

PERSPECTIVE

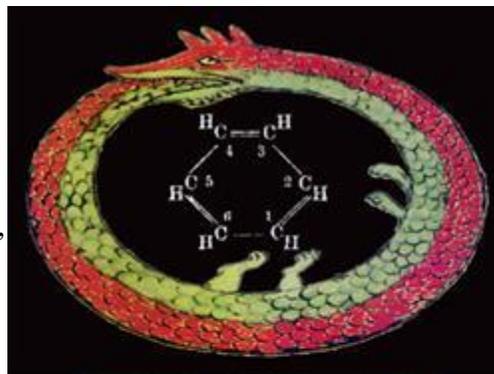
# The Many Guises of Aromaticity

Is hype debasing a core chemical concept?

[Roald Hoffmann](#)

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Aromaticity is one of the core concepts of organic chemistry. The idea began as a descriptor of the special stability of the ring of six carbons, benzene,  $C_6H_6$ . And importantly, of the ability of that ring to be transformed by chemically substituting the hydrogens attached to it. The reactions involved were relatively easy, the products often stable and useful. Aspirin, TNT, mescaline, vanillin, and serotonin all contain an aromatic, benzenoid core.



As chemistry evolved, it was natural to seek other gauges of stability and the capacity to change while retaining the  $C_6$  core. Clothed in various measures, wonderfully expanding in scope, mental catnip for my fellow theoreticians, aromaticity, the concept, flourished. I will sketch its flowering, from the seminal paper of German chemist August Kekulé that proposed the correct structure of benzene 150 years ago, to those new measures.



Today, an inflation of hype threatens this beautiful concept. Molecules constructed *in silico* are extolled as possessing surfeits of aromaticity—"doubly aromatic" is a favorite descriptor. Yet the molecules so dubbed have precious little chance of being made in bulk in the laboratory. One can smile at the hype, a gas of sorts, were it not for its volume. A century and a half after the remarkable suggestion of the cyclic structure of benzene, the conceptual value of aromaticity—so useful, so chemical—is in a way dissolving in that hype. Or so it seems to me.

## Kekulé

It is the sesquicentennial of Kekulé's proposal of the cyclic structure of benzene. The  $C_6H_6$  molecule was first isolated from compressed illuminating gas by Michael Faraday in 1825. Many organics, not just benzene, have distinct olfactory characteristics, ranging from pleasant to downright foul-smelling. But already by Kekulé's time, the adjective "aromatic" was associated with the group of molecules related to benzene.

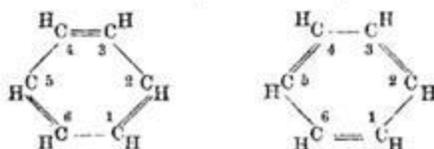
The structure of benzene remained a stumbling block to mid-19th century chemists. The road to the structure we now know was not simple—nothing in the real world is; Kekulé himself went through four distinct graphic representations in the seven seminal years of formulating benzene's structure. Let me show you two of these.

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Kekulé's first formulas didn't look at all like the representation we use today. From his first 1865 paper comes a "sausage" (*Wurst*) formula, shown on the top of the figure at right. The arrows in the image, his very first published representation, are Kekulé's way of communicating, within the constraints of a linear representation, that the left end of the molecule is connected to the right. In the middle of the same figure is a roughly contemporary image of a physical model of the structure, possibly made by Kekulé himself in Ghent, Belgium. The ovals in the top figure and the four black balls welded together in the middle represent the four valences (bonding capabilities) of the carbon atoms. The solid model develops a more direct representation of that connection.



Ghent University Museums - History of Sciences



Within a few years of this proposal, the structures were rewritten in a graphic form close to the contemporary one, as in the "Kekulé structures" shown at the bottom of the figure on the right, here taken from an 1872 paper by him. The two structures just differ in the placement of the double bonds in the molecule.

Kekulé's two structures, which we now would call cyclohexatrienes, posed an immediate problem to him and to other chemists—how to reconcile the equivalence, at every level (physical, chemical) of all six carbons of benzene with the existence, on paper, of two cyclohexatrienes. Kekulé proposed a microscopically detailed (and erroneous) theory of bonding forces in atoms, involving their oscillations around their equilibrium positions, resulting in timed collisions with other atoms. His *ad hoc* hypothesis saved the day. As Yale University's Jerome Berson wrote in his 2003 book, in a most perceptive analysis of Kekulé's ideas:

The history of organic chemistry shows that even though this theory was not really understood by most organic chemists of the 19th century, it was applied nearly everywhere. Chemists of the time quickly suppressed any remaining distaste, swallowed this awkward bolus, and pressed ahead. Their subsequent achievements under the aegis of the theory vindicated their action. The tremendous flowering of synthesis and the discovery of an abundance of new reactions and structures during that time all took place in an atmosphere of growing conviction *that, for whatever reason*, the C<sub>1</sub>–C<sub>2</sub> and C<sub>1</sub>–C<sub>6</sub> bonds of benzene were structurally equivalent, as Kekulé had said.

Benzene derivatives were and are ubiquitous in chemistry. Aside from the selection of compounds I mentioned, several of the amino acids and all nucleic acids contain a benzenoid entity. Why so many benzenes? It's not just the inherent stability of the six-membered ring, but I

think two other matters of architecture and reactivity. First, the flat skeleton of benzene allows us to “disperse” chemical functionality (through substituents) in a plane, radiating out of the ring. And second, while the molecule is relatively stable to decomposition, it is also moderately reactive. That reactivity, with acids, bases, and radicals, permits one to substitute a subset of the hydrogens by other groupings of atoms— $\text{CH}_3$ ,  $\text{Cl}$ ,  $\text{OH}$ ,  $\text{NH}_2$ ,  $\text{NO}_2$ . Function comes from the properties of these substituents—benzene is like a mug that allows one to detach and attach a number of handles to it, each with its own chemical capabilities.

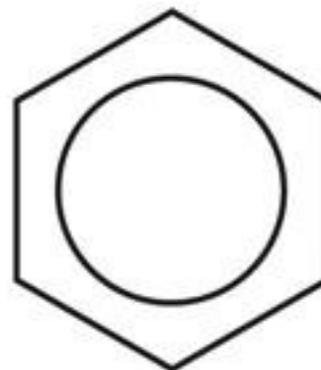
In 1890, long after the events, Kekulé describes his famous dream (here translated from German by Alan J. Rocke):

I was sitting there, working on my textbook, but it was not going well; my mind was on other things. I turned my chair toward the fireplace and sank into half-sleep. Again the atoms fluttered before my eyes. This time smaller groups remained modestly in the background. My mind’s eye, sharpened by repeated visions of a similar kind, now distinguished larger forms in a variety of shapes. Long lines, often combined more densely; everything in motion, twisting and turning like snakes. But look, what was that? One of the snakes had seized its own tail, and the figure whirled mockingly before my eyes. I awoke in a flash, and this time, too, I spent the rest of the night working out the consequences of the hypothesis.

Kekulé’s ouroboric vision did not hurt the molecule’s popularity.

## Stability

Aromatic compounds, meaning compounds containing benzene rings, became common. So were they particularly stable? Yes and no. Let’s take benzene itself. Here is one measure, an energetic one, of what is special about it. A common reaction is hydrogenation, the addition of a  $\text{H}_2$  to a  $\text{CC}$  double bond, as in cyclohexene going to cyclohexane, shown on the right.



The experimental heat of the reaction shown, at room temperature, is  $-118$  kilojoules per mole. That’s a lot of heat emitted—it would heat a liter of water from  $0$  to  $28$  degrees Celsius.

If benzene were cyclohexatriene, with its three double bonds, the heat of the triple hydrogenation (cyclohexatriene to cyclohexane) should be thrice that of cyclohexene, or around  $-354$  kilojoules per mole. Experimentally, the energy produced when three molecules of hydrogen are added to benzene is much less,  $-206$  kilojoules per mole. To put it another way, benzene is more stable than a hypothetical cyclohexatriene by about  $150$  kilojoules per mole.

That was actually the first simplistic estimate of the extra stabilization of benzene, called its *resonance energy*. With a more careful definition, the stabilization is seen to be even larger. The word “resonance” came from Linus Pauling, the premier American theoretical chemist and

structural chemist of the mid-20th century. He used a mechanical metaphor of resonance—the seeming ambiguity of two Kekulé structures was transformed by Pauling into an extraordinary stabilization. A nomenclature not introduced by Pauling but roughly contemporaneous—the circle in a hexagon symbol, shown at right (hydrogens understood, in the typical way of organic chemistry)—took over. The circle represents the symmetric, stabilized disposition of the six highest energy electrons of the benzene molecule, the ones the Kekulé structures wrote as double bonds.

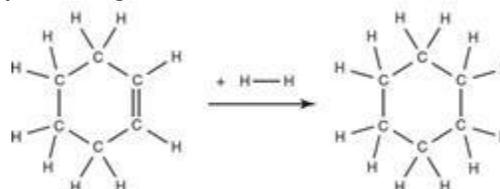
At the same time that Pauling's ideas flourished, Erich Hückel in Germany came up with a molecular orbital (MO) theory of the stability of benzene. Each carbon has six electrons—two are in a 1s orbital (orbitals are quantum mechanical places for electrons to move, wave functions that are solutions of Schrödinger's equation), too low in energy to bond. Three more electrons per carbon are in orbitals (2s and 2p) that form single bonds to the other carbons and hydrogens. There remains on each carbon one orbital perpendicular to the plane of the ring, a 2p orbital, and one electron. These form what is called the  $\pi$ -system of benzene.

From the six atomic orbitals, Hückel constructed six molecular orbitals, combinations of atomic orbitals, [as seen here](#). Three of them were at low energy, and with two electrons per molecular orbital, they had room for precisely six electrons. The  $\pi$  electrons in the ring were delocalized, no longer associated with any carbon, but shared equally among them. And six was the magic number. Here, in the language of quantum mechanics, was the aromatic sextet, the special feature of benzene.

The Hückel model was initially neglected (the story of why that happened is well told by Berson), but got a second life in 1950s. In the hands of physical organic chemists,

[+ enlarge image](#)

who could see in it pointers not just to the aromatic sextet but also to stable  $\pi$ -electron systems with two and ten electrons, Hückel's theory blossomed. I remember the excitement (it was when I was starting out in chemistry); a nexus between quantum mechanics and organic chemistry took shape. With time, the delocalization of electrons, part classical yet governed by quantum mechanical phase relationships that Hückel uncovered, became the distinguishing feature of aromaticity.



## The First Inflation

Mid-20th century, a time in which I studied, in retrospect was also the time of the first inflation of the concept of aromaticity. Guided either by a simplistic idea of “the more resonance structures, the better,” or by seeing aromatic sextets of electrons in too many places, much sweat in organic synthesis was spent in chasing down molecular phantoms. No matter, some fascinating molecules were made, and we gained a better understanding of the factors governing molecular stability.

All along there was a thermochemical corrective on our romance with benzene, and I don't mean its carcinogenicity (which eventually imposed controls on the laboratory use of this ubiquitous

solvent). As stable as benzene is, its heat of formation, that is, the heat of the reaction  $6\text{C}$  (graphite) and  $3\text{H}_2$  (a gas) to form benzene (a liquid) is +49 kilojoules per mole. The elements are more stable than benzene. And benzene is quite flammable.

## New Criteria for Aromaticity

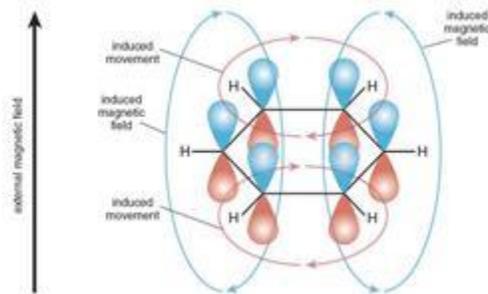
One hundred years ago, during World War I, chemical crystallography was born. Advancing slowly at first (the details of benzene's structure did not emerge until the 1930s), the field exploded with the advent of computers—today from the diffraction of x-rays by crystals we know the metrics of over 700,000 organic compounds. You can bet that there are tens of thousands of benzene rings in molecules in this cornucopia. All have C–C distances close to 1.39 angstroms, and quite far from the extremes of a localized double and single bond alternating (1.34 and 1.48 angstroms, respectively) in a hypothetical cyclohexatriene, one of the two Kekulé structures.



So came about another measure of aromaticity, *bond equalization*. There are many molecules part-way aromatic, and for those the disparity (or lack thereof) of bond lengths, expressed in a variety of ways, is a good measure of aromaticity. For instance, in the partially aromatic  $\text{C}_4\text{OH}_4$  molecule of furan, shown above, one has a sextet of electrons, but the bonds are, as shown, closer to being localized (double bonds shorter than single bond) than completely delocalized (all bonds approximately equal).

Nuclear magnetic resonance (NMR) provides another, most useful gauge of aromaticity. A magnetic field is applied to a molecule; the molecule's electrons respond by moving to counteract the applied field (see the figure on the right).

The field [enlarge image](#) actually experienced by a nucleus in the molecule (say that of hydrogen) is the sum of the external magnetic field plus the induced one. That local field is different at every distinct hydrogen; this difference, a *chemical shift*, allows one to identify hydrogens in an organic molecule. This is what has made NMR the prime analytic tool of modern organic chemistry. And, as magnetic resonance imaging (MRI), a common if expensive medical diagnostic procedure.



In benzene's delocalized electrons, a *ring current* of some magnitude is induced, substantially bigger than in a "saturated" organic analogue, such as cyclohexane. As the figure on the right shows, the ring current (producing a net magnetic field opposite to the induced one) runs around the molecule in such a way that at the periphery of the benzene molecule, which is just where the six hydrogens reside, the external magnetic field is actually augmented. The chemical shift of aromatic protons is identifiably different from normal protons. This became a hallmark of aromaticity, and not just in benzene. A related theoretical indicator, called *the nucleus*

*independent chemical shift* (NICS) introduced by the University of Georgia's Paul von Ragué Schleyer, has been cited as a measure of aromaticity (or lack thereof) in more than 4,000 papers.

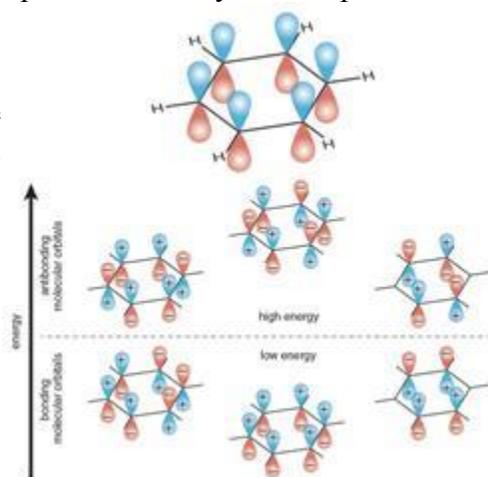
We had bond length variations from the 1930s, NMR chemical shifts from the 1960s. Both became ways to measure the extent of aromaticity.

## Bench-Stable, Bottleable

Computers made the determination of the structure of molecules in crystals easy—what took half a year in 1960 takes less than an hour today. They also made computations of the stability of molecules facile.

Whoa! What do you mean by stability? Usually what's computed is stability with respect to

decomposition to [+ enlarge image](#) atoms. But that is pretty meaningless; for instance, of the four *homonuclear diatomic molecules* (composed of identical atoms) that are most stable with respect to atomization,  $N_2$ ,  $C_2$ ,  $O_2$ , and  $P_2$ , two ( $C_2$  and  $P_2$ ) are not persistent. You will never see a bottle of them. Nor the tiniest crystal. They are reactive, very much so. In chemistry it's the barriers to reaction that provide the opportunity to isolate a macroscopic amount of a compound. Ergo the neologism, "bench-stable." "Bottleable" is another word for the idea. A lifetime of a day at room temperature allows a competent graduate student at the proverbial bench to do a crystal structure and take an NMR scan of a newly made compound. Or put it into a bottle and keep it there for a day, not worrying that it will turn into brown gunk.



Of course, one can also observe molecules in noble gas matrixes at 10 kelvin, or flying down a molecular beam, a stream of relatively few molecules. And one can obtain proof of their existence from a variety of spectroscopic techniques. Such molecules are very real; a molecule is a molecule, no matter how long it lives. But if one allows such fleeting molecules to approach each other, or approach acids or bases (water is both) they react, going away in a jiffy.

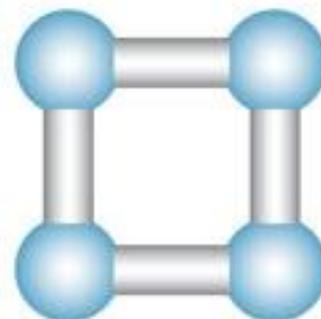
## Hype

Here is where hype comes in—not of advertisers, where we expect it, but of scientists. People calculate a new molecule, estimate its energy, find that it will not fall apart. To me the existence of such molecules, if attested to by spectroscopy, suffices. They are real. But there is a natural human tendency to want our molecular children to be exceptional. So, like the parents of the kids in Lake Wobegon or on City X's West Side, the conceivers of such new molecules look for something special. Could it be that the molecule is "aromatic?" Aromaticity is good, it has been good for 150 years. Perhaps the molecule is more aromatic, or maybe it is endowed with

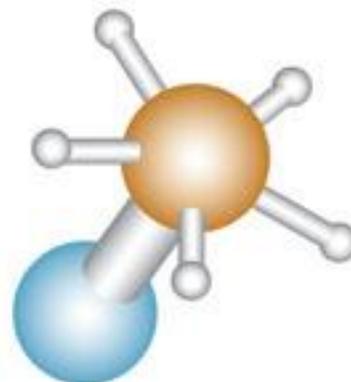
aromaticity of a different kind? There it is! Suppose the  $\sigma$  orbitals of the molecule (the orbitals in the plane of a molecule) also complete a shell, a group of occupied orbitals. Then the molecule is  $\sigma$ -aromatic. That's surely better than just plain old  $\pi$ -aromatic.

But, very often, the molecules conceived in a computer have minimal kinetic persistence. They would never survive aggregation at ambient laboratory conditions, or an encounter with the chemical killers in the air—water, oxygen.

Let me show two molecules for which such claims of extra aromaticity have been made. Both are illustrated in the figure at right: The top one is  $Al_4^{2-}$ , a square planar molecule; the bottom one is  $PtZnH_5^-$ . These molecules are beyond a doubt real, their structures established spectroscopically, and with reliable theory. What grates on me are claims of aromaticity, single or multiple, accompanying the fine experimental and theoretical work on these molecules. I would be willing to bet a good bottle of NY State Riesling (I will leave a sum for the eventuality in my will) that salts of these will not be made in milligram quantities in my lifetime or yours.



Or take  $C_6$ , known for decades. The molecule exists in cyclic (benzene denuded of hydrogens) and linear forms.  $C_6$  is observed in the interstellar medium and in the laboratory in a molecular beam. Not one of the good spectroscopists working on these carbon “clusters” (there are other  $C_n$  species) has made a claim of multiple aromaticity for them. Yet there are theoretical papers claiming just such double aromaticity for  $C_6$ . Carbon clusters, of which  $C_6$  is a small example, are patently reactive in a laboratory flask, moving on with a vengeance to graphite or, if oxygen is present, to  $CO_2$ . Until  $n=60$ , when one reaches a really persistent molecule.



The beautiful construct of aromaticity, sailing along for 150 years, enriched by new measures (bond equalization, ring currents) is vitiated by the idea being used as a marker of supposed singularity in a reaching for approbation. What bothers me is not the hype—I and most scientists have a finely tuned sensor for it. But I am pained by the damage done to this beautiful, eminently chemical idea that I can trace back a century and a half.

## Will Aromaticity Survive?

Oh, it will. It is in the nature of humans to both create a great idea, a new way of seeing one piece of the chemical universe, a way that lets us see similarities and differences. And then, equally human, to weaken the exemplary construction by bringing under its roof ideas or molecules that do not belong. There are reasonable extensions of aromaticity—to three dimensions, to different topologies of orbital interactions, such as those in Möbius strip arrangements of orbitals. But to me the labeling of the molecules cited in the last section as

aromatic (and of other hypothetical molecules in too many papers I have seen) appears to be less motivated by an intellectual desire to probe what aromatic means than by a reaching for distinction.

Aromaticity will survive the current wave of cheapening. The concept will survive because in its strong form—in the shape of benzene and other smaller ring systems with delocalized bonds—it singles out a group of molecules whose kinetic persistence and thermochemical stability go hand in hand. That's a correlation worth thinking about.

Another reason the concept will survive comes from its inherently chemical and, therefore I would argue, changeable nature. Here is what Paul Schleyer, an organic and computational chemist who has contributed immensely to the field, writes:

Historically, aromaticity has been a time-dependent phenomenon. Aromatic implies various features, properties, or behaviors to chemists with different backgrounds. While “benzene-like” still suffices for some, the “cyclic delocalization of mobile electrons” description now seems paramount. Its general implication for energies and structures, both geometrical and electronic, as well as magnetic and other properties, necessarily results in an ever increasing widening of the 19th-century aromaticity concept.

And Henning Hopf, a lover of aromaticity in all its guises, writes:

150 years after Kekulé's benzene dream, aromatic chemistry has reached a cultural richness and variety which the originator of the hexagonal benzene structure could not have imagined in his wildest fantasies.

Human beings need reasons for doing things. Aromaticity provides at least three motivations—first a search to better define the concept, hoping against hope that there is a unique measure of this elusive property. Second, one wants to explore all of its experimental manifestations. This has changed with time, as our tools have—we could not measure internuclear separations and chemical shifts in 1900. Third, and this is well said by Hopf, people have been inspired by aromaticity as a design principle to make ever more interesting molecules. The hype is seen through, the molecules, fleeting or persistent, remain real and beautiful.

## Acknowledgments

I am grateful to Paul Schleyer for his critical comments and many suggestions. Even as in the end he would not have been happy with what I have written (sadly, he passed away as this article went to press). Thanks to Martin Rahm for discussions and providing me with some illustrations.

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