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## Cover Story

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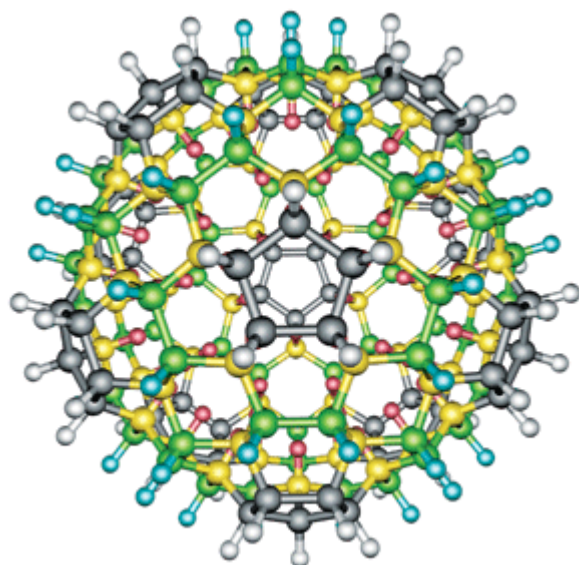
## Molecules That Could Be

### Calculations reveal stable but imaginary molecules that push the limits of what chemists know of chemical bonding

Jyllian Kemsley

**YOU HAVE THE ENTIRE** periodic table at your disposal. So what do you want to make?

That is a question that some theoretical chemists like to play with. Although many in the field use computations to shed light on existing molecules, some also take on the challenge of predicting molecules that haven't yet been observed or synthesized but could exist.



Courtesy of Tapani A. Pakkanen

Inside and Out The icosahedral C<sub>180</sub>H<sub>180</sub>

At the same time, theorists generally don't just throw atoms together willy-nilly. Says theoretical chemist and Nobel Laureate [Roald Hoffmann](#) of [Cornell University](#): You can take any group of atoms you want, throw it in a computer, and ask the computer to blindly search for a compound. The computer will find one. "Atoms really do want to bind with each other—they're unhappy as just atoms," Hoffmann remarks. The resulting molecule might be stable at absolute zero, but most likely, it would also be unhappy—and that would mean reactive. "You could keep a lot of graduate students busy—there are a large number of permutations that anyone can calculate, but that's not an intelligent use of humanity's talent," he says.

Molecules are predicted theoretically for the same reasons that synthetic chemists create them in the lab—to make compounds for specific applications, such as lubricants or fuels, or just to push the boundaries of what we know. "It's probing the limits of what we can do, and the limits

cage has 60 hydrogens bonded inside the cage (shown in red) and 120 on the outside (shown in white or blue). often give you information about the center," Hoffmann says. By looking at where theories break down, we get some ideas of how reliable those theories are.

Tetracoordinate carbon is a classic example. One of the basic lessons of introductory organic chemistry is that tetracoordinate carbon has tetrahedral geometry, with bond angles of  $109.5^\circ$ . But could those bonds be arranged differently, say, in a planar square?

"We can predict a huge number of organic molecules using the conventional concepts, but that doesn't really increase our understanding of bonding. In my view, the rule-breaking molecules reveal something new," such as new bonding motifs for carbon, says theorist [Paul v. R. Schleyer](#), a chemistry professor at the [University of Georgia](#).

Although synthetic chemists often chafe at the idea of theorists leading the way to synthetic targets, they do sometimes admit that good ideas can come from theory. For example, [Philip P. Power](#), a professor of chemistry at the [University of California, Davis](#), says his own work on synthesizing ethylene-like divalent tin and germanium hydrides was inspired by theoretical predictions of Georges Trinquier of [Paul Sabatier University](#), in France.

Sometimes, however, "it can be bad to listen to too much theory," Power says. "Theorists may predict that something can't be made or would be so unstable that you would never go into the lab and try it." That's a bigger issue with large compounds, he notes. Complex structures with many atoms push the limits of computations, so the results may not be as reliable as for smaller compounds. Nevertheless, Power sees huge benefits from synergistic interactions between theoretical and experimental work. Regardless of who inspires whom, theorists like to see their predictions validated experimentally, and synthetic chemists are often indebted to theorists for explaining bonding and elucidating experimental results, such as confirming spectroscopic band assignments.



Flat—and loving it

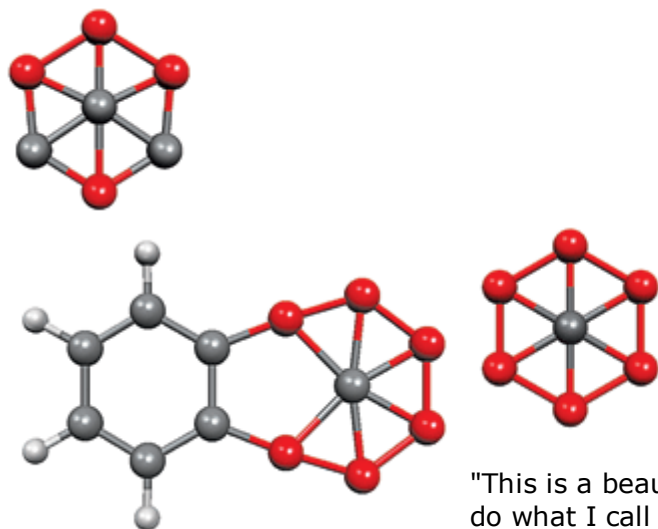
The structure of dimethanospiro[2.2] octaplane forces tetracoordinate carbon into a planar geometry.

**FOR THEIR PART**, theorists do caution that there's not much use in simply envisioning molecules with no thought as to whether there's a chance they could exist. "The literature is rife with loose statements about molecules being stable when there's no chance that they'll survive for a day nor do the calculations give any hint that they will," Hoffmann says. "The calculations don't probe the reactivity; they just probe whether something is a minimum" in potential-energy space. Ideally, theoretical studies should also include calculation of the energy barriers to rearrangement or dimerization, as well as reactions with  $O_2$ , water, and common acids and bases—"all the stuff floating around in a typical lab," Hoffmann notes. For a molecule to persist, at least for a few hours, these barriers must be at least 15–20 kcal/mol.

The first to tackle the question of whether tetrahedral carbon could be planar was Hoffmann, in 1970, along with chemistry professors [Roger W. Alder](#) of the [University of Bristol](#), in England, and [Charles F. Wilcox](#) at Cornell. Through theoretical analysis, they found that square-planar  $CH_4$  has a lone pair of electrons in a 2p orbital perpendicular to the molecular plane (*J. Am. Chem. Soc.* **1970**, *92*, 4992). They suggested that the square-planar form could be stabilized by using electron-acceptor ligands to delocalize those electrons. Several groups have now synthesized planar tetracoordinate carbon using metal ligands that function as electron acceptors.

Theorist [Leo Radom](#), a chemistry professor at the [University of Sydney](#), in Australia, used a different tactic, tackling the question of whether planar tetracoordinate carbon could exist in a neutral, saturated hydrocarbon. Instead of using electron-acceptor ligands to electronically stabilize the square planar carbon, Radom and former graduate student Danne R. Rasmussen developed a molecule that would physically constrain the bonding geometry around a central carbon.

Through ab initio molecular orbital calculations, the scientists progressively capped a planar tetracoordinate carbon above and below with cycloalkane moieties (the resultant molecule was christened "octaplane"), then added two new C–C bonds between opposite pairs of  $\alpha$ -carbon atoms (spiro[2.2]octaplane), and finally linked the top and bottom caps by methylene bridges (dimethanospiro[2.2]octaplane) to achieve—at least theoretically—a truly planar four-coordinate carbon in the center (*Angew. Chem. Int. Ed.* **1999**, *38*, 2876). Although the group did not investigate all reaction pathways to determine specific barriers to decomposition, a limited study indicated that the structure could well be stable enough to synthesize.



Courtesy of Paul v. R. Schleyer (3)

Spoked wheels Calculations suggest that carbon can bond to six other atoms in a plane, as illustrated by  $\text{CB}_6^{2-}$ , one isomer of  $\text{C}_3\text{B}_4$ , and  $\text{C}_7\text{H}_4\text{B}_6$  (shown with boron in red; carbon, gray; and hydrogen, white).

"This is a beautiful example of the use of computational chemistry to do what I call designer chemistry," Radom says. "To do this experimentally would be a nightmare—to make any one of these types of molecules is a major, major task. By doing it computationally, you can test all of the various possibilities and come up with the conclusion that this is the best target molecule for synthesis."

If planar tetracoordinate carbon isn't enough to set your mind spinning, theorists also have determined that planar pentacoordinate and planar hexacoordinate carbon could be viable synthetic targets.

Having carbon accept more than four bonds is not new; carborane cages include five- and six-coordinate carbon atoms. To force those bonds into a plane, however, is a much more demanding task.

Georgia's Schleyer, who made significant contributions to the theory of planar tetracoordinate carbon, took on the further challenge of predicting whether and how planar hexacoordinate carbon atoms could exist in a molecule.

Schleyer and former postdoc Kai Exner started with the idea of adding a carbon atom to the center of a benzene ring. Calculations showed that such structures are extremely unstable because of crowding around the central carbon. They turned instead to a carbon surrounded by six boron atoms; the longer B–B and B–C bond lengths allowed more room for the central carbon. They computed centrosymmetric  $\text{CB}_6^{2-}$  to be an energetic minimum, with  $n$  molecular orbitals similar to benzene's (*Science* **2000**, *290*, 1937). The octet rule is not violated because the central carbon has only partial bonds to the six boron atoms.

Exner and Schleyer also investigated planar hexacoordinate carbon in three isoelectronic, neutral  $\text{C}_3\text{B}_4$  isomers, which also are aromatic with six delocalized  $n$  electrons. All three isomers are energetic minima and have rearrangement barriers around 20 kcal/mol or greater.

In the seven years since Exner and Schleyer's paper, neither  $\text{CB}_6^{2-}$  nor  $\text{C}_3\text{B}_4$  has been synthesized. Recently, Schleyer and colleagues at the University of Georgia and [Beijing Institute of Technology](#), in China, suggested how planar hexacoordinate carbon molecules based on  $\text{CB}_6^{2-}$  might be more amenable to synthesis.

According to their calculations, when a peripheral B–B bond of  $\text{CB}_6^{2-}$  is broken and the ring opens, the central carbon retains its six bonds and planar structure. The opened boron ring then provides sites for substitution, allowing  $\text{CB}_6$  units to be grafted onto olefins, arenes, or saturated carbon systems (*J. Am. Chem. Soc.* **2007**, *129*, 1510).

Schleyer hopes that planar hexacoordinate carbon systems will be crafted. "The history of planar tetracoordinate carbon teaches us that such outlandish structures can be realized," he says.

Sometimes, surprising molecules are predicted not by design, but as a result of researching something else. For example, when postdoc Pradeep Gutta and chemistry professor [Dean J. Tantillo](#) of UC Davis were using theoretical methods to study the mechanisms of terpenoid cyclizations that lead to complex natural products, their calculations turned up a unique cation. A "formally tetracoordinate proton is seemingly suspended between two C=C bonds on opposite sides of a cyclooctadiene ring," the authors wrote (*Angew. Chem. Int. Ed.* **2005**, *44*, 2719).

When stripped down to a cyclooctadiene ring plus a proton, this so-called proton sandwich contains a symmetrical five-center, four-electron bonding array. The central proton is shared equally by the four "alkene" carbons, with carbon-hydrogen bond distances of about 1.5 Å. Computed nuclear magnetic resonance chemical shifts are about +13 ppm, indicating that the central hydrogen is very electron deficient. For comparison, bond lengths for three-center, two-electron cations  $[\text{C}\cdots\text{H}\cdots\text{C}]^+$  are typically 1.3 Å with chemical shifts of –7 to –3 ppm, consistent with an electron-rich environment.

Gutta and Tantillo's proton sandwich, although energetically a minimum, would easily rearrange to a structure with the proton bonded exterior to the ring. Still, perhaps some substituted system could be devised to stabilize the sandwich structure.

When it comes to predicting by design, other researchers are targeting fullerene variants. For all the work that has gone into making, purifying, and using fullerenes, their fully hydrogenated counterparts—fulleranes—are poorly understood. Finding stable fulleranes opens the door to further substitution, and with that could come new material properties. For example,  $\text{C}_{60}\text{F}_{60}$  has long been sought as a lubricant.

**PAST ATTEMPTS** to model  $\text{C}_{60}\text{H}_{60}$ , by chemistry professor [Martin Saunders](#) of [Yale University](#), predicted that the molecule would be most stable if 10 of the hydrogens point toward the center of the cage (*Science* **1991**, *253*, 330). Hydrogenating  $\text{C}_{60}$ , however, compromises the stability of the structure. To accommodate  $\text{sp}^3$  hybridization, the near-planar five-membered rings must buckle.

$\text{C}_{80}$ , in contrast, is composed of 12 pentagons linked by carbon atoms that are part of hexagons. Chemistry professor Tapani A. Pakkanen and coworkers Mikko Linnolahti and [Antti J. Karttunen](#) of the [University of Joensuu](#), in Finland, added hydrogens to  $\text{C}_{80}$  by creating an "in-out" isomer with 20 hydrogens bonded inside the cage and 60 hydrogens on the outside (*ChemPhysChem* **2006**, *7*, 1661).

The structure of the cage allows the linking hexagons to buckle, yielding a conformation similar to the boat conformer of cyclohexane. Those linking carbons get the interior hydrogens. Meanwhile, the pentagons remain planar and get the exterior hydrogens. Moving any hydrogen of a pentagon inside would distort the optimal planar arrangement of the five-membered ring, and moving any hydrogen of an interconnecting carbon atom outside would increase the steric hindrance between hydrogen substituents, the researchers explain.

Energy calculations indicate that  $\text{C}_{80}\text{H}_{80}$  is at least 96 kcal/mol lower in energy than dodecahedrane,  $\text{C}_{20}\text{H}_{20}$ , which is the only fullerane so far synthesized (*J. Am. Chem. Soc.* **1983**, *105*, 5446).

The next largest icosahedral fullerene is  $\text{C}_{180}$ , in which pentagons are connected through two fused hexagons. Pakkanen and coworkers created  $\text{C}_{180}\text{H}_{180}$  in silico by hydrogenating the hexagons alternately inside and outside the cage, leading to a total of 60 hydrogens in the interior. The  $\text{C}_{180}\text{H}_{180}$  structure is calculated to be even more stable than  $\text{C}_{80}\text{H}_{80}$ .

Theorists also have tackled other parts of the periodic table, including the transition metals. Metal complexes in very high oxidation states are often synthetic targets because they may be useful oxidation agents. But just how high can oxidation states go?

Chemistry professor [Martin Kaupp](#) and former graduate student [Sebastian Riedel](#) of [Würzburg University](#), in Germany, have theoretically evaluated the viability of Ir(VII), Os(VII), Os(VIII), and Tc(VII) complexes. Ligands used for such complexes are typically fluorine or oxygen because these atoms are small and highly electronegative.

The highest oxidation state complex of iridium synthesized to date is IrF<sub>6</sub> (*J. Chem. Phys.* **1960**, *33*, 436), but periodic trends indicate that Ir(VII) should exist. Kaupp and Riedel's computations indicate that IrF<sub>7</sub> could exist and would have a pentagonal bipyramidal structure (*Angew. Chem. Int. Ed.* **2006**, *45*, 3708). One possible decomposition

pathway—elimination of F<sub>2</sub> to form IrF<sub>5</sub>—is "appreciably endothermic." The other pathway—homolytic dissociation of an Ir-F bond to yield IrF<sub>6</sub>—is exothermic; however, structural rearrangement leads to a calculated barrier of about 24 kcal/mol. Thus, IrF<sub>7</sub> should be stable enough to isolate.

In the case of osmium, Os(VIII) is already known experimentally as the established oxidation agent OsO<sub>4</sub>, but reported syntheses of OsF<sub>8</sub> and OsF<sub>7</sub> have not been reproduced (both were likely OsF<sub>6</sub>). Addressing the question of whether OsF<sub>8</sub> and OsF<sub>7</sub> could exist, Kaupp and Riedel found that theoretically they can (*Inorg. Chem.* **2006**, *45*, 10497). OsF<sub>8</sub> likely has a fluxional structure, interconverting between two geometries. Decomposition pathways are unfavorable—F<sub>2</sub> elimination to give OsF<sub>6</sub> has a calculated barrier of more than 48 kcal/mol, and homolytic dissociation of an Os-F bond to give OsF<sub>7</sub> has a calculated barrier of 34 kcal/mol.

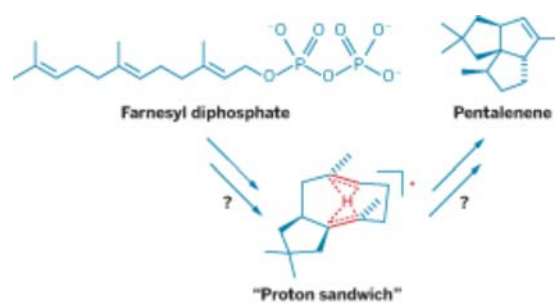
For its part, OsF<sub>7</sub> would, in theory, be even more stable. F<sub>2</sub> elimination to OsF<sub>5</sub> is endothermic, and homolytic bond cleavage has a high barrier of 57 kcal/mol, likely due to structural reorganization.

Finally, Riedel and Kaupp, along with graduate student Manuel Renz, found that TcF<sub>7</sub> is a viable synthetic target (*Inorg. Chem.* **2007**, *46*, 5734). Like OsF<sub>8</sub>, it appears to have a fluxional structure, interconverting among three forms. Computed decomposition barriers are nearly 72 kcal/mol for F<sub>2</sub> elimination to yield TcF<sub>5</sub> and nearly 48 kcal/mol for homolytic dissociation of a Tc-F bond to produce TcF<sub>6</sub>. If TcF<sub>7</sub> were synthesized, it would be the first heptafluoride of a 4d element.

That makes four stable structures, not one of which has been successfully synthesized. One problem, Kaupp says, lies in the occurrence of bimolecular reactions—for example, the reaction of two OsF<sub>8</sub> molecules to produce two OsF<sub>7</sub> molecules and F<sub>2</sub>. Such reactions tend to be exothermic. The way around that would be to switch from condensed-phase reactions to gas-phase or matrix-isolation techniques, in which reactive material is embedded within an unreactive host matrix.

**THE OTHER PROBLEM** lies in the chemistry of synthesis. Synthetic chemist [Karl O. Christe](#), a professor at the [University of Southern California](#), says that as one increases the oxidation state and number of fluorines around the central atom, it becomes easier for a new F atom to oxidize and abstract a ligand to produce F<sub>2</sub> rather than oxidize and form a bond with the central atom. "From a practical synthetic point of view, there's no easy and good solution," Christe says. "That's why we have been desperately trying to make compounds like these for many years."

Theorists also have led the way in making predictions about polynitrogen compounds, which are of interest for fuels or explosives. The reason for this lies in nitrogen bond energies—the average bond energies of N-N (39 kcal/mol) and N=N (100 kcal/mol) are significantly less than one-third and two-thirds, respectively, of the N≡N bond energy (228 kcal/mol) in N<sub>2</sub>. Consequently, decomposition of



proton sandwich A proposed intermediate in the pathway from farnesyl diphosphate to pentalenene features a proton suspended between two C=C bonds. Question marks indicate that the "proton sandwich" appears in only one of two possible computed pathways.

any polynitrogen compound to  $N_2$  will result in substantial energy release.  $N_2$ , being a major natural component of the atmosphere, is also an environmentally friendly product.

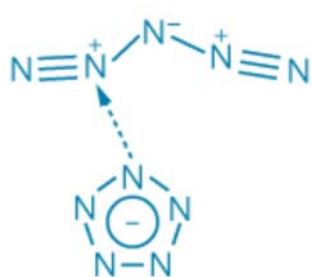
Of course, the very properties that make polynitrogen compounds desirable as fuels also make them difficult and dangerous to synthesize. By identifying compounds with sufficiently large barriers to decomposition, theoretical studies identify not only possible but also, researchers hope, safer synthetic targets.

Beyond the common nitrogen species  $N_2$  and  $N_3^-$ , many pure polynitrogen compounds have been investigated computationally:  $N_3$ ,  $N_4$ ,  $N_5^+$ ,  $N_5^-$ ,  $N_6$ , and  $N_8$ , to name just a few. Several have multiple structural forms; for example,  $N_4$  is calculated to be stable as a tetrahedron (analogous to  $P_4$ ), a four-membered ring (analogous to cyclobutadiene), and a chain. Of the above-mentioned species, only two have been synthesized in gram quantities: cyclic  $N_5^-$  as phenylpentazole (*Chem. Ber.* **1957**, 90, 2914), and  $N_5^+$ , first as  $N_5^+AsF_6^-$  (*Angew. Chem. Int. Ed.* **1999**, 38, 2004).

While phenylpentazole and other substituted pentazoles have been well-characterized experimentally, cyclic  $N_5^-$  alone has proven to be a much greater challenge. Early theoretical studies by [Rodney J. Bartlett](#) of the [University of Florida](#) and [Kim F. Ferris](#) at [Pacific Northwest National Laboratory](#) predicted a stable structure with bond lengths of about 1.3 Å (*J. Am. Chem. Soc.* **1992**, 114, 8302). The activation barrier to decomposition to  $N_2$  and  $N_3^-$  is calculated to be greater than 25 kcal/mol. There is some theoretical evidence, however, that  $N_5^-$  could decompose by tunneling through the barrier.

$N_5^-$  has been seen in the lab, at least fleetingly, through negative ion mass spectrometry by USC's Christe and coworkers (*Angew. Chem. Int. Ed.* **2002**, 41, 3051), as well as a group led by Henric [Stammark](#) of the [Swedish Defense Research Agency](#) (*Chem. Phys. Lett.* **2003**, 379, 539). Chemistry professor [Richard N. Butler](#) of the [National University of Ireland](#) and coworkers also claim to have observed  $N_5^-$  using solution nuclear magnetic resonance spectroscopy (*Chem. Commun.* **2003**, 1016). There is some debate over interpretation of the NMR spectra. Work from the Christe lab indicates the species was likely  $NO_3^-$  (*Chem. Commun.* **2005**, 1607), and computed spectra forthcoming from Bartlett may help to elucidate the experimental results.

In addition to  $N_5^-$  alone, the complex  $N_5^+N_5^-$  has been a hotly desired target for fuels. Bartlett and coworkers have predicted that compared with hydrazine ( $N_2H_4$ ),  $N_5^+N_5^-$  would release nearly twice as much energy per unit mass (*J. Phys. Chem. A* **2002**, 106, 4639). The ion pair is likely less stable than  $N_5^-$  alone; both the addition of  $N_5^+$  to  $N_5^-$  to form  $N_{10}$  and loss of  $N_2$  from  $N_5^-$  have calculated barriers of only about 15 kcal/mol in the solid state. Attempts by Christe and coworkers to synthesize the similar  $N_5^+N_3^-$  resulted in "violent reactions with spontaneous nitrogen evolution" (*J. Am. Chem. Soc.* **2004**, 126, 834).



Energetic dream The  $N_5^+N_5^-$  complex has long been a synthetic target for fuels.

Whether  $N_5^-$  or  $N_5^+N_5^-$  will ever be made in quantity remains to be seen. Despite the danger—the Christe lab has seen its share of accidents, including a Raman sample tube destroyed while characterizing  $N_5^+$ —Christe says that continuing to try for polynitrogen compounds is worth the risk. It's possible that the research may turn more toward compounds with multiple nitrogens as well as other atoms. Christe, for example, is currently working on the W-shaped  $N_7O^+$  ion.

"The carrot that's held out to make theory fascinating for those of us that do it is that if we can solve the equations accurately, we know all there is to know about that molecule," says Florida's Bartlett, adding that he has no doubt that  $N_5^-$  will one day be observed experimentally beyond mass spectrometry.

As for Cornell's Hoffmann, he has left behind planar tetracoordinate carbon and moved on to new challenges. Two current projects in his lab further illustrate the breadth of options for theoretical chemists to predict molecules.

**ONE PROJECT** involves the Bergman cyclization of a 3-ene-1,5-diyne to a 1,4-didehydrobenzene diradical, a reaction common in the biosynthesis of several antibiotics. Hoffmann, Cornell postdoc Edyta M. Brzostowska, and chemistry professor [Carol A. Parish](#) of the [University of Richmond](#), in Virginia, computationally replaced a C of the parent enediyne with Os(PH<sub>3</sub>)<sub>3</sub>, or a CH with Os(PH<sub>3</sub>)<sub>3</sub>H or Rh(PH<sub>3</sub>)<sub>3</sub> (*J. Am. Chem. Soc.* **2007**, *129*, 4401). Substitution of Os(PH<sub>3</sub>)<sub>3</sub> for C resulted in a decrease of 13 kcal/mol in the barrier to rearrangement. The substitutions for CH had less significant effects. Enediyne antibiotics are antitumor agents; the results for osmaenediyne may suggest a new family of organometallic enediynes that could provide useful biochemical properties if synthesized.

Another current project in the Hoffmann lab involves taking two elements that don't form any compounds under ambient conditions—for example, lithium and beryllium—and looking at whether there are any conditions favorable for compound formation. Unpublished theoretical work by Hoffmann, graduate student Ji Feng, and Cornell professors Neil W. Ashcroft and Richard G. Hennig shows that, at extremely high pressure, a handful of "compositions" of lithium and beryllium can form. They're "not quite molecules, but extended structures," Hoffmann says.

Who knows whether any of these in silico constructions will ever be made and their interesting properties verified? If the experience with planar tetracoordinate carbon is a valid model, it would be only a matter of time for synthesis to catch up with theory. Meanwhile, theorists will continue to push the limits of chemical bonding with their computers. As Hoffmann says about thinking up molecules, "It's just sheer fun."

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