemists want to make new substances. According to Joachim Schummer's figures, chemists synthesised 1.3 million new ones in 1996 [1997: I. 2.].

This figure is bound to rise dramatically with the advent of *combinatorial* chemistry, the science of synthesising large numbers of substances at once. According to a review article of 1996, methods have been developed that allow the production of on the order of 100,000 distinct substances [Thompson and Ellman 1996: 557] in one experiment. To the casual observer such a figure is almost incredible. Combinatorial chemistry is a new field – the *Journal of Combinatorial Chemistry* first appeared in 1999 – and thus is a live example of scientific advance.

We can start our look at synthetic chemistry by looking at Schummer's 'flowchart' illustrating the motivations and sources for synthetic chemistry (figure 1). Chemists, working from a variety of 'background methods', work to produce substances for internal aims, improving present methods, and external aims, such as the testing of new medicines. The chart is in parallel to a similar kind often found in philosophy of science, but therein theories, not substances, are manufactured. That is not what the synthetic chemists are doing; what they are doing is best understood by looking at the ends of the arrows. The 'external aims' can include, as mentioned, the building of pharmaceutical agents. The internal aims can include numerous considerations towards an improved science. In the preparation of substances, chemists can discover new general *methods* of producing others, provide starting *materials* for others, or investigate reaction mechanisms of particular chemical reactions[2].

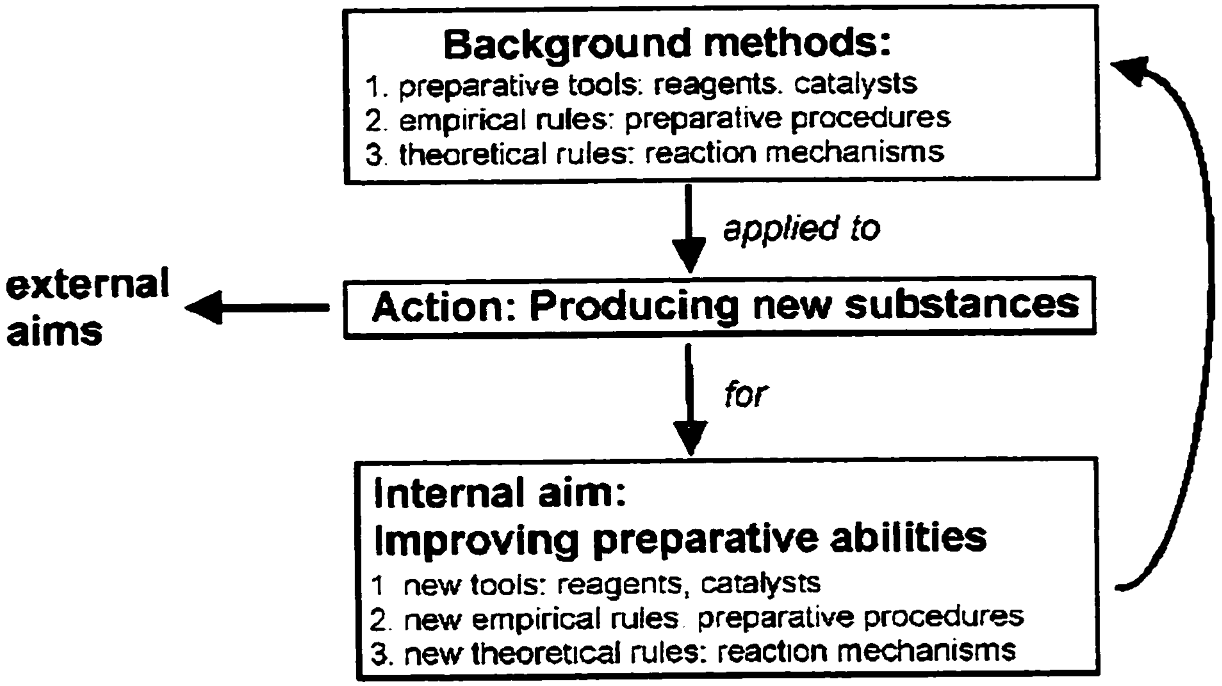

Figure 1: Schummer's flowchart of synthetic chemistry. Reproduced directly from Schummer 1997.

Synthesis in all forms is utterly dependent on the ability to draw *molecules* and examine bits of those drawings, in relative isolation from others, in the light of general principles that predict their behaviours. In the domain of synthesis, the general principles usually take the form of guidelines only, or else highly approximate use of physical-chemical theory. I take it that most working chemists would agree that the bulk of instruction in synthetic chemistry is in the interpretation of these drawings, together with

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[2] A *chemical reaction* is the transformation of one or more substances (*reactants*) to one or more others (*products*). A *reaction mechanism* is a detailed account of the steps in such a process.

consideration of purported physical correlates. The instrument of interpretation is in practise an informal cluster of ideas Del Re calls 'valency theory' [1998: B.1]. Description of this instrument in the next section shall supplies many considerations bearing on the reality of molecules.

While synthetic chemists are not in the business of confirming fundamental physical theory directly, they nonetheless have an interest in exploring regularities of chemistry. In particular, chemists need not be interested in a specific compound, but in a series of them. This is seen in the literature of neo-classical synthesis (for example, figure 4). Efficiency's sake dictates that we adapt synthetic successes in obtaining one molecule to its close cousins. Furthermore, the examination of numerous similar compounds can provide information regarding reaction mechanisms and the fine details of structural variation. These are the elements of physical chemistry, which studies the dynamics of molecules, again taking for granted the terms of neo-classical synthesis. As well, and of particular pertinence to the interest in combinatorial chemistry, is the interest in testing series of compounds for possible biological activity[3].

Neo-classical synthesis prescribes purification and unambiguous product identification. Of frequent interest is the *optimisation* of syntheses, finding the most efficient method of production of a given molecule. Thus the mere identification of a desired product in a reaction mixture may give way to repeated trials, under now more narrowly identified parameters, to find such a method. Here is one sort of task that suggests methods approaching combinatorial ones; we can imagine running numerous

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[3] In neo-classical synthesis the paper of Merrin, *et. al.*, represents investigation of possible anti-carcinogens; recent monographs of combinatorial chemistry are replete with references to the rapid production of drug test series; see back covers of Terrett's *Combinatorial Chemistry* and Wilson and Czarnik's *Combinatorial Chemistry: Synthesis and Application*.

reaction mixtures, in parallel, to find the optimal one.

The neo-classical chemist, upon reaching a successful synthesis, will wish to characterise the product as much as possible. Numerous procedures will be performed on the compound, and collectively their outcomes serve to define the compound uniquely and to demonstrate the correctness of the chemists' assertions of its structure. Some of them, such as elemental analysis (the determination of the relative abundances of elements) can in principle be done by classical methods, mostly prequantum, but are in practise done by modern methods of microseparation and spectroscopy. There is one characterisation done literally according to the method of early modern chemistry: melting point determination[4]. Others are modern-physical in origin, including molecular spectra. Of particular interest is X-ray crystallography, which ultimately produces an image resembling drawings that chemists use. Obtaining such characterisations is the standard of publication in neo-classical chemistry[5]. The ideal is discovery of easy synthesis of compounds in purified form, with all standard characterisations done.

Section 2: The 'Theory' of Synthetic Chemistry

It is mentioned above that chemists have all sorts of ways to make inferences that are independent of assumptions proper to fundamental theory (quantum mechanics). For definiteness, this section presents an account at the ways in which chemists' logic licences such inferences. This reasoning tends to be of a highly qualitative kind in synthesis laboratories. The details cannot be captured with mathematical equations so it

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[4] One heats the compound, watching it and a thermometer under a microscope. It is interesting to note that that theoretical calculations of melting points are unable accurately to predict measured melting points due to the enormous computational resources required for such a detailed calculation.

will be clear that a comprehensive presentation would be difficult to achieve. Really, the inferential practises in question seem often to be implicit in the shared folklore of chemists, pronounced in detail relatively rarely. While some bits and pieces are to be found here and there in elementary textbooks, some rational reconstruction is needed to provide the reader an opportunity to work out the implications of claims regarding chemical practise.

Synthetic chemistry overwhelmingly deals in molecules and immediate derivatives as their objects of study as individual objects. Molecules are assumed to have an identity separate from their surroundings. The posited isolation is subject to the same considerations as Cartwright's for that of hydrogen atoms, which considerations thus apply to derivative practical theories as well as fundamental ones. For example, it is usual in chemistry to denote water by 'H_2O'. However, a glass of water, say, must be understood as containing not only H_2O but also H_3O^+, OH^-, and numerous aggregates of those three. This might seem to lead away from molecular realism, but it is clear that the same system can be modelled by macroscopic objects: there is nothing proper to molecules' 'scientific' status in this sort of indeterminacy.

The drawings used by synthetic chemists represent molecules as consisting of atoms placed in more or less fixed relative positions. Consider butane as a prototype. Its standard chemical representation, its *Lewis structure*, is shown in figure 2a. The positionings implied by the figure are not to be understood literally; standard conventions assign the shape shown in figure 2b (the wedges are understood as being nearer the viewer than the plane of the paper, and the dashes as farther). The molecular shape

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[5] In the case of synthesis of series of similar compounds, the chemists may elect to do a limited number of full analyses.

implied by the latter drawing *is* taken literally by chemists[6]. Now, because carbon atoms are limited in their usual geometric connections, it is possible to abbreviate the pictures to figure 2c, the 'condensed' formula of butane.

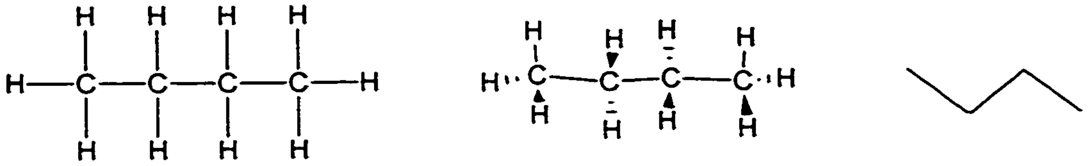

Figure 2: Three pictures of butane. 2a (left) is a Lewis structure. The C's are carbon atoms; the H's are hydrogen atoms. 2b (middle) shows the three-dimensional geometry of butane. The hydrogen atoms at the ends of the solid wedges are understood to be closer to the viewer than is the plane of the paper, the ones at the end of the dotted ones farther. 2c (right) shows the minimum picture needed to represent butane. The number of missing hydrogen atoms can be determined from position of each carbon atom in the chain (here two for the middle, three for the terminal carbon atoms of the chain).

Trained chemists can derive any of these drawings from the others in seconds using valency theory. Briefly, a limited number of connectivity possibilities are posited for each sort of atom, and geometry adjusts so as to minimise the interaction between electron pairs that correspond to directions about atoms. The possibilities follow a pattern corresponding to that of the periodic table of the elements, but which cannot be *predicted* from it. The details are to be seen in any elementary chemistry textbook, under the chapters dealing with the topics:

- Lewis structures
- VSEPR theory[7]
- periodic trends of atoms[8]
- acid/base reactions
- oxidation/reduction reactions
- organic chemistry

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[6] This technically is an oversimplification because it is expected that the angles in actual molecules follow those in Platonic solids only approximately.

[7] Valence-shell electron-pair repulsion theory. This is normally sufficient for all intents and purposes in organic chemistry; in other branches of synthetic chemistry things can be more complicated, and require use of more mathematical theory for rationalisation of structures. In those cases, though, the predictions of geometry are still got using rather low-level heuristics. Those that cannot be got so easily tend to be treated as brute empirical data.

[8] Based upon, cohering with, rationalised by, but not deductively inferred from, the periodic table [Scerri 1994].

The position of the element on the periodic table indicates how many bonds (to other atoms) are to be assigned. VSEPR theory and periodic trends indicates geometries. These ideas comprise the main part of valency theory. The study of acid/base, oxidation/reduction, and elementary organic reactions indicates which molecular fragments are expected to interact, and in what ways. More complex interactions as presented in advanced textbooks are typically elaborations of these.

The 'tetrahedral' placement of bonds about carbon atoms (four directions roughly forming the vertices of a tetrahedron) historically was proposed some forty years before modern physics[9]. This shape is in fact derivable from more fundamental theory – quantum-mechanical equations of motion and so on – in the most elementary cases only[10]. In other cases, the geometry cannot be motivated by fundamental theory – it is got from valency theory. As succinctly put by Del Re,

> ...the criteria of existence of molecules are provided by the building laws formulated in the theory of valency quite independently of the fact that quantum mechanical computations lead to the same molecules if the right input data and definitions are provided. [1998: B.1]

These techniques, it appears, would stay current even if fundamental theory were to change drastically, for these drawings are not to be understood as frozen objects: these shapes have numerous consequences in practise. For example,

> ...given six carbon atoms and six hydrogen atoms, the rules of valency predict 217 different molecules (and hence 217 different chemical substances) formed with the same atoms ('isomers'). ...[N]o chemist has any doubt that those 217 and only those 217 can be synthesised. [Del Re 1998: B.1]

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[9] Commented upon at the end of chapter 4, section 1.

[10] In those cases group-theoretical methods can be applied to transform high spatial symmetry in a molecule to symmetry in the equations of motion. Even then, when calculations are done on molecules those symmetries are always entered through input inferred from drawings.

The heuristic procedures described above allow the transfer of knowledge concerning certain molecules to relatively reliable ways of predicting behaviour of others. Many consequences arise, mainly through commonalties in molecular fragments. Certain fragments of organic molecules have histories of generations in chemistry[11], and there exist literal libraries devoted to the typical behaviour of such fragments. In fact, speaking relatively to what might be possible considering only the great diversity of chemical elements, a very small number of typical fragments dominate chemistry. These are commonly known as *functional groups*[12].

Noting that the individuation of atoms in definite positions violates quantum theory as standardly interpreted, we expect the drawings to be useful only if the atoms are highly localised in space in the quantum version of the molecule. This is indeed the case, and the result is that modern-physical effects can be treated, more or less, as perturbations in the more naïvely understood pattern of molecular evolution. Students become familiar with their behaviour at the intermediate stage of university chemistry, and drawings used by synthetic chemists are the same as in elementary textbooks. See figure 3.

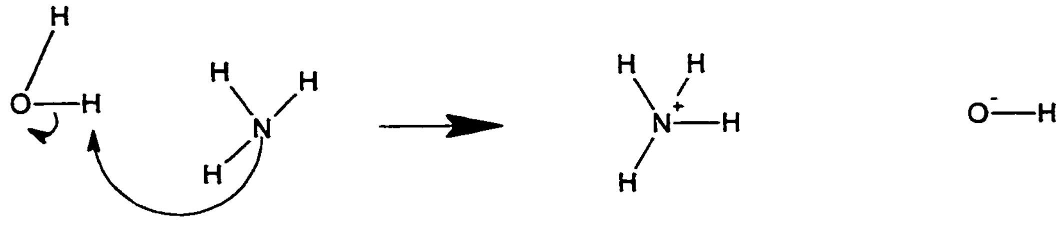

Figure 3: Arrows and lines used by synthetic organic chemists to show transitions from one molecule to another. Here the base ammonia (NH_3), a constituent of such household cleaners as Windex™, reacts with water (H_2O). The arrows show formal changes in electron associations. NH_4^+ (ammonium) and OH^- (hydroxide) are formed.

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[11] The beginnings of this work seem to have been crucial to the atomic debates of the 1800's: see chapter 4, section 1.

[12] I wish this to be understood in a broad sense, so all the commonly manipulated groups of chemistry will be termed here 'functional groups'. It is clear that synthetic chemistry is dominated by -H, -CC, -C=O, -NO, -NC, -NH, and -OH in various guises. For example, if one looks at a 'chemistry of transition metals' book, those groups are ubiquitous, and constantly employed without comment.

The letters show the positions of atoms. The arrows show the course of fragment rearrangement; formally, they represent the evolution of electrons of the molecules from certain associations to others.

This picture of the molecule is ubiquitous in organic chemistry, and is the stock-in-trade of neo-classical (organic) synthesis. Historically, it represents an improvement upon a less systematised version, after input from modern physics. It depends on the ability to accurately represent molecules in this way; the picture has proven astoundingly successful throughout the last century.

The attitude to idealisation exhibited here is notable. These principles are not all formalised, and chemists view a continuum of possible degrees of molecular isolation. I suggest that the ability to use chemists' drawings like photographs is symptomatic of realism. Our ability to jump out of the syntax – to be productive in the logico-mathematical sense – partakes of the same as the intuitions that guide our ordinary existence judgements. I explain with two elementary applications.

I. *The use of size as a criterion for judgements of likely reactivity.* The ketones $(CH_3)_2CO$ and $(CH_3CH_2)_2CO$ can both be converted to the corresponding alcohols $(CH_3)_2CHOH$ and $(CH_3CH_2)_2CHOH$ by a variety of processes. The same process is expected to work for both in virtually every case. Most importantly, though, it will be expected that the 'larger' ketone, $(CH_3CH_2)_2CO$, will always react slower. The reason is that the larger carbon chains in that case, CH_3CH_2, better block the reactive CO fragment than do the smaller fragments CH_3. No calculation necessary.

II. *The ability to predict number and nature of isomers straight from drawing of molecules.* Isomers are different molecules having the same number of atoms of each element – formally, rearrangements of each other. Schummer notes that there are clear visual criteria of isomerism for molecules [1996: 257-259] – the drawings are different! He gives the examples of butane (figure 2 above) and isobutane (figure 4). The very fact of isomerism has been given, historically, as a reason for believing in atoms and molecules (see next chapter). More to the present point, the activity of distinguishing molecules by looking at drawings is the same as detecting differences in, say, automobile designs, by looking at blueprints.

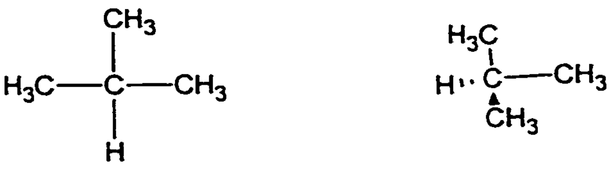

Figure 4: Isobutane. Rather than a chain of four carbon atoms there is a chain of three with one bonded to the middle. The figure on the left is an abbreviated Lewis structure; that on the right is a three-dimensional representation.

I focus here specifically on spatial reasoning since it seems so elementary and so elementarily analogous to dealings with normal things.

Section 3: Story of a synthesis

Consider now the actual job of going from one molecule to another. This discussion focuses on work, mentioned earlier, in which the author participated. The synthetic work described was done in the laboratory of Dr. Keith Vaughn in 1987-90, with some additional work after the author's departure. It is reported in the Merrin, *et. al.*, article of 1992. Everything was done using standard reagents (i.e., bought chemicals) available in the one-room laboratory.

Let us start with a transformation from the molecule in figure 5 to one of those in the series of figure 6. The difference between the molecules is clear, consisting in the difference of one fragment. There are standard methods of switching these fragments. Thus we straightforwardly can apply them to effect syntheses. We need reaction conditions that allow for the desired modifications to take place, and not others. Furthermore, we want to be able to identify, purify, or otherwise manipulate the product. In practice, this work is a trial-and-error process, ruled by numerous practical factors and constrained by chemical folklore, particularly the common stock of knowledge of functional groups' behaviour.

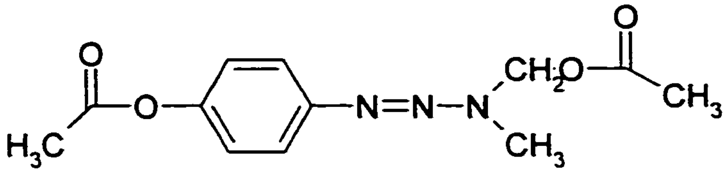

Figure 5: Starting material for the syntheses of Merrin *et. al.* [1991]. As usual in the literature, numerous abbreviations are used. For example, the benzene ring (hexagon near the left) stands for a specific cluster of carbon and hydrogen atoms. The structure features numerous abbreviations for various well-known fragments. The fragment in the top right (led by 'O', ending with CH_3) is referred to as '-OAc' in the text.

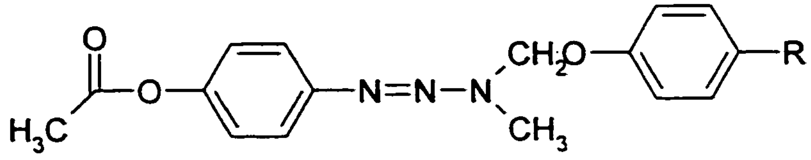

Figure 6: Main products in the syntheses of Merrin *et. al.* [1991] Reproduces structure 2 of that reference [page 144]. The '-R' stands for the various products obtained in this series. 6a: '-OCH_3', 6b: '-CH_3', 6c: '-H', 6d: '-Cl', 6e: 'Br', 6f: '-COO', 6g: '-CN', 6h: 'NO_2'. Together with the adjacent benzene ring and oxygen atom, it is referred to as '-OPhR' in the text.

In the case of the syntheses under consideration, the fragments required to replace the fragment '-OAc' in figure 5 were on hand in laboratory *reagents*, chemicals with a proven track record of producing those fragments. This 'starting material' was itself synthesed using a method perfected and published by the senior author years earlier. Thereafter we proceeded in numerous ways to induce the relevant fragments to rearrange as desired, using many of the methods of our less informed forebears of the nineteenth century: the dissolving of solids, the mixing and boiling of liquids. This is the source of the neologism 'neo-classical synthesis'.

Comparing figures 5 and 6, it is clear what we were doing. In each case an '-OAc' fragment was replaced by an '-OPhR' fragment, where 'R' stands for one of a variety of carbon-containing groups. For a chemist – based on valency theory – the route is clear. We need a way to remove the -OAc. This was done by using a strong acid, sodium hydride. The reason for doing this is to turn '–OAc' into '-HOAc', which is readily removable because of the stability of HOAc molecules (acetic acid, i.e. vinegar) and their strong tendency to leave the reaction mixture for the solvents tried. When the acetic acid molecule escapes, the way is clear for the incoming 'O'-containing fragment. In each case, the fragment was furnished by the corresponding 'phenol', HOPhR.

We should note that when chemists refer to fragments and their various combining possibilities, they do not distinguish between certain minor variants. So OAc^- (acetate) and HOAc (acetic acid) are regarded as basically the same, because the H atom in the latter is labile, that is, easy to remove and restore, in the form H^+. The ready removal and reintroduction of H^+ from O bonded to C is one of a short list of ubiquitous chemical phenomena that animate chemical synthesis in all its branches.

It is helpful to inquire as to why chemists are so sure this sort of procedure is likely to work. It is that '-OAc' fragments are relevantly similar to '-OPhR'. As with some other philosophical issues that arise in this thesis, similarity as such will not be explored. The sort of similarity to which the neo-classical chemist appeals in this case is strictly *spatial*; the two sorts of fragments are taken to have the same *shape* around the 'O' atom. Here we have another example of scientists jumping out of the syntax of the formal theory – or more precisely, ignoring it. We expect that compounds with similar structure (figure 6) will be synthesised by similar conditions. But there is no theorem of quantum theory that shows this must work; this sort of understanding is expressed in words, not in a mathematical language. This is an entirely prequantum understanding – an understanding of chemical fragments as being like blocks of Lego™.

The course of syntheses is not dictated by theory. There are no calculations telling chemists, say, whether boiling a sample for an hour, or an hour-and-a-half, is optimal in terms of product yield. It is of great consequence that the calculations of molecular wavefunctions from theory are of insufficient accuracy to provide detailed practical guidance to synthetic practise, owing to the incredible computational resources required. It is only in relatively recent times that university chemistry departments even have required detailed study of quantum theory for undergraduates. In the practical attitude appropriate to synthesis, quantum theory provides guidelines only. Theoretical chemists, too, speak in their language.

Therefore chemists proceed by trial and error, informed by previous experience. Laboratory solvents, many in use by the nineteenth-century chemists, have been highly standard for generations. The specific laboratory conditions are determined largely by previous experience in synthesising similar compounds. In practise, these can be quite capricious. Adjustment of conditions can be by changing solvents, reaction times, temperatures.

Methods of trial-and-error also rule in classical methods of product identification[13]. Samples can be removed from reaction mixtures according to various schedules of time in order to compare compositions as a function of time. A key classical method is thin-layer chromatography. Therein, a plate of a material resembling photographic film is 'spotted' (treated with tiny drops) from the reaction mixture(s) and pure starting material. Those spots, observable under ultraviolet light, will move, showing by the comparisons of velocities the presence of a new substance (or several). By comparing films prepared at various times, we can establish roughly when no further reaction will occur. This method was applied liberally in the syntheses reported upon

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[13] This task is technically *analytical*, not synthetic chemistry. Synthetic chemists tend to employ only well established methods of analysis; folks who work to improve these methods are called 'analytical chemists'.

here.

We can note in passing that this completely classical method of analysis is fully analogous to certain operations on macroscopic stuff. It is possible to mix normal things, like salt and water, and devise methods that will show us when the dissolution is complete. We could even survey people as to the subjective saltiness of the water at given time intervals, and assume that the salt is fully dissolved when there is no difference in taste as given by a statistical analysis of the surveys. Chromatography relies on this principle, but samples the molecules directly.

Another sort, *column chromatography*, was used to separate reaction mixtures and ultimately to isolate products. In this method, the contents of a flask are poured down a column of porous material from above. As with thin films, different substances have different velocities through the various materials usable for these columns. The various 'fractions' (selected samples from the bottom of the column) can again be subjected to the thin-film treatment to verify product separation. For purposes of product isolation in the cited experiments, these fractions were evaporated. Ultimately crystals of the products were got from the fractions.

Reflection on chromatography does not, to be sure, support molecular realism in detail. At best it shows that *discrete substances* exist in the mixture which is separated[14]. There is no coherent way of thinking of the mixtures as an undifferentiated mass. Historically, chemists explained the phenomenon in terms of molecular realism from an initially skeptical or at least cautious point of view, as we will see in the next chapter. This realism is no showpiece or theoretical add-on required for a tendentious philosophy; it is a working presumption with consequences. Any alternative one will have to tell us why, if molecular realism is to be rejected, that substances exhibit coherence with common-sense spatial reasoning.

Section 4: The Significance of Molecular Spectra

If some product detection methods are prequantum, some are anything but. The tool of choice is spectroscopy, the use of spectra to identify molecular features. And the miracle of chemistry is that the presence of functional groups can be *highly* reliably correlated with common patterns of spectra, on instruments available for routine use by researchers and students alike. The issue for philosophy of chemistry suggested here is a fresh consideration of the implications for molecular realism that is suggested by this multileveled system of correlations with the presence of well-studied molecular fragments.

Certainly a certain attitude to molecular realism is suggested by practise of chemists' use of spectroscopy, sometimes glib to the point of crudity. Let us consider spectroscopy's most powerful tool for synthetic chemists, proton nuclear magnetic resonance spectra (NMR). These were available for routine use of individual scientists at the time of the work reported upon here (but the samples shown below were done with an instrument of higher precision following the syntheses). Not present in the write-up of Merrin *et. al.* which we have been considering is a description of a technique of product detection using such spectra:

> (i) Be sure, based on previous knowledge, that the spectrum for the precursor molecule is right.
> (ii) Attempt a synthesis under conditions expected to possibly work with available materials.

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[14] These discrete substances have come to be known as 'chemical atoms'.

(iii) Allow the reaction to run for a while, and take a spectrum of the reaction mixture. Overlap this spectrum with that of the precursor, and *hold it up to the light*. An appearance of a small difference, with most of the pattern intact, indicates change, though not necessarily to the desired product.
(iv) (looking at figures 5 and 6) Where the unchanged part of the pattern is plausibly assigned to the unchanged part of the molecule, the desired product is possibly indicated. We can then check if the patterns expected of the new fragments appear.

In practise, the assumption of realism is made in product identification by this method. Compare the proton NMR peaks for the target molecules 6a and 6b (table below). The difference of one peak, with others substantially the same (and substantially the same as the peak locations in the starting material of figure 5 excepting -OAc), is attributed to the difference of fragments. Chemists' confidence that this can reliably be done is underscored by the coherence of the spectra with the expectations raised by literally construing the geometry of the molecule. The instrument can, for example, confirm findings got in the past using wholly classical methods of analysis. It would be a routine matter to extend demonstration of coherence to molecular geometry by further examples.

compound	fragments and peaks substantially the same (units: ppm, temperature 20°C, solvent CDCl)					different fragment
	left CH_3O	left ring	NCH_3	NCH_2	right ring	R
figure 6a	3.91	8.03-7.41	3.29	5.66	6.95-6.80	3.75 (OCH_3)
figure 6b	3.91	8.03-7.43	3.29	5.69	7.07-6.83	2.28 (CH_3)

Note the similarity to chromatography in terms of practical interpretation in the use of this method. Like chromatography, we can understand this approach to detecting product formation without understanding the underlying principles (hyperfine spectrum structure) that are proper to the construction of the instrument. The quantum-mechanical principles required to interpret spectra are of course alien to the understanding of the early chemists, yet they would have no problem using NMR as a 'black-box' tool – certain peaks correspond to certain functional groups. Chemists today routinely employ this method, often with the dimmest understanding of the physical principles underlying the instrument.

There are numerous other sorts of spectra in routine use by chemists. Some, such as infrared spectra, tend unlike NMR spectra to mark small differences in molecules with radical changes in the spectrum and retention of only a few key features. On the other hand, it may be surprising that spectra should ever correlate strongly with molecular structure. These correlations can be predicted in theory, but only using the assumption that the relevant signal-carriers (hydrogen nuclei, in the case of proton NMR) are in the positions predicted by drawings. The structure of the signals is comprehensible only with the independently gained knowledge of molecular reality, because the equations of spin motion do not furnish any natural theoretical constructs for the relative positions of hydrogen atoms.

Concerning spectra, I must say that my bias is clear and unabashed: spectra are the proof of a compound's presence. (This is the same as the bias of astronomical spectra researchers, but perhaps better supported since we have the stuff of chemical spectra at hand.) Chemistry operates under constraints that from one point of view are stringent. There are no *truly* exotic molecules: they are all made of atoms. Within this framework, we reach the conclusions of molecular structure by coherence of molecular spectra. Circumstances that would render spectra ambiguous as between structures are easy to rule out under careful study. In practise then, spectra are conclusive. They are the fingerprints of molecules.

As I noted earlier, we can have an understanding of the outcome of spectra, correlated with molecular structure, independent of understanding of the spectrometer. The coherence of evidence leads us (or at least, the chemists) to the conclusion that certain fragments are present in given combinations. This does not have to lead to a commitment to the truth of any *particular* theory, only to the truth of a family of theories – the ones that do not deny the observations. In an enormous number of particular cases – thousands every day – researchers are lead to the presence of literal bits of matter. The reasoning they employ, we have seen, does not require any final picture of the molecule in all its attributes. There is no inference to the truth of any particular theory, but inferences to the presence of molecules, informed by theory, yet preservable in the face of theory-change.

This chapter has presented a *post hoc* viewpoint of molecular reality as a working hypothesis in synthetic chemistry, relying on abductive judgements which weigh crucially in contemporary practise. The body of data under consideration is completed in the next chapter, consisting of a short series of snapshots in the evolution of this hypothesis in chemical history.

CHAPTER 4: HISTORICAL ILLUSTRATIONS: SYNTHETIC CHEMISTRY PAST AND PRESENT

The previous chapter presents some of the ways that contemporary chemists draw inferences concerning molecular structure, and how they bear on molecular realism. This chapter presents selection of topics bearing on molecular realism in historical perspective.

The growth in popularity of the molecular hypothesis in the nineteenth century saw ever-increasing use of arguments similar to those now in routine use which utilise features of atoms and molecules got by assuming an atomic/molecular realist position. These gained strength among chemists due to their apparent explanatory power, steadily gaining in scope. Their success in providing tools for chemists of increasing utility caused the anti-atomist arguments to lose professional popularity in many places. Numerous historical discussions regarding this issue mirror contemporary argument concerning scientific realism. Section 1 here discusses Dalton's proposal and its context, followed by selected episodes in this discussion in which the spatial properties of molecules provided explanations for observed macroscopic behaviour: the substitution of dissimilar elements for one another, the reactive properties of benzene, and the optical activity of substances.

It is widely acknowledged that the work of Jean Perrin in the early 1900's, along with novel discoveries of modern physics, spelled the end of anti-atomism as a serious metaphysical discussion in chemistry. His own work in counting molecules through the phenomenon of Brownian motion[15] was celebrated for its painstaking precision and

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[15] Small pieces of pollen or other substances jiggle randomly in fluids.

ingenuity. As well, his writing represented a brilliant synthesis of the independent counting experiments of others. This synthesis is commented upon briefly in section 2.

Sections 3 and 4 describe some aspects of historical change in the practise of synthesis, as they relate to the issue of molecular realism. The transition from classical to neo-classical synthesis offers much of interest to this matter. Finally, a short description of the new practise of combinatorial chemistry is given. As a newly founded branch of synthesis it also offers some considerations of interest.

Section 1: Atomic Debates of the Nineteenth Century in Retrospect

Nineteenth-century chemistry began following widespread adoption of Antoine-Laurent Lavoisier's systemisation of chemical classification, which had spelled the end of the phlogiston era [Brock 1992: 121ff. Levere 2001: 79]. Lavoisier's work is frank in its lack of a clear conception of separate substances independent of observer's operations on them [Lavoisier 1965: 175-182]. He is agnostic as to the ultimate nature of the 'elements', which are pragmatically defined as those substances not separable with *available* means. Compounds were viewed as compounds of elements, the nature of such compounding unknown. Within this milieu there was plenty of scope for speculation concerning those natures Lavoisier left up to posterity to work out.

At this point it is useful to introduce the terminology of *chemical* and *physical* atoms, commonly used by the parties to the atomic debates and in contemporary discussion of them. The word 'atom' denotes indivisibility; chemical atoms of elements are not separable technologically (through 'chemical' means[16]) whereas physical atoms are literal little particles of matter which today's chemistry textbooks usually call simply 'atoms'. The distinction allows us easily to describe the pragmatic treatment of certain substances as basic, without a necessary connection to the metaphysical makeup of those substances (and is recognised as such by Lavoisier).

Chemical atomism gained hold of the mainstream of chemistry by the 1790's. Careful weighing of products and reactants seemed to show that elements, in forming a given compound, always combine with their weights in a definite proportion: there are a limited number of ratios of weights of different elements in the single or several compounds formed by any given set of elements. This finding was challenged most notably by Claude-Louis Berthollet, an early supporter of Lavoisier, on the basis of some of his elemental analyses of reaction mixtures [Brock 1992: 144-145, Rocke 1984: 6, 7]. His key opponent in this debate, Joseph-Louis Proust, concluded that Berthollet's findings were due to insufficient separation of the substances involved; Berthollet was analysing various amounts of different compounds rather than discrete substances [*ibid.*]. That interpretation is retained to this day[17].

The difficulty of achieving precise weighings and other experimental difficulties made it difficult for chemists to decide between the competing interpretations of the data. Nonetheless, by 1810 the doctrine of definite proportions was ascendant [Brock 1992: 145]. It may be said here that chemists perhaps could not help but be inclined in favour of definite proportions, for that doctrine at least offered the possibility of quantitative

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[16] In the contemporary age of nuclear technology this 'chemical' caveat is needed; there is a brief discussion on this matter at the close of section 2.

[17] It is now known that in some cases, Berthollet's view is the correct one. For example, certain minerals and glasses exhibit elemental proportions with some variability. However, this sort of substance is

comparisons, whereas Berthollet's view seemed to lead to a vacuum as far as this matter is concerned. So skepticism concerning chemical atoms seemed to die out quickly.

The British chemist John Dalton was working out his theory of *physical* atoms at about the same time, publishing the work that brought about his recognition in most of today's elementary chemistry textbooks as the founder of modern atomic theory. Dalton was impressed by findings concerning the combining powers of gases and noted that some of the observed regularities were consistent with particle models, provided the forces between the particles were assumed to vary with the *size* of the constituent particles [Brock 1992: 142]. One might get the impression from the textbooks that Dalton's ideas quickly achieved hegemony, but in truth the debate was just getting started, with no decisive victory one way or the other until Perrin's celebrated work one hundred years later.

Dalton assumes that for each element there is an ultimate, indivisible particle, tiny and spherical, a structureless incompressible body always with the same weight. This is a physical atom. Elements as macroscopic substances are comprised of collections of such atoms that behave as individuals [Dalton 1964: 163]. Compounds consist of what are now called molecules: literal aggregates of individual atoms in definite proportions. For example, one atom of hydrogen and one atom of oxygen form a molecule of water (modern: two of hydrogen, one of oxygen). Thus, each molecule of a given compound is of same weight. Where more than one compound can be prepared from two given elements, the compounds are held to consist of molecules with differing numbers of atoms. For example, Dalton includes (in modern notation) NO and NO_2 [165]. Since the

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relatively exotic and the vast majority of chemical substances always exhibit fixed proportions under usual conditions of experiment.

atoms of each given element are identical in weight, the law of definite proportions follows. The macroscopic ratios of atomic weights in compounds are the same as the ratio of the corresponding atoms of each molecule of a compound.

Dalton predicts specific ratios for the weights of any two atoms of different types (elements). However, the numbers of atoms supposed to be in molecules of compounds were in general selected by what are poorly motivated, if not entirely arbitrary simplicity rules [Rocke 1984: 35-36]. In any case, Dalton came quickly to be regarded as having at least provided a basis for a research program by providing a rationale, however incomplete, for formulae of compounds [39], and a conceptualisation of the way that matter can combine (also incomplete) [Brock 1992: 135].

It is clear that many chemists who used Dalton's ideas took an instrumentalist attitude to the theory [Rocke 1984: 57]. Numerous reasons are explored in the historical references [Rocke 1984, Brock 1992, Levere 2001, etc.] but for the present discussion we can note that the theory does not seem to have any measurable consequences other than relative weights. Moreover, there was for a long time much confusion regarding correct molecular weights [Brock 1992: 228-230]. The molecules were strictly hypothetical; they could not be used to affect things directly, as Hacking would like to see from entities purported to be real. The chemical atoms frequently were referred to variously as 'atoms', 'equivalents' or 'volumes', indicating ambivalence at best concerning Dalton's theory.

On the other hand, the theory did not actually contradict any established findings, so chemists were certainly entitled to speculate if they wanted, and Dalton's drawings had heuristic value for presenting results. For us as for the chemists of his time, Dalton's ideas provide a useful articulation of molecular realism, a sort of generic minimum for physical atomism with its implications.

Contemporaneous with Dalton, a clue was provided for the mechanisms of chemical combinations through the new science of electrochemistry. The invention of the electrical battery in 1800, constructed from "alternating disks of metals and blotting paper moistened with a salt solution, " [Levere 2001: 87], clearly implicated electricity as a driving force behind chemical action. A new means was provided for the separation of substances, and soon new elements were discovered [90]. Electrochemistry proved fruitful not only in the finding of regularities among the behaviour of various substances, but also in inspiring classification schemes for those behaviours based on electrochemical properties of substances.

Celebrated studies from eminent electrochemist Jöns Jacob Berzelius provided a new consensus in European chemistry by the 1830's concerning the classification of substances [Levere 2001: 101]. Berzelius and other electrochemists systematically studied various radicals – compounds that retain their identity through series of reactions (now called variously fragments, functional groups, and polyatomic ions). He classified the behaviour of elements and radicals alike in terms of their electrochemical properties [92], and introduced notations for substances and reactions recognisably similar to the modern ones [Brock 1992: 212-213]. Within this milieu, knowledge of observed regularities in chemical reactivity rapidly increased, and led some chemists to seek explanatory hypotheses through physical atomism.

Berzelius, at the peak of his fame in the 1830's, was engaged in a lively correspondence with the younger August Laurent concerning the latter's hypothesis of *atomic positioning within molecules* as a factor, competing with electrochemical behaviour, which determined the course of certain reactions [Levere 2001: 101-103]. Laurent used the concept of positioning to explain the reactive regularities of differing substances through similarities of positioning, and differences in properties through differences in positioning.

It was Berzelius who had coined the term 'isomerism' for the existence of different compounds from the same combinations of elements, and Laurent explained this, as well as the phenomena of *allotropy* and *crystal isomorphism*, by positing physical atoms. Allotropes, different forms of the same element, result from different arrangements of the same sorts of atoms. Isomers similarly result from positional permutation of the atoms. Finally, isomorphic crystals – minerals of drastically different chemical composition but similar shapes – result from the *same* arrangement of *different* atoms or molecular fragments.

As well, Laurent explained some cases of similar reactivity of compounds of rather different composition through positioning arguments. For example, trichloroacetic acid, a compound heavy in the element chlorine, has, under some conditions, very similar reactivity as acetic acid. (Moreover, they smell the same to me.) Laurent argued that in substituting chlorine (Cl) for hydrogen (H) in acetic acid, trichloroacetic acid resulted from replacement of H for Cl in the same *physical positions* of the molecule. Figure 1 shows modern structures for these molecules.

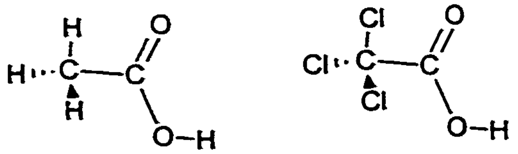

Figure 1: Acetic (left) and trichloroacetic acid (right).

Laurent did not immediately gain a consensus in favour of his views, and much work remained until his sort of explanatory argument began to gain real ascendancy in chemistry. As data mounted and agreement was reached on previously disputed atomic weights [Levere 2001: 114-116], systematic knowledge grew, as famously embodied in the periodic system first advanced by Dimitri Mendeléev in the 1860's [117]. The rapid growth of systematic classification lead to Peircian irritation for an explanation, and numerous chemists sought a scratching-post within molecular realism.

Molecular realism remained a controversial hypothesis in chemistry up to the time of Perrin, but it achieved numerous triumphs that put its detractors on the defensive. Laurant's work was a major inspiration for the research program of type theory. For the first time, chemists began to draw pictures with links between 'types' – our modern functional groups [Brock 1992: 218-220, Crosland 1962: 324].

One of the best-known of type theory's achievements, Friedrich Kekulé's (1866) rationalisation of benzene's (C_6H_6) behaviour by assuming it is made of a *closed ring* of six carbon atoms, is discussed in detail in the Del Re article (as well as in virtually all standard historical surveys such as those of Brock [1992] and of Levere [2001]). Briefly, if bromine (Br) is substituted twice for hydrogen (H), only three substitution products result; that only three twice-substituted products are possible given this hypothesis is clear (figure 2).

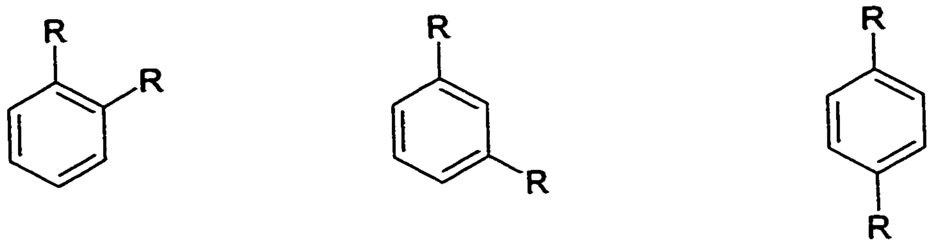

Figure 2: Assuming that the carbon atoms in benzene form a closed ring and are mutually equivalent, only three possible bisubstitution products can result, as seen in the macroscopic observations.

Another discovery of interest for the present discussion is the explanation of *optical activity* by means of topological arguments concerning organic molecules. Optical activity is the ability of certain substances to rotate the plane of oscillation of plane-polarised light[18] passing through those substances or solutions thereof. For example, there are two forms of tartaric acid, which rotate the plane in mutually opposite directions. For a doctoral thesis awarded in 1847, Louis Pasteur synthesed an equal mixture of the two forms (which did not rotate the plane of light) in crystalline form [Partington 1964: 751, 752]. He found in the mixture two sorts of crystals. These were, in physical appearance, mirror images of each other, yet not identical, like opposite hands. They turned out to be the two forms of tartaric acid.

Figure 3: Two mirror image molecules that are not identical. They can be superimposed only if one is passed through a mirror or has two R's switched. The central vertices, as is customary, represent carbon.

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[18] In electromagnetic theory, then (1870's) as now, electromagnetic radiation is considered to be waves that propagate (travel forward) in one direction, and oscillate (go back and forth) in the directions perpendicular to the forward motion. *Plane-polarised* light, as it travels in one direction, confines its oscillations to a geometric plane (straight up and down, say).

Jacobus van't Hoff and Joseph Le Bel, in the 1870's, worked out a geometric theory that dared to posit physical molecules [Le Bel 1874]. In the modern theory, molecules whose three-dimensional drawings form mirror images which are not identical are assumed to give rise to oppositely plane rotating variants. One consequence of the theory is the now-ubiquitous view of carbon as tetrahedral in its connections; see figure 3. Whenever tested, Le Bel's hypothesis always holds true.

It will be clear especially to readers with anti-realist sympathies that these explanatory hypotheses alone could not be enough to establish molecular realism, and they failed to convince a plurality of the chemical community through the end of the 1800's. More impressive is that atoms and molecules, historically, continued to do what existents are supposed to do, in ways independent of the data leading to those hypotheses. By the beginning of the twentieth century, scientists were ready actually to *count* those particles.

Section 2: The Counting of Atoms and the End of Serious Anti-atomism in Chemistry

Jean Perrin's celebrated work in the early 1900's came at a time of a more famous upheaval in science that followed the discovery of radioactivity and anomalies in classical electromagnetic theory. The coming of nuclear physics and the beginning of quantum theory intersected with the work of Perrin and others in establishing a common proportionality factor between atomic weights and number of atoms for all elements. This proportionality factor, got by arbitrarily assigning an atomic weight of 12 to carbon and others by reference to carbon, is now known as Avogadro's number. The effect of numerous measurements of this number was to quickly erase doubts concerning molecular realism for most chemists.

Perrin became famous for ingenious measurements of that number, and his work *Atoms* reviews his and others' independent determinations. He provides a table of these measurements, thirteen in all [1918: 206]. They mutually agree to less than 20% error, and subsequent measurements only improved their agreement [Nye 1972: 161]. Four of them come from his studies of the phenomenon of Brownian motion, the random jiggling of small but visible particles in fluids. All depend on deriving an equation in which *particle number* appears, and in which all other quantities are known or independently measurable. Other phenomena leading to such an equation include various sorts of radiation, X-ray diffraction, and electrochemical measurements.

Salmon [1984: 216-222] discusses at length the implications of such a variety of means to obtain Avogadro's number, and his conclusions are similar to some drawn in chapter 3 concerning practise in synthetic chemistry. There is no clear point of commonality concerning the various sorts of measurements aside from the molecular hypothesis. The same conclusion was drawn by the scientific community at large by 1913 [Nye 1972: 157-159]. As Henri Poincaré put it, "...we see them since we know how to count them" [translated in Nye 1972: 157]. To this day no one has explained why so many different quantities readily interpretable as particle number should exhibit agreement, without the molecular hypothesis.

To be sure, this was not the end of the line for refinements in the understanding of atoms. Nuclear physicists had prepared substances that appeared to be of the same element, yet with different atomic weights. The atomic theory had to be modified to assume that elements could have various sorts of atoms or slightly differing weights; the phenomenon is now known as isotopy. Assuming that these atoms are statistically distributed in molecules according to their natural abundances allows the molecular hypothesis to be retained. Today, the concept of an element is no longer viewed as a pragmatic one by chemists. The atoms of a given element all have the same nuclear charge; elements so construed are coextensive with those that can be prepared chemically with the exception of those not available in amounts amenable to chemical manipulation. While the distinction between chemical and other (i.e. nuclear) methods is not sharply definable, the enormous qualitative difference is always clear in practise.

Not long after Perrin's famous work, the present system of drawing molecules was devised in the work of G. N. Lewis and others [Partington 1962: 960-962]. By the 1920's standard methods of drawing molecules were essentially as they are now.

Section 3: Evolution of Synthetic Practise: Classical to Neo-classical

There is no doubt that neo-classical synthesis is a different activity than was classical synthesis[19]. Scientists today are using instruments and techniques that go far beyond what could have been imagined in an earlier phase of the history of chemistry. It should be understood, though, that this has done nothing but put chemists even further towards a molecular realist view. Their history, in fact, seems to display a steady progression towards techniques of compound identification and synthetic planning, both of which rely to an ever-increasing extent upon assuming this view.

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[19] These terms are defined at the opening of chapter 3.

Chemists have always boiled, burnt, mixed, poured substances, and more, in hopes of obtaining new ones. Moreover, where new substances were created, chemists have always sought methods to verify their composition. It is clear that before a reasonable degree of systemisation was achieved in the late 1700's, this must have been a largely hit-or-miss, ultra-empirical affair. Before the time of Lavoisier, systematic knowledge was slender indeed, and the number of substances which chemists succeeded actually in producing was by today's standards incredibly low (in the hundreds perhaps) [Crosland 1962: 110-113, cf. Lavoisier 1964: 175-198]. Nevertheless, even very early chemists occasionally succeeded in syntheses of substances followed by analyses back to known materials[20]: Crosland attributes this feat to chemists who created cinnabar *circa* 1100 [1962: 112].

The growing adoption of Lavoisier's system, along with chemical atomism and electrochemistry, drastically and rapidly expanded the range of available tools for chemical analysis. Numerous methods of analysis had been available for hundreds of years [Brock 1992: 177]. But the new tools of the 1800's brought the exciting possibility of successful analyses of new, previously unknown substances rather than only the verification of known ones. All references seem to agree that the post-1800 period saw an expansion of synthesis and analysis hand-in-hand: "relationships between organic compounds could be seen for the first time" resulting in "a burst of activity and an immense clarification of the chemical evidence" [208]. Routine standardisation of analytical methods was clearly a boon to the individual synthetic chemist, who could now have a greatly increased confidence in the results of chemical machinations.

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is the original meaning of the phrase 'chemical analysis'.

At the same time, different analytical chemists used various mutually incompatible methods of classification by analytical behaviour [Crosland 1962: 312-317], leading to confusion regarding elemental composition of some compounds. Radicals, discussed in the previous section, quickly influenced analysis, as did type theory, predecessor of today's systematic knowledge of functional groups [314]. These classification schemes can all be explained, in modern notation, with short series of drawings in terms of common fragments, the competing schemes emphasising different aspects.

Chemists officially remained skeptical of physical atoms, but when the theories of Kekulé, van't Hoff and Le Bel were put to the test, the result was fruitful for both analysis and synthesis. "Chemists could now work out, in their notebooks or on the blackboard, the structures of new substances and their probable reactions" [Levere 2001: 147]. Every step towards something recognisably closer to the modern picture of molecules brought about a large expansion in new substances and their systemisation, even when the methods were applied with a wink.

The twentieth century brought one important new innovation to synthetic practise that amounted to taking the geometric picture of the molecule more seriously. This was the practise of describing molecular reactions through drawn mechanisms showing the interaction between molecules according to formal conventions. C. K. Ingold systematised the essentials of the methods still in use in a 1934 article [Brock 1992: 535]. These methods made it easier than ever to understand the interactions of specific functional groups in molecules. Moreover, not only stable molecules but hypothesised reaction intermediates (transient species formed from starting material and ultimately turning to product) could be treated. Understanding of intermediates grew immediately, and chemists could then make spatial judgements concerning intermediates to infer products, cohering with actual observations. This adds an additional element of coherence between the geometrical picture of molecules and macroscopic observation: we can point at microscopic observations caused not only by the spatial properties of stable molecules but also those of intermediates.

Molecular spectra are, as noted in detail in the previous chapter, an important tool for neo-classical synthesis. NMR spectrometers became available for unambiguous molecular structure interpretation by the 1960's. Before long, protracted disputes concerning structures became a thing of the past [Brock 1992: 630]. With time, it became possible for chemists to use NMR and other tools of analysis on a routine basis.

Modern tools of analysis, or course, assume molecular realism *ab initio*. Chemists still boil, burn, mix, pour substances, and more, in hopes of obtaining new ones. But now the possibilities, thanks to the molecular hypothesis, can be sharply delineated, often down to two or three, prior to even trying something. Neo-classical chemists do the same thing as the classical chemists. The real difference is in a full-blooded acceptance of the molecular hypothesis and the use of analytical techniques that depend upon it.

Section 4: Combinatorial Chemistry

The ideal of achievement for the neo-classical chemist is, as mentioned in chapter 3, full characterisation and isolation of product. The deviation from this ideal marks the distinction of the new science of combinatorial chemistry from neo-classical synthesis. When fantastic numbers of different compounds are prepared together, these full characterisations are an extreme bottleneck. Combinatorial chemistry offers easy access to numbers of compounds far in excess of the number of molecular spectra one would care to analyse. Instead, combinatorial chemistry is in large measure dominated by the large-scale testing of combinatorial libraries (i.e. large series of compounds obtained simultaneously) for drug precursor activity[21]. Until recently, the testing was the bottleneck; now "robotic samplers can screen more than 10,000 compounds per week" [Wilson 1997: 5]. Thus combinatorial chemistry deliberately builds a haystack from which needles are to be identified [1997: 2].

There are at least three ways to obtain large numbers of products. Chemists may prepare mixtures in solution, prepare various solutions in parallel, or form products on 'solid supports', solid materials that trap molecules.

The principle of synthesising mixtures is clear. Instead of introducing a single functional group for attempted introduction upon a substrate molecule to obtain small numbers of products, a chemist may opt to mix numerous ones with other molecules, under conditions such that many combinations are possible. Where the functional groups in use can link to each other, the number of possible outcomes grows exponentially with the number of reactive fragments. The distribution of these outcomes is not necessarily uniform, and it cannot always be known if some of the possibilities are not present. Thus this method seems to represent one extreme in the trade-off between quantity and quality of product. There is likely no hope of full separation and characterisation of thousands of compounds together in one vessel, dissolved in the same phase.

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[21] Discussion in Terrett's [1998] and in Wilson and Czarnak's [1997] anthologies is in many places dominated by this consideration.

Nonetheless, some straightforward methods of identifying compounds with desirable biological activity are possible. For example, a researcher could introduce viruses to the mixture; where these react with certain of the compounds in the mixture, the reaction can be detected by removing and analysing the viruses. Even if particular compounds can not be observed in this way, a technique called *deconvolution* is available. Briefly, by selectively excluding certain fragments and testing mixtures of compounds from the others, chemists can narrow down those particular compounds that might have some desired activity.

Requiring more work, but potentially offering new compounds in a form easier to characterise, is the use of parallel solutions. Let us suppose that fragments A, B, and C can be linked together in any combination. Then suppose we introduce A into three samples, then flood two of them with B and C respectively. All three mixtures will contain A-A; one only will contain A-B, and another, A-C. The generalisation to more fragments is clear.

Naturally, combining large numbers of such fragments is likely to be a logistical challenge. Robotics is the answer; robot arms can perform specified operations on thousands of tiny reaction mixtures. Each is grist for a separate test of whatever chemical activity may interest the researcher. Follow-up may dictate larger-scale repetition of certain syntheses, as might interest in molecular spectra. The physical separation of the molecules allows separate spectra to be taken. Since the syntheses are on the micro level, however, these spectra will not be of high quality unless some syntheses are repeated on a larger scale. It may be anticipated that more powerful spectrometers will be developed to make high quality spectra available straight from reaction vessels. This may be coupled in the future of better robots that can physically prepare the samples for all kinds of spectra. The more help that can be obtained this way, the more it can be expected that combinatorial chemistry will routinely offer the quality of product generally demanded in neo-classical syntheses.

Probably most combinatorial chemistry to date, though, routinely uses solid-phase synthetic techniques. That is, products are formed onto a solid surface underneath the liquid reaction mixture. Forming on a solid surface facilitates removal of separate compounds. Thanks to technology developed through the efforts of past chemists and materials researchers, numerous substances are available for trapping compounds. These are in routine use in neo-classical synthesis also. Commonly chemists employ resin beads that trap molecules. This has the advantage of allowing products to be removed with the beads, and being reliably able to trap substrate molecules to allow attack by fragments with which we might treat them. Now, spectroscopic techniques are available for scanning molecules on these beads [Terrett 1998: 153-170], though it should be kept in mind that attachment to the beads is a very different environment than those in which molecules might be in application; this affects spectra. Products on beads can also be detected through encoding with compounds known to react with certain combinations of fragments.

Combinatorial chemistry's symbiotic relationship to technology is notable, and continues a trend in contemporary science of all kinds. For chemistry, though, the trend to robotics brings the science to a new kind of practise. The tendency is to take out the labour (the non-brainwork, that is) from the laboratory. The enormous scope made possible by the use of robotics is astounding: no person can be counted upon to keep track of thousands of reaction vessels. I would like to emphasis how this makes chemical discovery of a quasi-Baconian kind more quickly available. While we have many assumptions about the general nature of chemistry, we can imagine the performance of thousands of reaction vessels 'to see what happens'. We need not have any idea of what products might form. This has often been an element of neo-classical chemistry, and truly classical chemistry, but now the haste with which purely exploratory chemical research can be carried out gives us an opportunity to explore permutations of chemical treatment on a huge scale.

Combinatorial chemistry, though today a very different practise than neo-classical chemistry, is very far from being a rejection of it, or from superseding it. It is instead a different placement of emphasis. Combinatorial chemistry, in general, is more oriented to utilitarian employment of molecules than in the detailed study of their individual structure. At the same time, it can be a source of information for carrying out larger-scale individual compound syntheses. As its technology becomes available to the larger chemical community we can expect that the chemists will find ways to study very detailed individual compound data *as well as* being able to turn out huge numbers of new molecules at once.

There is a different metaphysic involved in combinatorial synthesis in opposition to neo-classical. Neo-classical synthesis uses the concept, and even the term, 'substrate': attention is drawn to a single entity which is *modified*. For combinatorial synthesis, there is less interest in the outcome for any particular molecule.

However, the story of combinatorial vs. neo-classical chemistry is not one of competing paradigms, in any strong sense. All the results of combinatorial chemistry are comprehensible by chemists of previous generations. The basis of the functional groups remains too. There is no incommensurability here. In fact, this seems to me an example of a cumulative advance, poised to propagate still more cumulation. There are no exotic molecules, no areas of fundamental theoretical concern. Computational studies of reaction mechanisms, for example, employ derivative, approximate theories. Hence there seems little room for Kuhnian anomalies.

At the same time, there is what might be called a revolution in chemical practise in the making. This mirrors the overall impact of technology on the practise of science in many other areas. The biggest difference likely to be of concern is the increased use of instrumentation. Here, discussion has been going on in chemistry for many years, particularly since the routine availability of molecular spectra. Each iteration of instrumentation and automation takes us one step back still from having the material literally on hand.

CHAPTER 5: COHERENCE OF INFERENCES PHYSICALLY INDEPENDENT AS A BASIS FOR MOLECULAR REALISM

The claim of this thesis is that on the basis of all sorts of observations concerning the practise of synthetic chemistry and its history, molecules are real in the same way as are rocks. Synthetic chemistry, I submit, is a realist discipline, and observers should agree with this construal. In very many ways the molecular fragments are studied according to considerations that guide our ordinary spatial intuition. Molecular realism explains these regularities and provides crucial aids to judgement and interpretation; no other available hypothesis does. Moreover, and crucially for the present argument, *whatever* exhibits the observations has a structure (broadly construed) that mirrors that of the 'molecules' that are drawn and modelled.

The 'best explanation' argument for scientific realism was reviewed in the first chapter. My argument, while related to it, is different in some important ways. Section 1 presents the ways in which it is crucially informed by the work of Hacking and Cartwright. Section 2, summarising the data that have occupied us for the past two chapters, presents the arguments in standardised forms. Section 3 compares synthetic chemistry to two other fields of science, contemporary nuclear physics and past population biology, in order further to clarify the role of the molecular hypothesis in synthetic practise. Section 4 addresses some anti-realist objections to the thesis' claims, and section 5 concludes.

Section 1: The Argumentative Strategy in Relation to Hacking's and Cartwright's

More than once above, Hacking is cited as an inspiration and source for the present argument. The work here shares Hacking's emphasis on individual happenings in laboratories as the best guide to scientific realism. However, it is important to acknowledge one crucial difference between his main argument in *Representing and Intervening* and the one here. His main argument does not require an *inference* as such to establish the reality of entities. It is enough that we are *doing* something.

> By the time that we can use the electron [in beams] to manipulate other parts of nature in a systematic way, the electron has ceased to be something hypothetical, something inferred [1983: 262].

We are not inferring; we are doing something with the electrons. Therefore electrons exist. In chapter 1 this view was rejected as an oversimplification, because we need some theoretical context to know that we are actually manipulating electrons.

There is, however, another argument for realism to be found in *Representing* which is very close indeed to the present one. Discussing his personal experiences in educating himself concerning microscopists' practises, Hacking argues that microscopic grids (in 'disc' form) manufactured from macroscopic analogues are real because

> ...we look at the tiny disc through almost any type of microscope and see exactly the same shapes and letters as were originally drawn on a large scale. It is impossible seriously to entertain the though that the minute disc, which I am holding by a pair of tweezers, does not in fact have the structure of a labelled grid...we *made* the grid to be just that way...[t]o be an anti-realist about that grid you would have to invoke a malign Cartesian demon of the microscope [because different sorts of microscopes work on physically independent principles] [Hacking 1983: 203].

I submit that this case is more convincing than that of the electron beam, if less interesting, invoking as it does a wider context of interpretation (prior acts of observation and manufacture). This context provides the needed "specific, concrete causal processes" [Cartwright 1981: 385] needed for inferring the presence of a microscopic grid.

Having engaged in a very short but detailed examination of the practises of synthetic chemistry and its history, we are in a position to make similar inferences for molecular realism. They follow, as mentioned in chapter 1, Cartwright's 'inference to the best cause' by citing the specific causal links needed to so infer.

The arguments in standardised form in the next section are intended to follow the schema:

> (i) citation of causal links from molecular structure to macroscopic observations or historical progress (mentioned in chapters 3 and 4 and summarised in section 2)
> (ii) the claim that these are understood in a relatively theory-independent way (defended in chapters 3 and 4)
> affirmation of the existence of causal agents responsible, here understood to be atoms and molecules

Section 2: The Claims of the Thesis

Molecules, with knowledge of their structures, are used to affect other, less well known things. As well, though, they are used to

- change other molecules.
- identify other molecules.
- build things.
- instantiate patterns of reactivity which can be inferred in practise *only* this way.

There is a discernible causal sequence in the way that molecules and their structures are employed in this way. As we have seen in chapter 3, the *shapes* and other geometrical properties of molecules are crucial to what can be done with them. They are used by chemists to decide which reactions are likely to work. For example, a molecule of the form ABA might be modified to ABC where C can *fit* in place of A; moreover, the resulting molecule ABC can then be modified to CBC. Similar moves are used in classical methods of product identification. Chemists rely upon the geometric properties of fragments; there is no alternative available. Numerous examples abound in sections 1 and 2 of chapter 3.

As well, the modern molecular hypothesis with valency theory provides inferences regarding observations

- often needing familiarity only with the concept of a three-dimensional object and which exhibit just the same regularities.
- which *always* rely crucially on hypothesised geometry.
- which allow planning of syntheses such that the planned moves, done with drawings of molecules, cohere with the behaviours of the molecules themselves.
- which in some cases *cannot* be inferred from theory.
- which in some cases are poorly understood in their theoretical implications by individual chemists.

Molecules are ubiquitous in chemical synthesis in a way that no single equation or theoretical construct is in any other science. In the textbooks, one sees indented pictures of molecules, over and over. Their shapes are crucial to virtually all specific (as opposed to abstract theoretical) inferences and modes of explanation. The theory of these pictures is described in section 2 of chapter 3.

The argument here is therefore

(i) The geometric properties are used in chemical synthesis to plan moves that might work.
(ii) Interpretation and use of these properties typically does not rely upon mathematical theory.
(iii) The use of spatial intuition without calculation gives results that cohere with the macroscopic observations in terms of the results of chemical reactions.
(iv) Molecules are countable in ways proper to the molecular hypothesis as well as by experiments independent of principles

> proper to chemistry (from the studies of Perrin and others, described in chapter 4, section 2).
> Therefore, there are causal agents responsible for the observations, which resembles macroscopic objects in many of their causally efficacious properties.
> Therefore, in the absence of an alternative, molecules exist.

Furthermore, molecules can be altered in a way that is directed by molecular realism

- such that many aspects measurable by independent physical processes remain unchanged through theory-change and technological innovation.
- such that new technologies of product detection always present constructs easily interpreted in terms of molecular structure even though the mechanisms of those technologies are independent of molecular realism, and the constructs *do not* appear in the theory of that technology.

Again, there is a discernible causal sequence in the analysis of molecules through devices. NMR spectra, for example, are used to identify molecules that are present, and their interpretation in terms of molecular geometries was discussed in section 4 of chapter 3. In similar molecules, most of the peaks of the spectra always turn out to be at almost the same position. Historically, as new technologies, such as NMR spectroscopy, have been developed, they have always been interpretable in terms of molecular geometries.

The argument that presents itself is

> (i) The geometric properties of molecules are interpretable in terms of constructs arising in the interpretation of analytical techniques.
> (ii) When introduced, new analytical techniques always can be interpreted in terms of molecular geometries where applicable, when it might be expected that each new analytical technique might fail to be so interpretable or even to falsify molecular realism.
> (iii) Typically, there is no connection between molecular geometry or other properties of molecules in the physical principles proper to these devices.
> Therefore, there are causal agents responsible for the observations, which resembles macroscopic objects in many of their causally efficacious properties.

Therefore, in the absence of an alternative, molecules exist.

Historically, the molecular hypothesis

- convinced an initially skeptical chemical community.
- displayed its features in a cumulative way.
- encouraged innovation and success in producing new substances even when construed instrumentally.
- finally provided a way to count those molecules, which counting agreed with that got from experiments independent of practises in chemistry.

Sections 1-3 of chapter 4 reviewed this sequence of events. As chemistry developed in the 1800's, more and more phenomena appeared that were interpretable and explicable in terms of molecular connections. This sort of interpretation advanced the pace of synthesis in a major way and is implicated in virtually all its lasting innovations.

The argument that presents itself is

> (i) The molecular hypothesis incorporating specific connections between atoms was scientifically progressive.
> (ii) Moreover, progress in chemistry gave rise to new puzzles that were solved with the aid of this hypothesis.
> (iii) The chemical community was initially skeptical. But even when the molecular hypothesis was treated instrumentally by many chemists, research gave rise to new regularities that cohered nicely with that hypothesis and for which no alternative presented itself.
> Therefore, there are causal agents responsible for the observations, which resembles macroscopic objects in many of their causally efficacious properties.
> Therefore, in the absence of an alternative, molecules exist.

In relation to the new science of combinatorial chemistry, reviewed in chapter 4, section 4, the molecular hypothesis (including molecular geometry)

- is needed for elementary comprehension.
- is the basis and rationale.

The reviewers of this new practise (Thompson and Ellman [1996], Terrett [1998], Wilson and Czarnik [1997]) constantly reference the same spatial intuitions used in more traditional synthetic chemistry. Moreover, the descriptions of what they are doing are in terms of molecular fragments and functional groups. Those features of practise that are shared with traditional synthesis continue to work, and are essential to its description.

The argument here is

> (i) A new innovation of synthetic practise depends on the
> molecular hypothesis for its exposition.
> (ii) This variant in its new findings coheres with the molecular
> hypothesis.
> Therefore, there are causal agents responsible for the
> observations, which resembles macroscopic objects in many of
> their causally efficacious properties.
> Therefore, in the absence of an alternative, molecules exist.

These arguments are not deductive of course, and instantiate Cartwright's 'inference to the best cause'. Moreover, I have reached the conclusion of molecular reality *via* an intermediate conclusion to a more general 'causal agent'. So the conclusion to molecular reality is an extrapolation. But it is less of one than it might appear to be at first sight. Because of the causal efficacy of those features of the causal agents corresponding to molecular geometry, whatever those agents are must somehow incorporate those features in their structures. The nearly *comprehensive* resemblance of those causal agents to actual little particles in many cases should make us ask how much resemblance is necessary for identification. The very conception of any alternative is strictly hypothetical. Any such alternative would have to be something quite complicated, and very difficult indeed to even distinguish from molecules as we know them.

Molecules exist. Further doubt would subvert the practise of synthetic chemistry: all moves by synthetic chemists assume them. Their use of molecular realism is not, as some imply, an add-on foreign to science (for example, van Fraassen 1980: 156). It is proper to the planning, execution, and interpretation of all synthetic chemistry work. In terms of chemical exposition, it is crucial also: there is no available alternative. The molecular hypothesis is, moreover, stable in the face of theory-change and new techniques, and can be understood independently of fundamental theory. New techniques that might have been expected to subvert it, like NMR spectroscopy, have done nothing but make it more plausible. And the hyper-modern variant of synthesis, combinatorial chemistry, depends upon it.

Chapter 2 discussed the criteria for realism, concluding that while no final judgement is available, there is no privileged, simple sort of observation that escapes the need for inferences if any attempt is made at systematic understanding. Molecules do so much that existents are supposed to do. We can use the geometric features of molecules to effect changes in others, in the way Hacking discusses, but we can also use those features to *detect* those same molecules. So we have both push and pull here. To doubt molecular realism, I submit, is to doubt the basis of many familiar judgements about normal things. Moreover, chemists' manipulations of molecules are relatively theory-independent. Many, many details of theory could be different without changing the molecular hypothesis. The convergence of so many findings entirely independent of the molecular hypothesis is sheer brute data without it.

Section 3: A Comparison to Some Other Scientific Practises

It is clear that the fact that synthetic chemists seem as a group to be molecular realists is not in itself a convincing reason to adopt molecular realism for an external observer. The arguments of the previous section are intended to go beyond this, claiming that molecular realism is needed to understand how their practises can work at all, let alone 'succeed'. A comparison to some other scientific practises may help show how very crucial this is. We can profitably compare synthetic chemistry to contemporary nuclear physics and to population biology before the discovery of DNA.

Nuclear physics studies the particles that make up the nuclei of atoms and the forces that hold them together. These nuclei have no macroscopic model to speak of and so the study is necessarily abstract even in its strictly experimental branches. Its mathematical theory displays numerous colourful features interpretable as manifesting truly odd behaviour of matter at the tiniest scale. For example, certain constructs can be identified as 'virtual particles', particles that temporarily violate (formally) the principle of energy conservation, and which 'carry' the nuclear forces. Moreover, the nuclear particles cannot be individuated.

It is probably too much to imagine that nuclear physicists as a group can be anti-realist about nuclear particles, but it is clear that they need not be realists about objects arising from interpretation of mathematical paraphernalia in their work. Virtual particles and the like are calculational devices. Their status cannot typically make a difference in practise because they have no identifiable features outside the mathematical formalism.

Now consider biology before the coming of DNA. Genes were originally an explanatory construct to account for the variation and similarities of biological organisms. As such, they need not have been physically instantiated in DNA, as they now appear to be. Population biologists, then and now, could make predictions on the basis of genotypes without worrying about possible physical instantiation. Much could be done and much still can be done without worrying about the ultimate physical basis of genes (though of course biology generally seems to be increasingly preoccupied with this since the dawning of biotechnology).

Both of these sorts of studies contrast strongly with synthetic practise concerning the realism issue. As discussed in chapter 3 and reviewed above in brief, the features of molecules *qua* actual three-dimensional bodies are referenced constantly in the planning and execution of syntheses. Moreover, they are referenced largely outside of mathematical formalisms: many inferences concerning what to do are got by simple spatial reasoning that would work for Lego also.

Section 4: Some Objections Addressed

Arthur Fine makes a case, which initially seems plausible in the abstract, against the use of abductive realism judgements in philosophy of science.

> Metatheoretic arguments must satisfy more stringent requirements then those placed on the arguments used by the theory in question, for otherwise the significance of reasoning about the theory is simply moot...No support accrues to realism by showing that realism is a good hypothesis for explaining scientific practise [1984: 262-263].

So we should not judge the reality of entities from a view outside science.

The above has done more, I hope, than to show that "realism is a good hypothesis for explaining scientific practise." Molecular realism is not simply a good explanation for chemical practise. The above account has identified a number of cases in which specific causal sequences can be traced to agents that strongly resemble molecules. Moves in the synthetic laboratory are not really informed by theory much; they are informed by simple geometric features with predicable causal consequences. I do not try to claim, as Hacking does, that we can put ourselves in a position to know entities without inference. However, many ‘arguments’ used in synthetic practise rely upon inferences to causes similar to those used in selecting traffic routes (or deducing the route that the criminal followed); they do not test fundamental theory or arguments got from it.

Moreover, it is difficult to locate chemists’ attitude in Fine’s natural ontological. I do not see what is here that is not comprehensible by an untutored observer. Certainly, only the trained can work with instruments to produce reliably correct results, and interpret them. But the practise is readily understood externally. While very brief, my presentation of synthetic chemistry is no oversimplification. Chemists really and literally treat drawings of molecules as being like photographs, in a way requiring no smoke and mirrors. The explanatory arguments made here are the same as the ones chemists have used to defend molecular realism. There is no intellectual gulf of the kind suggested by Fine's work, and that is all to the good, for philosophy of science *should* try to look at the internal machinations of scientists. Otherwise it is not philosophy of science.

An empiricist in the mode of van Fraassen might say that the coherence I have repeatedly cited is not reason for concluding molecular reality – just because molecules are unobservable. It is enough that the relevant theory is empirically adequate. It must be noted again that contrary to van Fraassen’s pronouncements, molecular realism is *in* the ‘theory’ of synthetic chemistry. In fact, in practise, there is little else to which to appeal in making laboratory judgements, as noted earlier. It is also necessary for interpreting the outcomes of synthesis experiments.

Moreover, if molecules are 'unobservable', it is not clear why their structures can in so many ways be exhibited in manifest consequences, and why independent, novel techniques keep showing their traces. While rejecting the instrumentalist view of an independent language of observation, van Fraassen still wants to believe in a simple, unadorned concept of observation that excludes theoretical entities, continuous with naked-eye seeing [1980: 13-19]. But this fails to work even for Hacking's microscopic grid, for as Hacking's discussion of microscope design makes clear, seeing through a microscope is not the same as seeing with the eye, only bigger [1983: 206-209]. Van Fraassen's view is overly restrictive, and fails to respect the enormous difference between a molecule, which can be applied in so many ways, and something far more speculative such as tachyons or black holes. It seems better to at least admit degrees of observability. In any case, as shown by Del Re's mountain example, plain seeing is not a clear criterion for observation.

Some readers may be unimpressed with the closing of the previous chapter, wherein the problem of instrumentation taking us away from the raw stuff is raised and rejected quickly. It could justly be said that this is done from an internal point of view (chemical practise) that cannot affect the judgement of an external observer. The argument there relies on an optimistic induction based upon the way in which previous expansions in instrumentation have tended to confirm rather than disconfirm molecules. As well, according to my observations, the mainstream of chemistry regard spectra and other gadgets as proxies for more direct seeing, and I think it is the incredible coherence of instrument-aided findings with those got independent of instruments that supports this view. To defend this inference would require an analysis of instrumentation as such that would require much more space than available now. So I admit this weak point, enjoining those readers who might be interested to follow combinatorial chemistry and other highly technology-dependant variants of synthesis as a test case for molecular realism.

Section 5: Conclusion

We cannot comprehend synthetic chemistry without a commitment to molecular realism, and neither can chemists. If there is some other causal agency responsible for the data, it must be a queer one indeed. We can not, as van Fraassen wants to be, agnostic on this matter, central to chemistry. It is *in* synthetic chemistry. Nor should we adopt the natural ontological attitude, which mystifies what is actually quite clear for external observers of chemistry.

The new tradition emphasising experiment, pioneered by Hacking and Cartwright, provides an excellent research program for philosophy of science. I proudly submit the study here concluded for this tradition, and enjoin all scholars of science to visit the laboratories themselves. Such visits just might bias them in favour of scientific realism.

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