

What might philosophy of science look like if chemists built it?

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Abstract Had more philosophers of science come from chemistry, their thinking would have been different. I begin by looking at a typical chemical paper, in which making something is the leitmotif, and conjecture/refutation is pretty much irrelevant. What in fact might have been, might be, different? The realism of chemists is reinforced by their remarkable ability to transform matter; they buy into reductionism where it serves them, but make no real use of it. Incommensurability is taken without a blink, and actually serves. The preeminence of synthesis in chemistry could have led philosophers of science to take more seriously questions of aesthetics within science, and to find a place in aesthetics for utility. The necessary motion twixt macroscopic and microscopic views of matter in modern chemistry leads to the coexistence of symbolic and iconic representations. And in another way to the deliberate, creative violation of categories.

Keywords Chemistry · Philosophy of science · Philosophy of chemistry

1 Introduction

Implicit in the title might be two presumptions. The first one, that there is (or should be) a single philosophy of science, is not a claim I intend—I do think one should look for a common core, in a way that allows for differences.¹ The second presumption, that philosophy of science, as it is construed today, would be different if it were based on chemistry, is what I wish to examine.

¹ Indeed, the French name of the discipline explicitly carries the plural “sciences.”

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And behind that latter supposition is the notion that philosophers of science, their professionalism and good will not impugned, nevertheless are likely to construct their world-view of science based on the sciences they know best. These are usually the sciences that they studied (a) as a part of their general education, or (b) the science they came from, so to speak, if they made their transition to philosophy at some later point in their career.

I have not made a rigorous examination of the education of philosophers of science. But my anecdotal feeling is that, for those who entered the profession directly, an exposure to mathematical logic is more likely than to geology or chemistry. And, for many of the philosophers of science who came to their field after an initial scientific career, their scientific expertise was likely to be in the first instance physics, after that biology, and rarely chemistry.

I will argue that this matters, for chemistry is different.

There are exceptions. In the English-writing community, the most striking one is Michael Polanyi, a very distinguished physical chemist. In the French philosophical community, Pierre Duhem, Emile Meyerson, Gaston Bachelard and H el ene Metzger had professional chemical backgrounds. Bernadette Bensaude-Vincent has argued convincingly that this background shaped their philosophical outlook, in contrast with the analytic philosophers of their time (Bensaude-Vincent, 2005).

In recent times the situation may have changed. A subfield of “philosophy of chemistry” has emerged, with annual meetings and two journals (*Foundations of Chemistry*, *Hyle*). The practitioners of this field are more likely to have had substantive experience in chemistry.

I feel we should put some blame for the situation on the chemists as well, asking why more of them have not wandered into philosophy. Are they so unreflective? If so, why? Is there something in the practice of chemistry that drives them toward becoming kings—à la Margaret Thatcher and Angela Merkel—rather than philosophers? Is the employment situation too good in chemistry?

2 What makes chemistry different: a chemical paper

Chemical Abstracts indexed in 2004 685,796 articles, 5,601 books, and 173,669 patents in chemistry and related fields. Let’s look at one such recent paper to get an idea of the science.

But . . . is that possible, to glean knowledge of all chemistry from one paper? The science is highly compartmentalized and the historical antecedents, modes of analysis and argument, and goals of a study in physical chemistry differ from those of medicinal chemistry or solid state inorganic chemistry.

As I value the differences that make chemistry and life interesting, I also believe in a poetic perspective on science. Archie Ammons wrote a small poem, “Reflective” (Ammons, 1990):

I found a
weed
that had a

mirror in it
and that
mirror

looked in at
a mirror
in
me that
had a
weed in it.

That weed, that dew drop on it, that particular weed and no other dew drop has within it the essence of the universe.

The paper is by a group from Kyoto University of Komatsu, Murata, and Murata, led by Komatsu (2005). It is in the field of buckminsterfullerene chemistry, that beautiful, metastable C_{60} allotrope of carbon which has been with us for only 20 years. C_{60} is made by unsporting methods (i.e. not by methodical construction from smaller pieces), by striking a carbon arc in just the right pressure of helium. There is a little room, not much, inside the nanometer-wide ball of buckminsterfullerene. But by equally unsporting (yet reproducible) methods, by brute force of discharge and high temperature covaporization, people have inserted atoms inside C_{60} –He, Sc, N. Nothing bigger, no molecule.

Meanwhile, there has sprung up a vast and ingenious chemistry around C_{60} . People, those manipulative experimenters, have added groups of atoms — few, many, changing in one way or another the buckyball. Two years ago, Komatsu's group carved a 13-membered ring orifice into C_{60} . Soon thereafter, they showed that H_2 entered that hole. Now, in this paper, they do something much more interesting, and important, and amusing — yes, all of these, and this is to reclose the hole by a sequence of chemical reactions. All the time the H_2 stays inside. At the end of this “molecular surgery” (a term introduced by Yves Rubin, another worker in the field, who had earlier made molecule **1** of this paper, and had found that some hydrogen goes into it), they have H_2 trapped in the fullerene, $H_2@C_{60}$. The @ sign here stands for a very fixed address, encapsulation.

Let's look at the illustrations in the paper. The drawings are important — the graphic content of the molecular science and its connection to issues of representation, of iconic and symbolic signing, are things I will return to.

The molecule the authors made previously, **2**, is shown in Scheme 1, along with another precursor, $H_2@2$. Then Fig. 1 of their paper shows the sequence of sewing up the hole after the H_2 enters. This is the subject of the Komatsu et al. paper before us. The last step of the reaction, a pyrolysis, kicks out many atoms. Figure 2 of the paper shows a proposed “mechanism” for this step, the presumed sequence of elementary reaction happening.

Figure 3 is the only illustration in the Komatsu paper which shows experimental measurements — nuclear magnetic resonance measurements (giving information on the magnetic environment of the carbons) and mass spectra (effectively weighing the molecule) of $H_2@C_{60}$. Figure 4 shows a first reaction (a dimerization) of the new molecule, $H_2@C_{60}$.

Does this paper look like a philosopher of science's typical paper? I know, I am about to take the easy road, set up a straw-man. Please forgive me, it allows me to enter a discussion on just how different this chemical enterprise is.

In my opinion, the Komatsu et al. paper bears no resemblance to a paradigmatic hypothetico-deductive, or Carnap's deductive-nomological, or inductive, or Popperian conjecture/refutation process. There are observations in the $H_2@C_{60}$ paper, of course.

a Encapsulation of Molecular Hydrogen in Fullerene C₆₀ by Organic Synthesis

Koichi Komatsu,* Michihisa Murata, Yasujiro Murata

In spite of their importance in fundamental and applied studies, the preparation of endohedral fullerenes has relied on difficult-to-control physical methods. We report a four-step organic reaction that completely closes a 13-membered ring orifice of an open-cage fullerene. This process can be used to synthesize a fullerene C₆₀ encapsulating molecular hydrogen, which can be isolated as a pure product. This molecular surgical method should make possible the preparation of a series of C₆₀ fullerenes, encapsulating either small atoms or molecules, that are not accessible by conventional physical methods.

Endohedral fullerenes, the closed-cage carbon molecules that incorporate atoms or a molecule inside the cage (1–6), are not only of scientific interest but are also expected to be important for their potential use in various fields such as molecular electronics (7), magnetic resonance imaging [as a contrast agent (8)], and nuclear magnetic resonance (NMR) analysis (9, 10). However, development of their applications has been hampered by a severe limitation in their production, which has relied only on physical methods, such as co-vaporization of carbon and metal atoms (2, 3) and high-pressure/high-temperature treatment with gases (9–14), that are difficult to control and yield only milligram quantities of pure product after laborious isolation procedures.

An alternative approach to synthesizing endohedral fullerenes is “molecular surgery,”

in which the cage is opened and then closed in a series of organic reactions (15, 16). For example, an open-cage C₆₀ derivative 1 with a 14-membered ring orifice has been synthesized (17), and the insertion of molecular hydrogen into 1 in 5% yield has also been achieved (15). However, the closure of its orifice was not attempted. A C₆₀ derivative 2, which we synthesized recently (18), has a 13-membered ring orifice with a sulfur atom on its rim and a relatively circular shape compared with the elliptical orifice of 1. This opening has enabled us to insert molecular hydrogen through this orifice in 100% yield (19). When matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry was conducted under enhanced laser power on compound 2 encapsulating hydrogen (H₂@2), we observed a molecular ion peak for H₂@C₆₀ at a mass-to-charge ratio (*m/z*) of 722 (19). This result suggested that H₂@2 could be a precursor for H₂@C₆₀ in an actual chemical transformation. We now report the synthesis of 100% pure H₂@C₆₀ from H₂@2 (Scheme 1).

Encapsulated H₂ escapes from the cage when the compound H₂@2 is heated above 160°C (19), so high temperatures must be avoided if the chemical synthesis of H₂@C₆₀ is attempted from H₂@2. With such a precaution being taken, we performed a stepwise reduction of the orifice size of H₂@2 and completed its closure by a thermal reaction. The application of heat to the last step did not cause a serious loss of H₂, because the orifice size was already reduced sufficiently to prevent such loss.

The first step involved the oxidation of the sulfide unit (-S-) in H₂@2 to a sulfoxide unit (>S=O) to give H₂@3. The resulting >S=O unit was removed by a photochemical reaction to produce H₂@4 (Fig. 1, steps A and B) (20). Both reactions proceeded at room temperature with yields of 99% and 42% (68% for step B based on consumed H₂@3), respectively. The MALDI-TOF mass spectrum of H₂@4 exhibited the molecular ion peak of H₂@C₆₀ as a base peak, indicating its enhanced accessibility from H₂@4 as compared to H₂@2. The spectrum, however, also showed the presence of empty C₆₀ in 20% yield relative to H₂@C₆₀, and indicated that further reduction of the orifice size was needed. Thus, in the next step, two carbonyl groups in H₂@4 were reductively coupled by the use of Ti(0) (21) at 80°C, to give H₂@5 with an eight-membered ring orifice (Fig. 1, step C).

At each process in these three steps, complete retention of encapsulated H₂ was confirmed by observing the characteristically upfield-shifted NMR signal of the incorporated H₂. The integrated signal intensity exactly corresponded to 2.00 ± 0.05 H for the signals at a chemical shift δ of -6.18 parts per million (ppm) in H₂@3, at -5.69 ppm in H₂@4, and at -2.93 ppm in H₂@5, with reference to the 2.00 H signal for two aromatic protons. The gradual downfield shift of the hydrogen signal

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Fig. 1 (a) First page of Komatsu et al. (2005) paper; (b) Second page of Komatsu et al. (2005) paper; (c) Third page of Komatsu et al. (2005) paper

But they are not passive, with the experimenters perplexed by what nature shows them. The measurements are willed, to achieve a transformation. There are no alternative hypotheses, just one developing narrative. There are further experiments, indeed (the n.m.r. and mass spectra), but they are more in the context of building a coherent story rather than falsification.

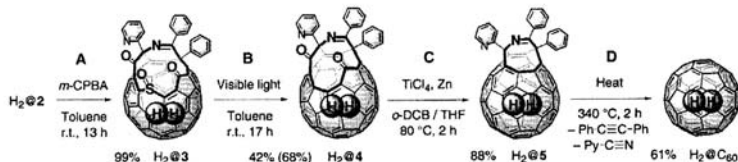
The various mid-20th century logical-positivist models of the scientific process by and large reduce experiment to mere observation.² They privilege theory construction and to me reveal indifference to the affective-cognitive link forged in the performance of experiment. A rotation in a laboratory would have been good for these philosophers.

What theories are being tested in this beautiful paper? None, really, except that this molecule can be constructed. The theory building in that is about as informative as the statement that Archie Ammons' poem tests a theory that the English language can be used to construct novel and perceptive insights into the way the world and our minds interact. The power of that tiny poem, the cleverness of the molecular surgery that Komatsu et al. perform in creating a new molecule, just sashay around any analytical theory-testing concerns.

² For what I think is a good account of these views, see Godfrey-Smith (2003).

b

Fig. 1. Size reduction and closure of the orifice of the open-cage fullerene encapsulating hydrogen, in a four-step process. Percentage values are product yields; that shown in parenthesis is that based on the consumed precursor. *m*-CPBA, r.t., and *o*-DCB stand for *m*-chloroperbenzoic acid, room temperature, and *o*-dichlorobenzene, respectively.



observed at steps B and C reflects the formation of each step, within the fullerene cage, of a fully π -conjugated pentagon, which exerts a strong deshielding effect through its paramagnetic ring currents (22).

Finally, complete closure of the orifice was achieved by heating powdery $H_2@5$ in a glass tube at 340°C for 2 hours under vacuum (Fig. 1, step D). The desired product $H_2@C_{60}$ (118 mg, contaminated with 9% empty C_{60}) was obtained in 67% yield by passing a carbon disulfide solution of the crude product through a silica-gel column. Similar results were obtained when $H_2@5$ was heated at 300°C for 24 hours, at 320°C for 8 hours, or at 400°C for 2 min. Thus, $H_2@C_{60}$ was synthesized in a total yield of 22% from $H_2@2$, which can be obtained in 40% yield from consumed C_{60} (18, 19).

We presume that the closure of the orifice takes place by way of a thermally allowed $[\pi 2s + \pi 2s + \pi 2s]$ electrocyclic reaction that produces two cyclopropane rings (Fig. 2). Sequential radical cleavage and a retro $[\sigma 2s + \sigma 2s + \sigma 2s]$ reaction produce C_{60} by splitting off 2-cyanopyridine and diphenylacetylene.

The ^{13}C NMR spectrum of the desired product exhibited a signal at $\delta = 142.844$ ppm together with a very small signal at $\delta = 142.766$ ppm (Fig. 3A), the latter corresponding exactly to the signal of empty C_{60} . In an expanded spectrum obtained with 56,576 data points for a 50-ppm spectral width, the integrated peak areas of these signals yield an estimated ratio of $H_2@C_{60}$ and empty C_{60} of 10:1.

We separated $H_2@C_{60}$ from C_{60} through recycling high-performance liquid chromatography on a semipreparative Cosmosil Buckyprep column (two directly connected columns, 25 cm by 10 mm inner diameter, with toluene as a mobile phase; flow rate, 4 ml min^{-1} ; retention time, 395 min for C_{60} and 399 min for $H_2@C_{60}$). Isolated $H_2@C_{60}$ was judged to be 100% pure on the basis of a single ^{13}C NMR signal at 142.844 ppm (Fig. 3B), the results of high-resolution fast-atom-bombardment mass spectrometry (calculated molecular weight for $C_{60}H_2$: 722.0157; found: 722.0163), and the agreement of the

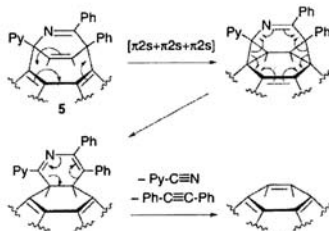


Fig. 2. Proposed reaction mechanism for the formation of C_{60} from compound 5 by heating. Only the tops of the molecules are shown. Ph and Py stand for phenyl and 2-pyridyl groups, respectively.

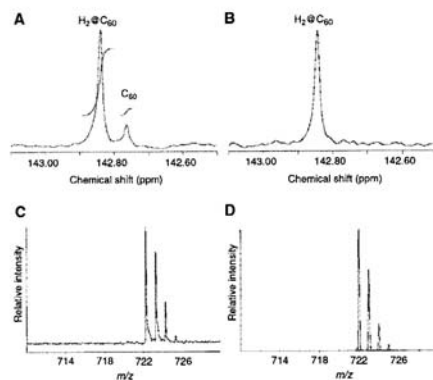
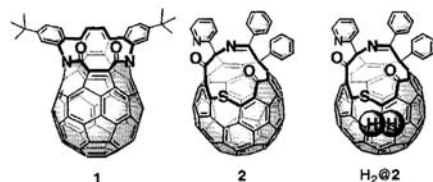


Fig. 3. Structural characterization of $H_2@C_{60}$. (A) Expanded ^{13}C NMR spectrum (75 MHz, *o*-DCB- d_4) of $H_2@C_{60}$ contaminated by 9% C_{60} . (B) Expanded ^{13}C NMR spectrum (75 MHz, *o*-DCB- d_4) of purified $H_2@C_{60}$. (C) MALDI-TOF mass spectrum (positive ionization mode, dithranol matrix) of purified $H_2@C_{60}$. (D) Predicted isotope distribution pattern for $H_2@C_{60}$.



Scheme 1.

Fig. 1 continued

Michael Weisberg, who read a draft of this paper, remarks that I should anticipate attempts to reconstruct out of my presentation and the Komatsu paper some sort of hypothesis (Weisberg, personal communication). He suggests I say:

“This paper gives us evidence that a certain theoretical statement — namely the procedure for making $H_2@C_{60}$ — is true. This could be given hypothesis-like form

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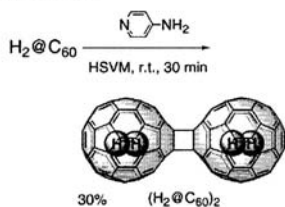


Fig. 4. Mechanochemical solid-state dimerization of $H_2@C_{60}$ by the use of a high-speed vibration milling (HSVM) technique.

observed and predicted isotope distribution patterns in the MALDI-TOF mass spectrum (Fig. 3, C and D). In addition to correct elemental analysis for hydrogen (calculated for $C_{60}H_2$: C, 99.72, and H, 0.28%; found: C, 99.04, and H, 0.24%).

The very small downfield shift (0.078 ppm) observed for the ^{13}C NMR signal of $H_2@C_{60}$ (as compared to empty C_{60}) indicates that the electronic property of the fullerene cage is largely unaffected by the encapsulation of H_2 . The ultraviolet-visible and infrared spectra of $H_2@C_{60}$ are also exactly the same as those of empty C_{60} . This situation contrasts with the cases of $Kr@C_{60}$ (13) and $Xe@C_{60}$ (12), in which larger downfield shifts are observed (0.39 ppm and 0.95 ppm, respectively), caused by appreciable electronic and van der Waals interactions between the C_{60} cage and the encapsulated atoms, which are much larger than H_2 .

The 1H NMR signal for the encapsulated hydrogen of $H_2@C_{60}$ in *o*-dichlorobenzene- d_4 was observed at $\delta = -1.44$ ppm, which is 5.98 ppm upfield-shifted relative to the signal of dissolved free hydrogen. The extent of this upfield shift is comparable to that observed for $^3He@C_{60}$ (6.36 ppm) (9, 10) in 3He NMR relative to free 3He . This result shows that the shielding effect of total ring currents of the C_{60} cage is nearly the same, regardless of the paramagnetic species inside the cage.

The irrelevance of the encapsulated H_2 to the electronic character of the outer cage was also demonstrated by cyclic voltammetry (0.5 mM in *o*-dichlorobenzene with 0.05 M Bu_4NBF_4 for reduction and 0.5 mM in 1,1,2,2-tetrachloroethane with 0.1 M Bu_4NPF_6 for oxidation). The voltammogram of $H_2@C_{60}$ exhibited four reversible reduction waves and one irreversible oxidation peak at the same potentials as C_{60} , within an experimental error of ± 0.01 V.

In order to clarify the reactivity of $H_2@C_{60}$, the solid-state mechanochemical [2+2] dimerization reaction (23) was conducted. A mixture of $H_2@C_{60}$ and 1 molar equivalent of 4-aminopyridine as the cataly

(24) was vigorously shaken by the use of a high-speed vibration mill for 30 min under N_2 according to our previous procedure (23, 24). The 1H NMR spectrum of the product mixture exhibited a signal at $\delta = -4.04$ ppm of the [2+2] dimer, $(H_2@C_{60})_2$, and a signal of unchanged $H_2@C_{60}$ at $\delta = -1.44$ ppm, in an integrated ratio of 3:7. This result indicates that the dumbbell-shaped dimer of $H_2@C_{60}$ is formed in the same yield as that for the reaction of empty C_{60} (24) (Fig. 4). No effect of the encapsulated H_2 was observed upon reactivity of the C_{60} cage. The extent of the upfield shift of the 1H NMR signal (2.60 ppm) observed for the dimer $(H_2@C_{60})_2$ was similar to that observed upon the same dimerization reaction in 3He NMR (2.52 ppm) (24) for 3He encapsulated in the ratio of $\sim 0.1\%$ in C_{60} (9, 10).

The endohedral fullerene $H_2@C_{60}$ is nearly as stable as C_{60} itself. For example, the encapsulated H_2 does not escape even when heated at $500^\circ C$ for 10 min. Thus, $H_2@C_{60}$ can be viewed as a stable hydrocarbon molecule that has neither C-H covalent bonds nor C \cdots H interactions. It is likely that our method could be used to synthesize endohedral fullerenes such as $D_2@C_{60}$ and $HD@C_{60}$, as well as the homologous series with C_{70} . Our work here complements the total chemical synthesis of C_{60} recently achieved by Scott and co-workers (25) and implies that organic synthesis can be a powerful means for the production of yet unknown classes of endohedral fullerenes.

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Supporting Online Material

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Materials and Methods

Figs. S1 to S9

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Fig. 1 continued

by putting it into a conditional: if you do such and such reactions, you get $H_2@C_{60}$. So yes, we get evidence for a hypothesis or theoretical statement. However, H-D and falsificationism also suggest a certain PROCEDURE for doing science. And this is what I am claiming is not present.”

I agree.

In a carefully reasoned book, replete with detailed examples from 19th and 20th century chemistry, Jerome A. Berson makes much the same point (Berson, 2003):

“It seems clear that much of the activity of synthesis seems to fall outside of the doctrine of conjectures and refutations. That set of guidelines envisions no important role for the largely confirmative aspect of an activity that has proven central to the concerns of chemists. Whether one wants to make a certain compound to confirm its structure, or to make a medicinally significant molecule, or to test a theoretical existence issue, or just because “it is there,” the point remains that the actual synthesis itself frequently has an inescapably confirmative purpose, not a refutative one.

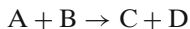
In trying to adapt falsificationist doctrine to the field of chemistry, we seem to have uncovered something arrestingly curious. If, as Popper says, confirmations count only if they are intended to test a theory, and if, again as he says, a valid test of theory must be refutative, we are led to a dilemma: if a confirmative synthesis succeeds, it doesn't count, but as any chemist knows, if it [RH:the synthesis] fails, it doesn't refute.”³

3 What is chemistry?

Let's move beyond this paper. Institutionally the enterprise is gigantic: the American Chemical Society has 158,000 members; I have already mentioned the estimate of $\sim 7 \times 10^5$ articles published per year. Underlying the cadres and their production is economic value: $\sim 70\%$ of the close to 2,000 US Ph.D.'s in chemistry find industrial employment.

Chemistry always was the art, craft, and business of substances and their transformation. I say “always,” because I want to emphasize that the protochemistries in food preparation, cosmetics, metallurgy, glass and enamel making, textile preparation, dyes and pigments, fermentation, medicinal preparations and many others *preceded* the formal development of the science. Chemistry remains this—the study (and utilization) of macroscopic matter and its changes. The transformed matter must be macroscopic if it has commercial value, but on the research plane, the actual amount manipulated may be tiny (think of the knowledge built on DNA gels).

With time, we've learned to look inside the innards of the beast, and reasoned out that in the macroscopic matter, static and undergoing transformation, there are atoms, and, much more interesting, persistent groupings of atoms which are molecules. So chemistry is also the art, craft, business and science of molecules and their transformations. It is, symbolically, and essentially



I will later add the arrow that makes this an equilibrium, and its consequences.

The reliable knowledge (a phrase I've borrowed from Ziman (1998), more than van Frassen's “empirically adequate”) gained of the molecular world came from the hot and cool work of our hands and mind combined. Sensory data, yes, but we did not wait for scanning tunneling microscopes to show us molecules; we gleaned their presence, their stoichiometry, the connectivity of the atoms in them, and eventually their metrics, shape and dynamics, by indirect experiments. The reasoning in these was rarely

³ See also Bensaude-Vincent (2000).

decisive, sometimes productively quasicircular (Hoffmann, 1988), and often in the nature of extending a story. Amazing that one could design the reality of physiologically active pharmaceuticals and billion-ton industrial production on such seemingly flimsy knowledge, isn't it?

Given this briefest sketch of chemistry, let me look at some leitmotifs of the last century of philosophy of science in the chemical context.

4 Realism, reinforced by transformation

You are not likely to find a doubter of realism, a skeptic on any level, in the chemical community. At the same time chemists realize the symbolic essence of their molecular representations and the multiplicity of ways of looking at a molecule. Chemists also are well aware of the ephemeral nature of theories. But underlying their productive activities is a solid realism. Whence the intuitive realism of the chemist?

I think it derives from the reinforcement of sensual perception by the transformation inherent in chemistry. The sensual perception I'm talking about is at one level just that, of some green crystals that precipitate in a flask and are filtered out in a separate process. The feeling that matter is matter is reinforced by a chemical appreciation of differences in chemical and biological behavior. Perhaps 15 million of the 17 million or so well-characterized chemical substances are white crystalline solids. Salt, sugar, penicillin and tetrodotoxin (the poisonous principle of the pufferfish, fugu) are such. The differences in their biological behavior (or in the nmr spectrum) are a continuous lesson in realism. Taste them, take their spectra.

By itself, the gestalt of sensual perception, though deceivable in its parts, makes a very big difference. No amount of exposure to text and images with sexual content diminishes the nervous wonder of a first sexual experience.

Transformation provides great, great reinforcement to a naïve realist perspective. It is one thing to make molecule A. You may be uncertain about its structure, always more uncertain if it is a molecule that you wanted to make and it was made by someone else. But when you take compound A, with the supporting chemical and physical evidence for its structure, and you transform it into compound B, and the spectroscopic clues for its structure check out, and then B is changed into C, and C into D, and it all makes sense—boy, do you then believe in A!

Ian Hacking says it well (Hacking, 1983):

“Experimental work provides the strongest evidence for scientific realism. This is not because we test hypotheses about entities. It is because entities that in principle cannot be ‘observed’ are regularly manipulated to produce a new phenomena and to investigate other aspects of nature. They are tools, instruments not for thinking but for doing.”

Hacking's outlook, reminding philosophers to pay more attention to experimental intervention, rings true.

The constructed realist confidence is perhaps more in the molecular, microscopic structure; there was never much doubt about the reality of those powders.

5 Reductionism

What's the use of flogging a dead concept, you might think. I agree. But simplistic reductionism, while retaining little standing in the philosophical community, is alive

and well within science. Aside from the general good feeling that comes from being at the bottom of a reductionist chain (and for chemists that may derive from providing explanations for biology), there are theoretical chemists who really think that all the concepts of chemistry would be clarified by rigorous definitions, of course based on physics (Bader, 1990).

My minor tirade against reductionism, stressing its unreality and futility, is elsewhere (Hoffmann, 1995). More positively, here's what I believe: In dealing with the complexity of this world, human beings adduce explanations in two modes (and then mix them up; more on this below). Vertical understanding is the classical reductionist kind. Horizontal understanding is expressed in the concepts, definitions, and symbolic structures at the same level of complexity as the object to be understood. Horizontal explanations, like dictionary definitions, but richer, are quasi-circular (Hoffmann, 1988). And none the worse for it. A poem is horizontally understood at the level of the language in which it is written and the psychology of the writer and reader; it is vertically (and impoverishingly) explained by the sequence of firing of neurons (and the biochemical actions behind them) in the author's or reader's mind.

My stronger claim is that most concepts in chemistry that have proven productive in the design of new experiments are not reducible to physics. By this I mean that they cannot be redefined adequately using only the language of physics. To be specific, I'm thinking of aromaticity, the acid-base concept, the idea of a functional group, a substituent effect, and that of a chromophore. And let us not forget the chemical bond.

Few, if any, new molecules would have been made if we had waited around for rigorous definitions of these productive thought constructions. Our icon, achieving that deserved status through its sheer utility, Mendeleev's Periodic table, would not have been drawn up for 56 years. The mechanism of the deceptively simple dimerization reaction that Komatsu runs on $H_2@C_{60}$ at the end of his paper is quite unclear. That doesn't stop him from making the molecule.

It might seem as if I am advocating a special logic for chemistry, or no logic at all. It's as if I were back in the period of 1700–1750, in which Georg Ernst Stahl, Guillaume-François Rouelle and Gabriel-François Venel (who wrote the *Encyclopédie* article on chemistry) set out a special philosophical basis for chemistry. Each in his own way privileged the actions of chemistry, the distinctive properties of compounds, the irreducibility of chemistry to physics.⁴

Perhaps I am. But I think the recognition that understanding is as much horizontal as it is vertical, in *any* science (as it is in the social sciences) gives me a way to express the distinctiveness of chemistry.

Let me say it another way: Reductionists claim that they labor to reach the roots. And once the elementary particles are understood, and all the forces too, then one could move upscale, and with the workings of those building blocks and forces, a bit of the aleatory thrown in, the macroscopic would emerge. At any level. I'm skeptical; I've hardly ever seen a soul move upscale.

I think chemistry does move upscale, climb ladders of complexity, create new molecules and emergent phenomena. It does so by alternating small riffs of reductionist analysis with lots of intuitive thinking on the horizontal level. Making up a story, while making molecules.

⁴ For a succinct review of the period, see Golinski (2003).

6 Incommensurability

In chemistry, revolutions may be less frequent than the grafting of a new way of thinking onto an old stock. Though some people think that neologisms are the way (*pace* the Condillacian side of Lavoisier), in the long run the the way to capture minds may be to introduce the new pretending to be the old.

My model here is the two-step evolution of the nature of the chemical bond. The first conflation is of the simple 19th century line, denoting association, with a shared electron pair in a Lewis structure. This was followed by Pauling's skillful association of the covalent wave function of the new quantum mechanics with Lewis' shared pairs, and through that with the 19th century bond. Meanwhile, other signatures of bonding—length, energy, vibrations—reified the chemical bond.

Another instance, a very recent one in my community of theoretical chemistry, is of using the supposedly unneeded (if not unreal) orbitals of density functional theory in the same ways as the orbitals of a so-called one electron molecular orbital approach to electronic structure. The latter is a poorer theory, with greater explanatory power, and in it my favorite molecular orbitals play the central role.

Still another grafting is that of explanations of electrostatics onto a quantum mechanical calculation which from the start has electrostatics built into it. This is going on, with a vengeance, right now.

Kuhn saw incommensurability as being the consequence of two competing paradigms, and he distinguished incommensurabilities of language, and of standards of evidence. I think incommensurability is no problem whatsoever to chemists. Differences in language are there, the result of different paradigms, but more so of history, and of education. Yet people, eager to make things, with no handwringing on how problematic it all is, graft one way of understanding onto another. So, to return to that electrostatic/quantum mechanical conundrum, a couple of decades down the line there is one language (of charges attracting, *and* of quantum mechanical explanations) which even though it is deeply inconsistent at its core, is rich enough to provide productive extrapolations.

There is a relation here to Peter Galison's concept of the utility of pidgin languages (Galison, 1997), with the addition I would make that the trading zone forms in the mind of every individual.

A not unrelated phenomenon in chemistry (and maybe not just chemistry) is the fecundity of flawed if not downright wrong theories (Berson, 2003, Ch. 8; Hoffmann, 2003).

7 Analysis and synthesis, creation and discovery

In a unique 1806 novel, "Elective Affinities," constructed on the metaphor of a theory already on the way out, in a time when analysis was at the center of chemistry, Goethe has this scene between Eduard and Charlotte (Goethe, 1971, p. 53):

"The affinities become interesting only when they bring about divorces."

"Does that doleful word, which one unhappily hears so often in society these days, also occur in natural science?"

"To be sure," Eduard replied. "It even used to be a title of honour to chemists to call them artists in divorcing one thing from another."

“Then it is not so any longer,” Charlotte said, “and a very good thing too. Uniting is a greater art and a greater merit. An artist in unification in any subject would be welcomed the world over.”

The H₂@C₆₀ paper I chose details the sequential transformation of molecules. Is that typical? And, if typical, what consequences do such papers have for the philosophy of science?

I would claim the Komatsu et al paper, beautiful as it is in its individuality, is indeed also typical of organic, polymer, inorganic, organometallic and solid state chemistry. But not of physical and analytical chemistry. In the formative years of modern chemistry, the primeval analytical question “What is it?” answered at the atomic level, was the dominant one. That query remains important, for Komatsu and his coworkers interrogate every molecule they make as to its identity. They must analyze their reagents, and the intermediate structures in their synthesis. And they most certainly must prove the consistence of their spectra with the structure they suggest for their heroic achievement, H₂@C₆₀.

But, as you can just see from the way the work is presented, the analytical enterprise is, if not taken for granted, subjugated. Most of the evidence is in the Supplementary Material to Komatsu’s paper. The emphasis is on the new molecule, on synthesis. Making it matters.

The concern may return that I have picked a certain kind of paper out of the multitude. Joachim Schummer has come to similar conclusions (Schummer, 1977a,b; Schummer, 2004). He has also taken a sample of 300 synthetic papers and analyzed them in detail, asking for the papers’ *aims*, i.e. why chemists do experiments. And how they accomplish them. Figure 2 shows the outcome.

Schummer finds the emphasis on synthesis I mention, as well as what one might call “propagation”—the making of new molecules “in order to improve the abilities to produce more new substances.”

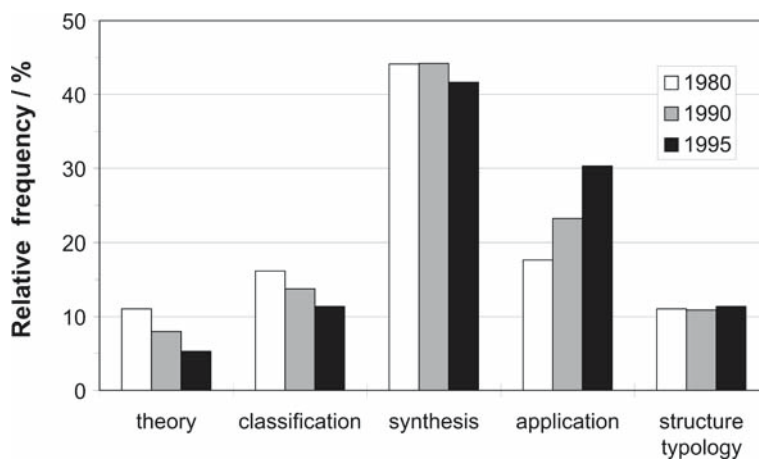


Fig. 2 Relative frequencies of aims in synthetic chemistry, 300 papers from *Angewandte Chemie*, 1980–1995. Schummer (1997b)

When did this change, when did synthesis begin to dominate chemistry? One locus is found in the in the second half of the 19th century, in Perkin's opening to aniline dyes, and the subsequent development of German dye and medicinal chemistry. Another is found in the twin explosions of activity in organometallic and solid state chemistry in the second half of the 20th century. Certainly an intellectual high turning point was provided by the synthetic *tour-de-forces* of R.B. Woodward's mid-20th century syntheses.

Michael Weisberg has made me aware that to some philosophers the distinction between creation and discovery may seem strange. In that they see a "context" (or logic) of discovery in science, accompanied by the (arational) generation of hypotheses. And contrast that with the context of justification, the way data is processed to build credibility in one or another set of hypotheses. In chemistry it's clear that making new molecules is a very, very different enterprise from analyzing what is in nature. And that synthesis creates in its practitioners different ways of looking at the world, in which theory building is not central. Making things is.

8 What could be different?

I believe the dominant interpretations of the nature of science by mid-20th century philosophers come out of a focus on theory formation and justification and view science as just discovery. And if those interpretations were instead based on the heart of chemistry, the creation explicit in synthesis, they would be different. As I said above, and as Berson argues convincingly, the extended philosophical discussion of falsification, the prevalent concern with testing theory, has little to with chemical preparative practice.

I fear that the even the chemistry-educated philosophers of note—from Freudentheim to Polanyi—have also come from a certain side of the tracks. This was physical chemistry, which shares much of its research ethos, though not all, with physics. Even as they do fascinating things, by and large, physical chemists don't make molecules.

Emily Grosholz reminded me that I should acknowledge a change in philosophical winds in the 1980s. Ian Hacking, Nancy Cartwright, Bas van Fraassen, Margaret Morrison, as well as others emphasized experiment, construction, and intervention. Their efforts paralleled by convergent activity in the history of science, have created a philosophical purview sympathetic to the story I tell. Grosholz remarks, that these philosophers "...might have developed their positions in even more interesting ways if they'd drawn their case studies from chemistry as well as physics." Indeed.

So what could have been different? Chemists make compounds/molecules, the objects of their own contemplation. That puts them close to art and artists. Lest we get too romantic about that (only someone who has not tried to make a living as an artist would), the centrality of creation also puts us close to engineers. The molecule is made, and often it is made for a purpose—a desired physical or biological property.

The connection of this one science to art—high and low—could have led philosophers to apply aesthetic theories to science. This would have certainly helped people to be more at peace with the obvious influence (not all for the good, mind you) of aesthetic factors—symmetry, order, telling a good story—in the acceptance of theories. Not just prediction.

The connection to engineering makes utility an important criterion to chemistry. Sulfuric acid, no. 1 on the chemical hit list for 75 years, is beautiful because all

100 billion lbs of it made in the US last year are *used*. And utility immediately creates a problem for my hypothetical new philosophy of science that incorporates aesthetics. Disinterested contemplation has been a central feature of aesthetic theories—vide Kant's *Zweckmässigkeit ohne Zweck*. I personally think (Hoffmann, 1990) this points to a failure of classical aesthetics, in not allowing utility to be a valid determinant in defining what constitutes art and beauty.

One more point: Chemistry is the truly anthropic science—our molecules can heal, and they can hurt, for they are on the scale of the molecules in our bodies. A consequence is that chemists must enter the arena of public ethical debates. Many do not do so willingly.

9 Semiotics, too

The number of drawings in the Komatsu et al paper is probably less than if this paper were published in a chemical journal—*Science* limits the number of illustrations. But it is high enough for you to see centrality of graphical representation in chemistry. And that means pictures of molecules more than curves of measurements.

Though describing compounds and their transformations requires representation (see the writing around the arrows in Fig. 1), it is the microscopic world-view, of molecules, which makes for a flowering of representation. Curious representations they are too, polyhedra floating in some neutral space, situated somewhere between the compact messaging of caricature, the conventions of “primitive” art, and cubist perspectives (Hoffmann & Laszlo, 1991; Laszlo, 1993).

And, all the time, trying desperately to evoke in the mind of the chemist reader who is privy to the primitive graphic codes used (for chemists, to whom three-dimensional representation of shape may be a matter of life or death, are not trained in art), the geometry of the molecule.

There is lots going on there, in those visual representations. Perhaps most important is the mixing of symbolic and iconic representations. The names of the compounds, and the elements of which they are comprised, are all symbolic. Even though these are real, tangible substances! The molecules, which are *not* seen directly, are given a more iconic representation—you see that hole in the buckyball, don't you? Though there are awful doses of symbolism hidden in those bond lines.

It seems like a holy mess, this conflation of representations. But it works. Elsewhere, Emily Grosholz and I have argued that the world bridging involved in dealing with a real chemical problem requires both symbolic and iconic representations. We write (Grosholz & Hoffmann, 2000):

How does the iconic form of the chemical structure expressed as a diagram that displays atom connectivities and suggests the three-dimensionality of the molecule, bridge the two worlds of the chemist? The most obvious answer is that it makes the invisible visible, and does so, within limits, reliably. But there is a deeper answer. It seems at first as if the chemical structure diagram refers only to the level of the microscopic, since after all it depicts a molecule. But in conjunction with symbolic formulae, the diagram takes on an inherent ambiguity that gives it an important bridging function. In its display of unified existence, it stands for a single particular

molecule. Yet we understand molecules of the same composition and structure to be equivalent to each other, internally indistinguishable. . . .

Thus, the icon (hexagonal benzene ring) also stands for all possible benzene rings, or for all the benzene rings (moles or millimoles of them!) in the experiment, depending on the way in which it is associated with the symbolic formula for benzene. The logical positivist in search of univocality might call this obfuscating ambiguity, a degeneracy in what ought to be a precise scientific language that carries with it undesirable ontological baggage. And yet, the iconic language is powerfully efficient and fertile in the hands of the chemist.

The iconic and symbolic languages are each incomplete—they cannot represent all. But that is not a failing; they are “productively ambiguous,” serving an essential bridging function.

10 Violating categories

Another characteristic of modern chemistry is the inseparable mixing up of the microscopic and the macroscopic perspectives in doing chemistry. Look at the Komatsu et al paper. It contains four figures of molecular drawings, and not a single photo of the material(s) undergoing transformation. The physicality of the processes is hinted at in the telegraphic (sorry, text-messaging) abbreviated reaction conditions around the arrows in Figs. 1 and 4 (“toluene, r.t. [=room temperature], 13 h”). The details are in the “Supporting Online Material;” the only amount of material mentioned in the text is the mass of $\text{H}_2\text{@C}_{60}$ obtained in the final step—118 mg, contaminated with some C_{60} .

The point here is not how far away (and why) we are from the format of scientific reportage of say, 18th century England. Rather it is that the practicing (and excellent) chemists inextricably mix macroscopic and microscopic viewpoints of substances and molecules in the productive work of their science.

I think there are philosophical implications in the violation of categories. I do not dispute that the philosopher’s job is to define the modes and levels of thought and action, and that upon such delineation one can superimpose the messy actions of often illogical human beings. This was Lavoisier’s program too, of really defining the elements. And it made modern chemistry possible. For instance, could we ever define impurity in chemical compounds except by getting compounds as pure as they can be (defying entropy in the process) and then comparing made-to-order mixtures with naturally impure substances?

I’m torn about this. I started out in chemistry perturbed by the mixing of categories around me, drunk on logic, mathematics, and symmetry. I was looking, as Primo Levi once was, for the theorems of chemistry. Eventually I came to peace with the multivalency of piecewise understanding around me. And I saw that partially irrational reasoning (oh, prettified for publication) led to stunning molecules and reactions.

My perception of human beings, not just chemists, is

- (a) that in the service of either creation or utility, they will naturally and deliberately violate all categorizations (here chemists inextricably mixing up molecules and compounds), and

- (b) that the process of creation of the new depends essentially on the transgression of categorization.

Point (a) is weak, and ultimately unimportant: people are people. Point (b) is stronger, with implications for philosophy: I want to claim that people are unlikely to make the new (art, science, religion, new people) without violating categories (Feyerabend, 1975).

I am here beyond philosophical holism, beyond intellectual bricolage, close to Feyerabend's prescription for "epistemological anarchism." Must be what too much poetry does.

One could imagine the last, strong variant as a restatement of Kuhn's revolutionary program; if so it represents a wholesale democratization of revolutions—they must be there in every creative act.

11 Change

So, Heraclitus was right. While equilibrium creates a stable, seemingly dormant middle (even as that middle is seen at the molecular level to be all flux), the chemical norm is change. Products are different from reactants. We can, and do, perturb equilibrium.

Could there be philosophical consequences of continuing, ever-present change? I'm not sure, but I wonder if cognizance of chemistry's emphasis on the arrow in $A + B \rightarrow C + D$ could have led people to spend more effort in constructing workable process philosophies. In doing so, perhaps one could learn something from the chemical analysis of complex reaction systems (the atmosphere, metabolism, oscillating reactions, surface catalysis) in building a philosophical frameworks that respect equally things and the changes between them. Some efforts in this direction have been made (Earley, 1981, 1998; Stein, 2004).

We are drifting in that direction in molecular biology, as the relative paucity of the genome does not easily explain the richer proteome and how the environment influences an organism. Evelyn Fox Keller has spoken interestingly of "verbing biology." I think we need thought from the philosophical community (with something to learn from artists) on how best to represent change.

Change is desired and resisted by individuals, and mostly resisted by our societies. No wonder then that society has an ambivalent view of the science at whose core is change. Even so, we are fascinated by change—be it a fire burning, a new dance tune, a child growing. As Mircea Eliade said (I paraphrase), chemists, screaming to high heaven that they had nothing to do with alchemy, accomplished everything the alchemists desired—to heal, to turn base things into gold (that's what Merck, Sharp and Dohme did). At the same time chemists—well, molecular biologists—transplanting genes have entered the transgressive region of free change that bothered the Church about alchemy. Bernadette Bensaude-Vincent writes well of this, of our continually transgressive science (Bensaude-Vincent, 2005).

And yet, as I said, we are fascinated by change. How to capitalize on that fascination, now that is a problem for today's chemistry. We desperately need the magic of alchemy, its natural hold on the imagination.

Philosophy of science changes too. To say that every decade a new "ism" is in, misses the point as much as the current rage for nano-this or nano-that in chemistry. Much more interesting is the wonder of something new made or said. In chemistry, all

of a sudden there is this new molecule, C_{60} , or H_2 in it—how come we didn't think of it, did not have it before? So into the library (I'm getting old) comes this new book, as Kuhn's did one day, and it shapes a new world, even as it has antecedents and ambiguities.

I think that philosophy has something to learn from my truly anthropic science, the one with synthesis at its center. That science is in the middle, but the middle—be it for human beings or molecules—is never static. Oh, it may seem quiet, but it is tensed, a perturbable balance of polarities: of natural/unnatural, macro/micro, pure/impure, harm/benefit, the same/not the same, of trust/doubt. Things change. Quiescent, they can be willed to change. They, we must change.

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