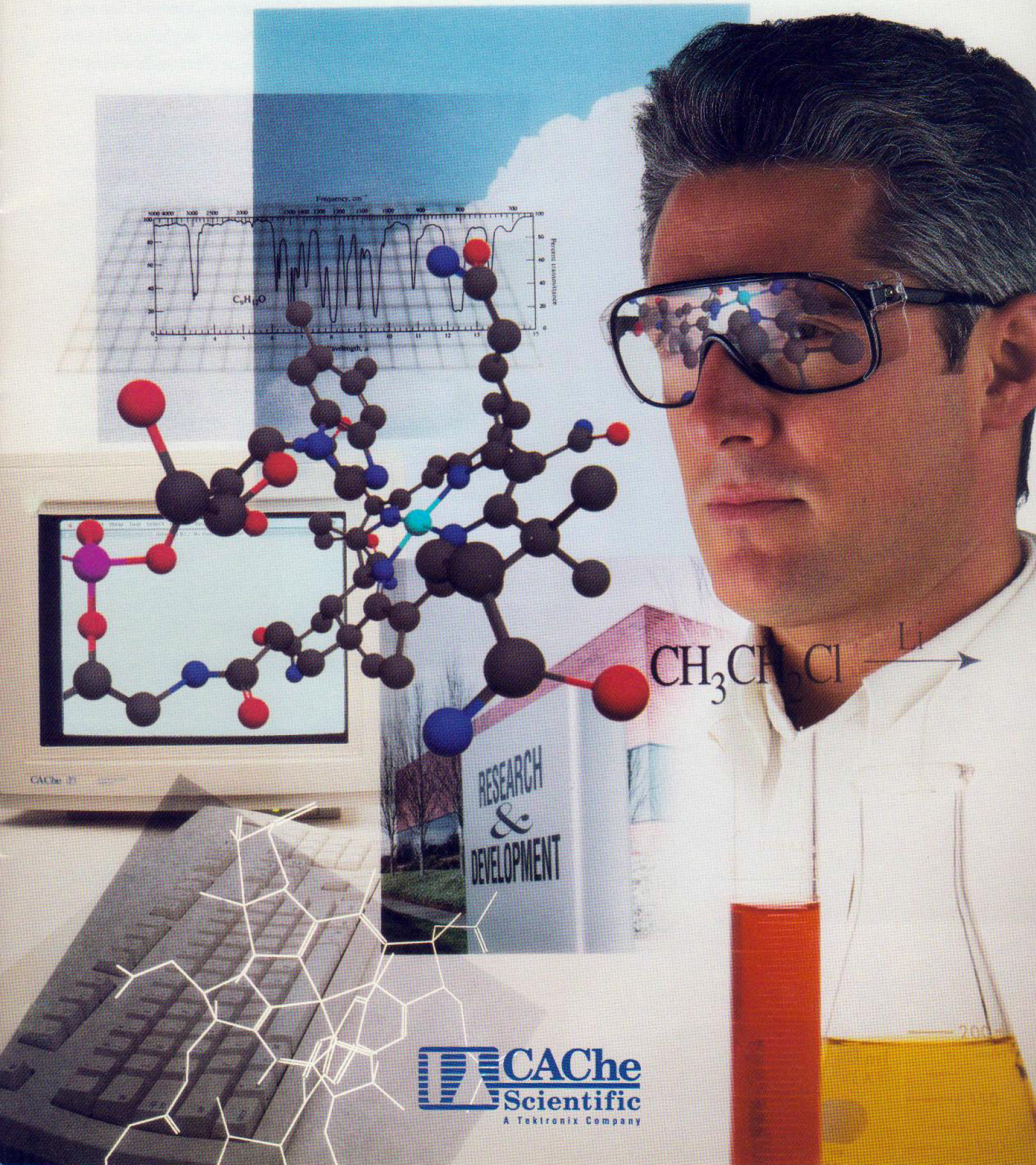
CHEMISTRY TAKES SHAPE WITH CACHE.

Practical Solutions for the Bench Chemist.

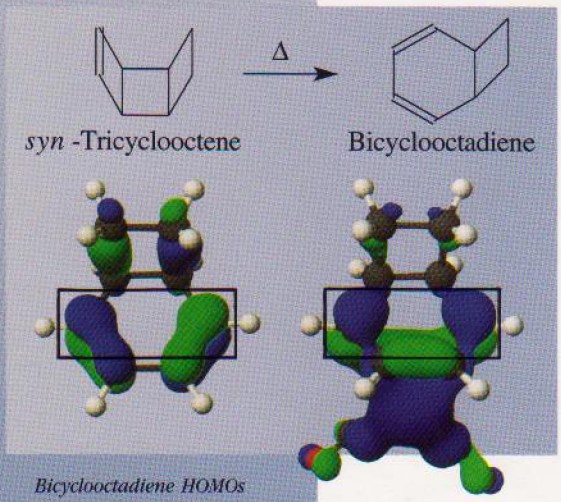


CACHe Scientific
A Tektronix Company

"EUREKA!"

Gary had been working on a reaction steadily in the lab with little success. Finally, under the stress of looming project deadlines, he walked down the hall to Steve's lab to ask for advice. Steve suggested looking at the reaction on his CAChe WorkSystem. ***"Maybe it can help us understand what's preventing the reaction. We can look at sterics, electrostatics, solvent effects and even frontier orbitals."*** Gary sketched in his reactants, and Steve showed him how to predict and display all the different aspects of the molecule's reactivity. The results were presented graphically, so they were easy to understand — and revealing. ***"Whoa! The orbitals show that this reaction isn't even allowed. But from the looks of the LUMO it could go photolytically."*** Steve also suggested testing the effect of various transition metal complexes to perhaps alter the reaction mechanism. ***"Let's try it on the CAChe system first so we don't go up any blind alleys."*** Sure enough, complexed with $Fe(CO)_3$, the ring opening was easy.

Later, heard back in the lab .... ***"That metal complex shortened the half life of the reaction from who-knows-what to two hours. By the way, can I get some time on the system later today? I have another idea ...."***

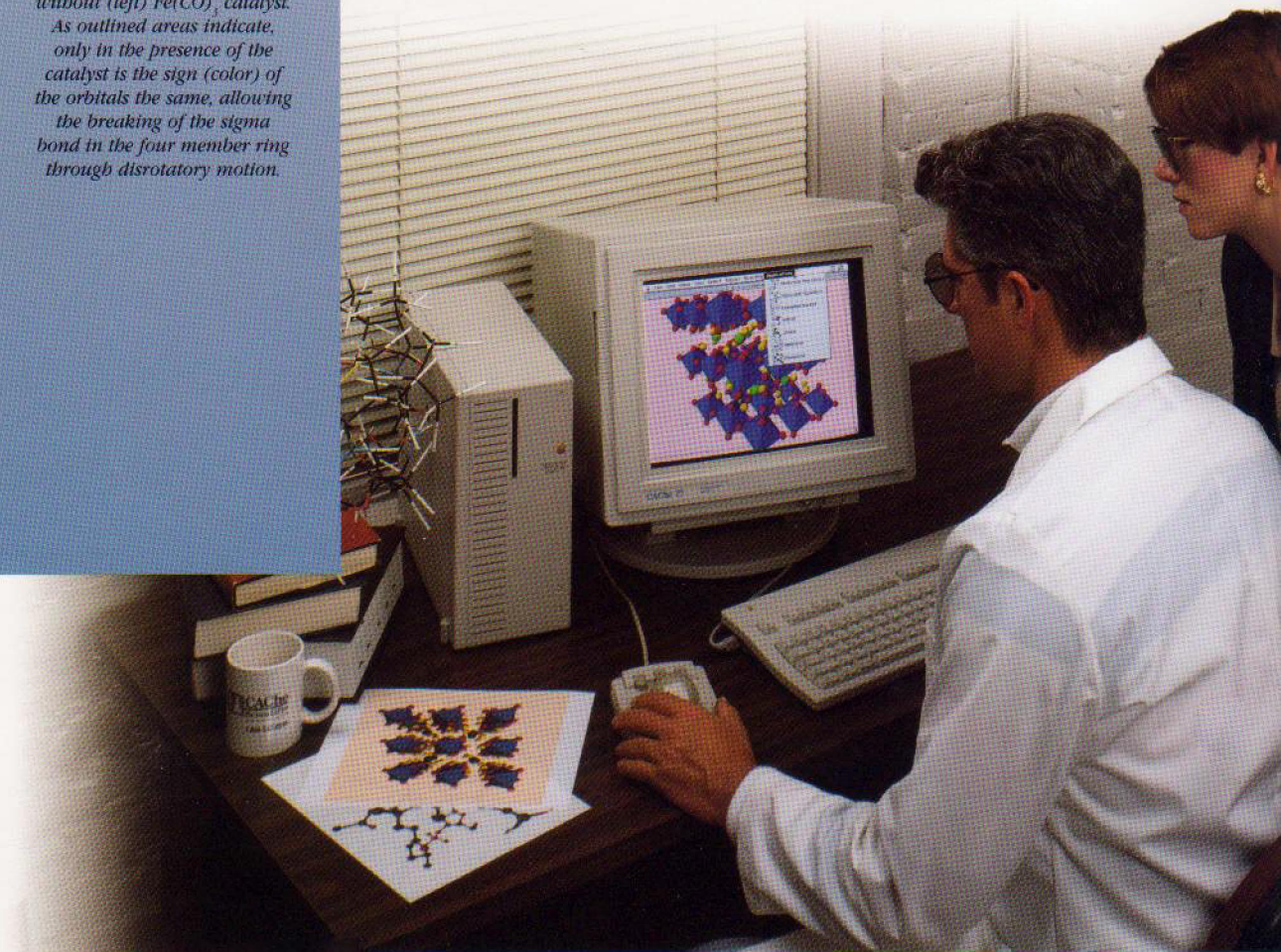


Bicyclooctadiene HOMOs shown with (right) and without (left) $Fe(CO)_3$ catalyst. As outlined areas indicate, only in the presence of the catalyst is the sign (color) of the orbitals the same, allowing the breaking of the sigma bond in the four member ring through disrotatory motion.

The last decades have seen dramatic changes in the chemist's laboratory. For instance, the experimental chemist no longer has to be an expert in ion physics to obtain useful information from a mass spectrometer, or an authority on optics and Fourier transforms to run an infrared spectrometer.

The most striking example of all is the revolution in computer-aided chemistry (CAChe). Beginning in 1989, CAChe has transformed computational chemistry techniques into practical, affordable tools which provide an intuitive user interface, automated analysis and visualization capabilities. These tools enable chemists to design and study structures and reactions without having to master computers or quantum mechanical theories. Bench chemists can test their ideas right at their desk on their personal chemistry system from CAChe Scientific.

With CAChe you need no longer be limited to your own area of expertise, or be constrained by expensive, dangerous or simply unavailable reagents. You're free to use the full force of your creativity to investigate the chemistry of compounds safely and



Visualize What You've Only Been Able To Guess At.

easily, without delay or added expense. Long-shot ideas that might take weeks of work in the lab can now be tested in just minutes or hours. And with CAChe, the possibility of discovering whole new classes of compounds could eclipse even the dramatic productivity gains you can realize.

CAChe has the only line of products developed specifically for the bench chemist. The CAChe product series provides insight into chemical structure, properties and reactivity heretofore not available by other experimental techniques. For example, with CAChe you can predict and visualize:

- Electrophilicity
- Nucleophilicity
- Bond orders
- Partial charges
- Reaction pathways
- Reaction mechanisms
- Activation energies
- Transition states
- IR/UV/Vis spectra
- Solubility
- Stability
- Conformational energy
- Heats of reactions
- and many more. . .

Founded in sound chemistry, CAChe is an invaluable tool in the design of a broad range of chemical products, including catalysts, dyes, surfactants, adhesives, polymers, drugs, herbicides, petrochemical products, process chemistry and ceramics. And unlike other visualization tools, CAChe has been designed to work with organics, inorganics and organometallics — all elements of the periodic table, in fact, right up to lawrencium.

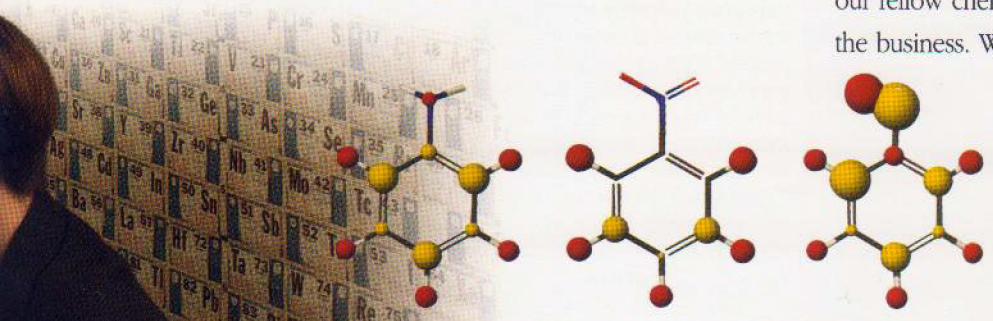
Focus on chemistry, not on learning to use a computer. The Macintosh-style interface featured in CAChe products requires no special training to use — and no knowledge of complicated computer operating systems or interfaces.

The whole process is simple, fast and intuitive — as easy as learning to use a Mac in the first place. To input structures, for example, simply sketch molecules from atoms and fragments using CAChe's patented three-dimensional editor. See results graphically in stereoscopic 3D, with real-time manipulation available at a touch. Interactively viewing structure, chemical properties and reactivity allows you to see new relationships, to literally visualize new chemistry.

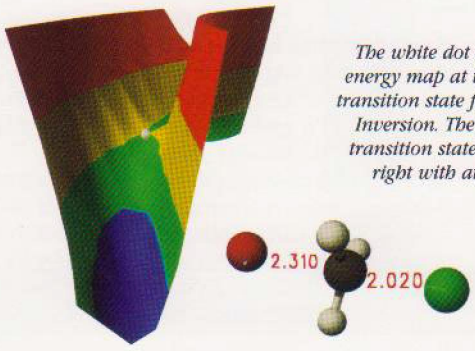
The work isn't over until your peers are convinced. You have to be able to convey your results at a conference — or justify them to your boss. CAChe products are 100% Macintosh-compatible, which means you can easily cut and paste CAChe visuals and data into numerous Macintosh applications to create publication quality documents. CAChe color printers and slidemakers give you high-resolution presentation materials in minutes.

It's not always easy to adopt new techniques, but CAChe is with you all the way. We're committed to providing our fellow chemists with the best support, service and training in the business. With your CAChe system you receive a full complement of user documentation, along with immediate access to software updates as they become available, product accessories to meet growing requirements, and CAChe Scientific's Hotline that puts you in direct touch with our application chemists who can assist you with your day-to-day chemistry challenges.

More than a set of tools, with CAChe you get a whole company's resources.

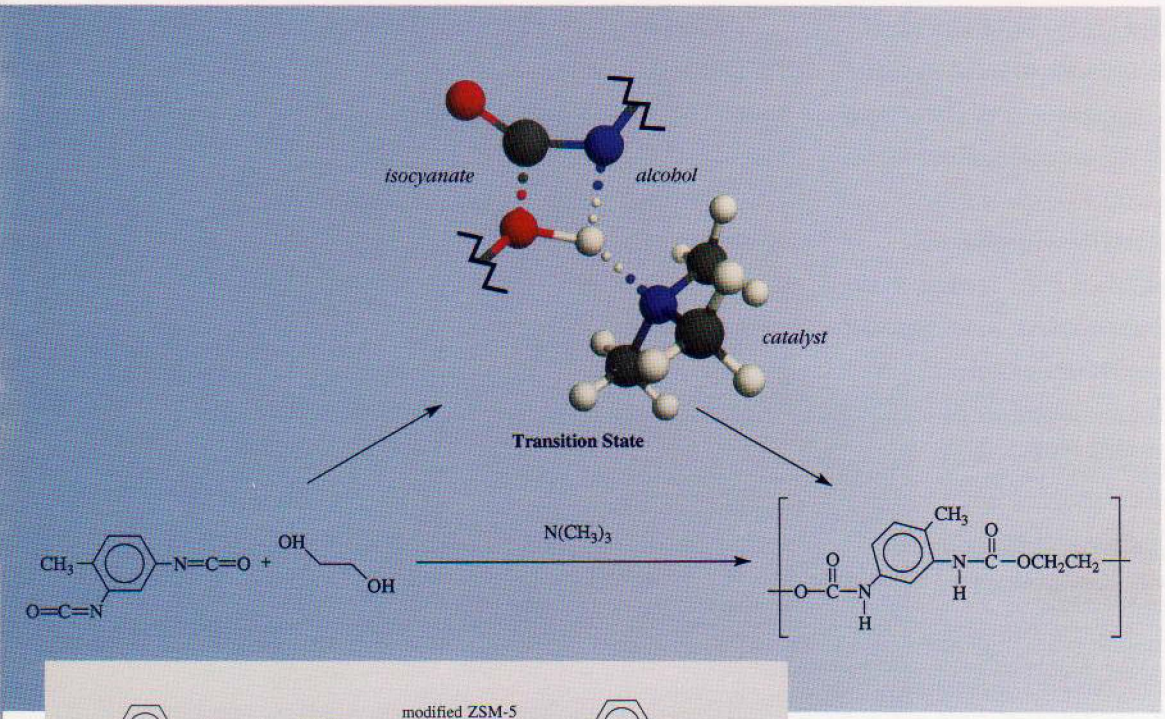


Analyzing partial charges from Extended Hückel calculations shows the pattern of aromatic electrophilic substitution. The radii of the red and yellow spheres are proportional to the magnitude of the partial charge; red is positive, yellow negative.



The white dot on the potential energy map at the left marks the transition state for the S_N2 Walden Inversion. The structure of the transition state is shown on the right with atom distances.

Picture It: Results Like This At Your Command.

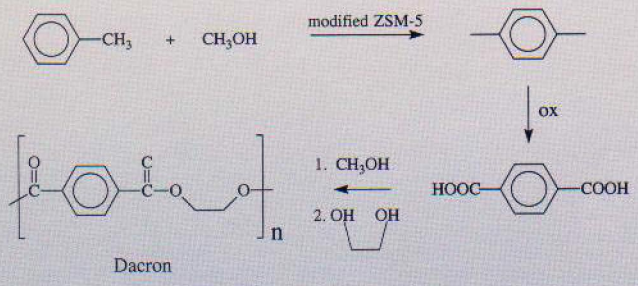


Polymers:

Polyurethane Catalysis

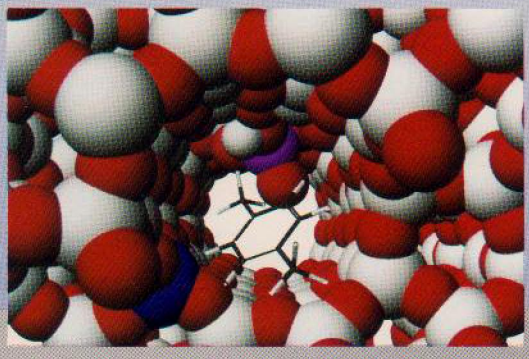
Polyurethane foam preparation involves reaction of a diol in a slight excess of a diisocyanate. Trialkyl amines catalyze the formation of a polycarbamate goop. To ensure optimal reaction efficiency, catalysts must be "tuned" by modifying the structure. ***But, how does the catalyst function?***

Until recently, the trialkyl amine was believed to complex with the carbonyl carbon to catalyze the alcohol-isocyanate condensation. CAChe calculations, however, discovered a novel transition state as shown on the left. Since this indicates the catalyst can function by activating the diol hydrogen, ***alternative catalysts which activate the diol need to be explored.***



Dacron

Phosphoric Acid modified ZSM-5

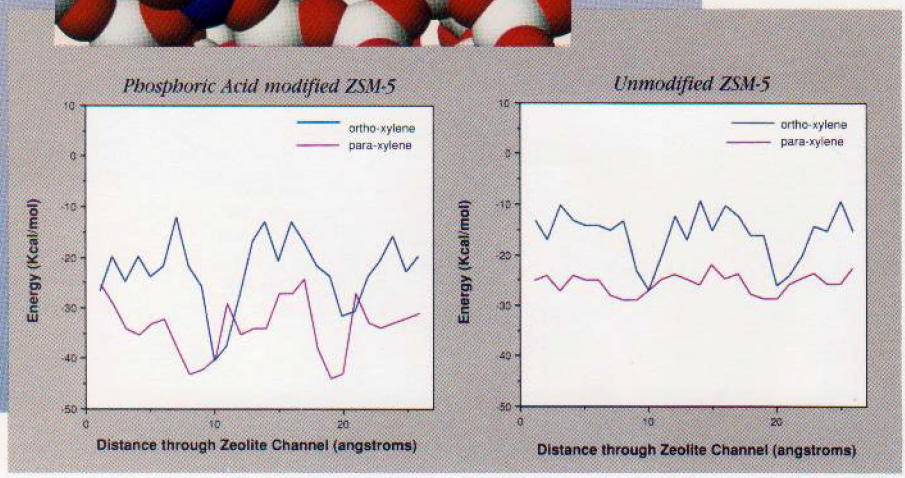


Process Chemistry:

Zeolite Catalysis

Polyesters are commercially important polymers made from terephthalic acid, which is produced via oxidation of the para isomer of xylene. The conventional process to make p-xylene depends on separation of the para isomer from a mixture of C_8 aromatics. Process economics are significantly improved if the concentration of p-xylene in the C_8 aromatic feed stock is high.

One way to produce xylene feed stocks having high concentrations of p-xylene is by shape selective catalysis using zeolites. A well-known example of such selectivity is alkylation of toluene with methanol using ZSM-5 catalyst.



How can the CAChe Worksystem help in narrowing the number of potentially useful zeolites, thereby reducing the number of experiments?

Zeolite reactivity analysis, including reaction thermodynamics, constraints of transition states, and transport inhibition in zeolite catalysts can be tested in a "what if" mode. For example, the graph below shows position dependent potentials for xylene isomers in the unmodified ZSM-5 straight channels. These calculations indicate that p-xylene experiences lower energy barriers to movement relative to the ortho isomer. Thus, transport inhibition of ortho-xylene is inherent in the shape of ZSM-5. Using CAChe, other molecules can be added to the channel system to test the effect on the mobility of xylene isomers. For example, p-xylene is shown passing through a channel of ZSM-5 modified with phosphoric acid, and the graph shows the energy potentials. CAChe results indicate that ***phosphoric acid modification is likely to favor the p-xylene isomer and that further experimentation is warranted.***

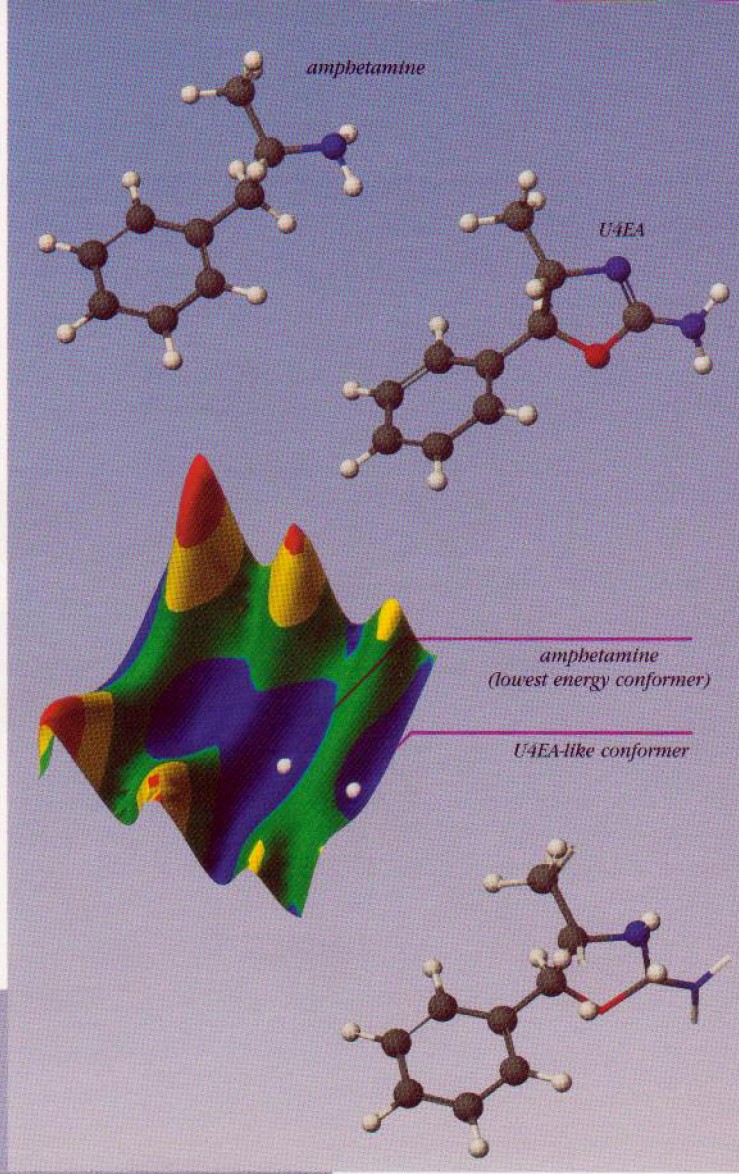
Medicinal Chemistry:
Forensics

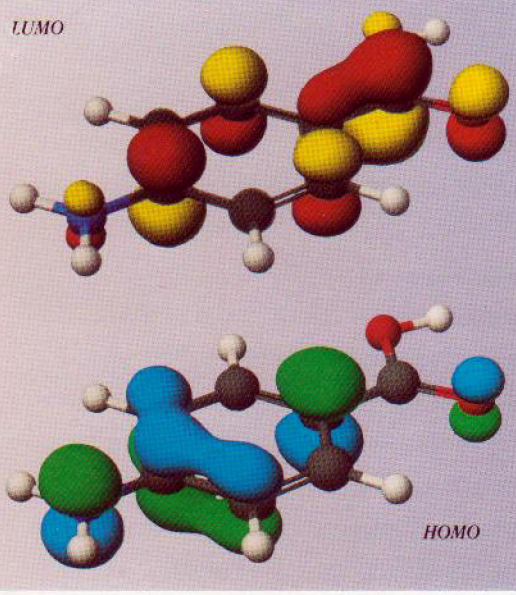
In the mid-1980s several cases of apparent amphetamine overdoses were reported in Miami. Crime lab analysis indicated victims used 4,5-dihydro-4-methyl-5-phenyl-2-oxazolamine, a designer street drug code-named U4EA. Although it structurally resembles amphetamine, it is much more potent. ***Why does U4EA exhibit 1000 times greater potency than amphetamine?***

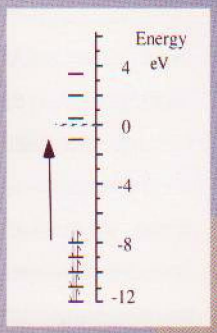
These two compounds (shown at right) have dissimilar low energy structures. Since receptor sites bind to similar structures, ***can amphetamine and U4EA assume similar shapes? And if so, at what energy cost?***

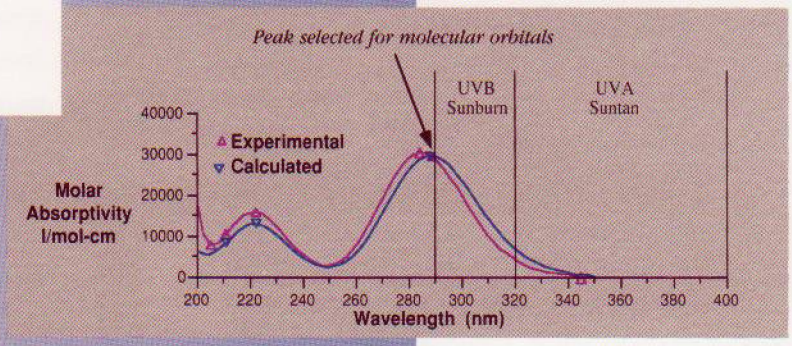
The flexible C_3 side chain for amphetamine allows many more low energy conformations compared to U4EA, which has a relatively rigid double ring structure. CAChe's conformational analysis of amphetamine revealed a slightly higher energy U4EA-like conformer which could readily interact at the same receptor site. Superimposing this amphetamine conformer on U4EA, using spheres for amphetamine and sticks for U4EA, illustrates their structural similarities.

The potential energy map (shown at right), generated by the same CAChe program, reveals the small energy barrier needed to convert amphetamine's most stable global minimum conformation to this U4EA-like conformer. CAChe's conformational analysis led researchers to conclude that ***amphetamine has lower efficacy than U4EA because it requires additional energy to move into the active conformation at the receptor site.***









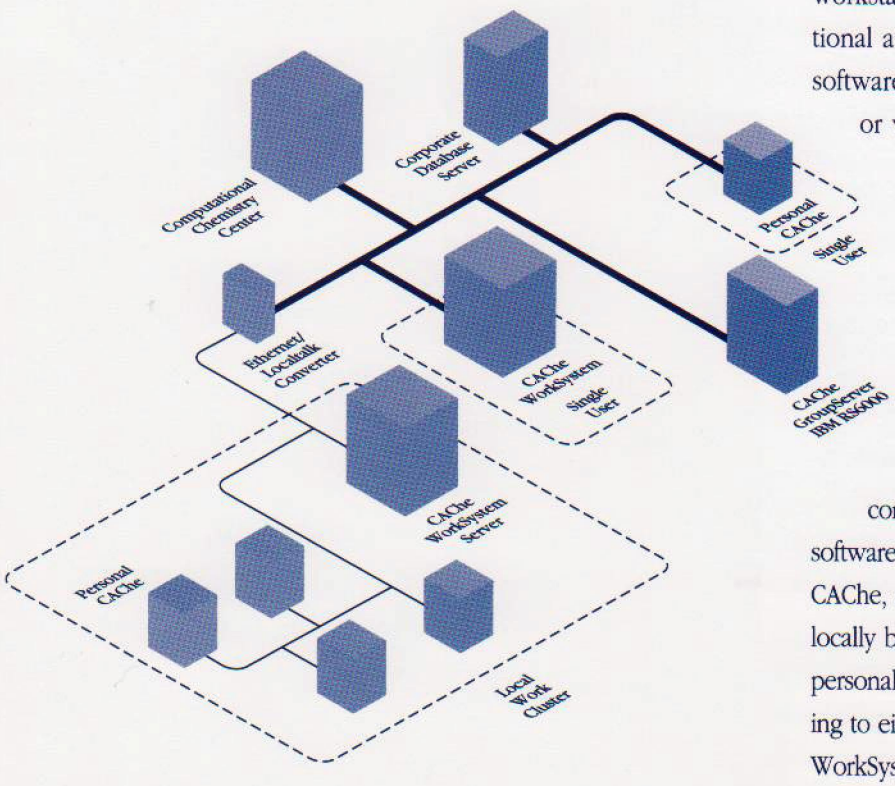
Color Chemistry:
Sunscreens

Sunscreens frequently contain PABA (p-amino benzoic acid) derivatives to block harmful UV radiation. Understanding the relationship between the molecular structure and UV absorption properties of these compounds can augment design of improved sunscreen materials. ***What insight can a CAChe visualization system provide?***

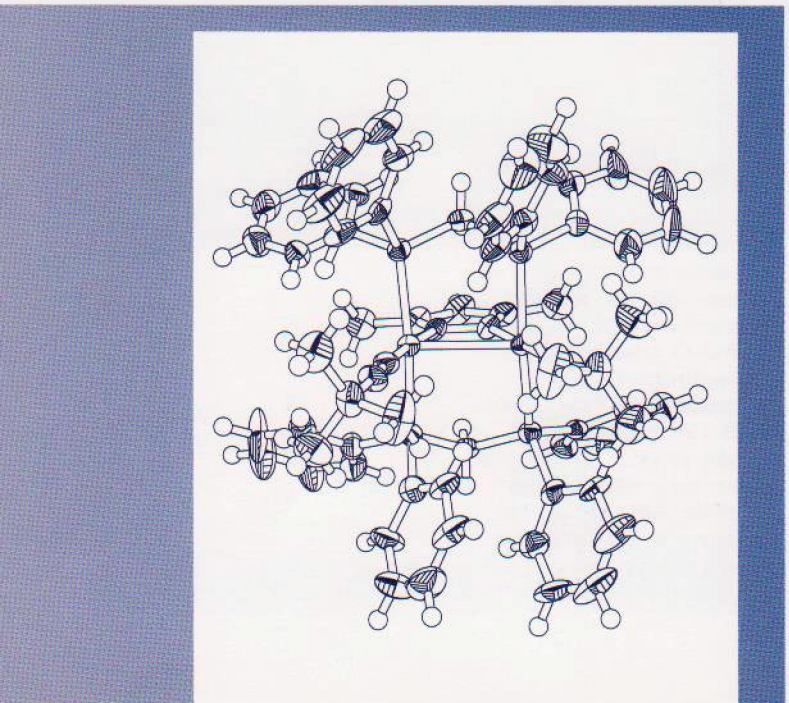
CAChe analysis predicted the UV/Vis absorption spectrum shown above, superimposed on the experimentally observed spectrum for PABA. ***How is the calculated spectral peak near 290 nm related to PABA's molecular structure?***

A click of the CAChe mouse on a spectral peak identifies the orbitals active in the absorption. In this case, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are displayed superimposed on PABA. This relationship between spectra and structure, which no analytical instrument can indicate, ***directly ties PABA's specific molecular chromophores to their corresponding UV absorption peaks.*** This unique CAChe capability provides insight useful in determining where to chemically modify PABA to change its absorbing wavelengths or their intensity, thereby improving its UV absorption properties.

From Affordable, Personal Tools To Powerful Network Resources.



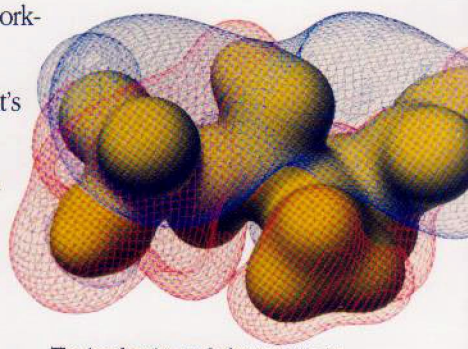
In addition to color prints and transparencies, black and white schematic representations are also easily produced. Here the schematic picture of the crystal structure of $[Rh_2(m\text{-}[(C_6H_5)_2PCH_2P(C_6H_5)_2])_2(m\text{-}N_2C_3H_2)(t\text{-}C_4H_9NC)_2]^{2+}$ is shown as thermal ellipsoids.



CAChe offers an expandable family of products available on platforms ranging from personal computers to scientific workstations. Because they meet a wide range of computational and graphical requirements, you can tailor a hardware/software solution for the unique needs of individuals, groups or whole departments.

Select standard packages or assemble your own CAChe-developed software for IBM and Apple, hardware components, stereo 3D graphics and coprocessor cards, and color printers and slidemakers. All supported by a dedicated development team of scientists and engineers.

Grow into your system, not out of it. The Personal CAChe product is a cost-effective entree to computer-aided chemistry techniques, offering chemistry software for your Macintosh computer. As you prove the value of CAChe, access to more advanced techniques can be achieved locally by adding CAChe's RISC-based coprocessor board to your personal computer or by networking to either a CAChe WorkSystem or the department's GroupServer (IBM RS6000).

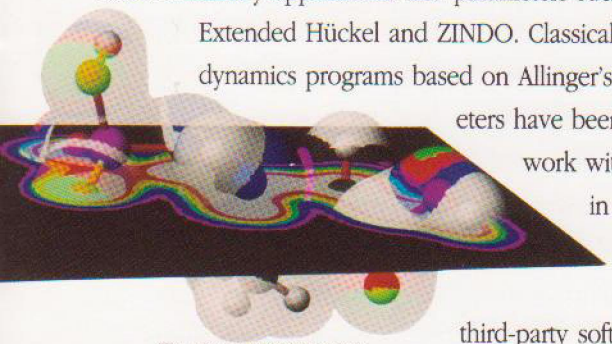


The iso-density and electrostatic iso-potential surfaces of phosphocreatine are shown. The iso-density is the yellow surface and the red and blue meshes are the positive and negative iso-potential surfaces.

For networking requirements, all products can be linked to remote computing resources and databases through Ethernet and AppleTalk. As a result, CAChe users are able to take advantage of, and complement, other computing resources within their organization. In addition, CAChe provides straightforward translation of structures extracted from standard databases including Molecular Design Ltd., Brookhaven Protein Databank and Cambridge Crystallographic database. And standard file formats such as Tribble, SHELX, Chem3D and ChemIntosh are all readable by CAChe.

Sound chemistry, sound solutions. With CAChe you can easily exploit quantum mechanics through a highly integrated user interface. Visualization replaces computer printouts of wave functions and eigen vectors. The graphic examples on this page demonstrate electronic properties predicted using quantum mechanical methods on CAChe.

CAChe chemistry systems embody established computational chemistry applications and parameters such as MOPAC, Extended Hückel and ZINDO. Classical mechanics and dynamics programs based on Allinger's MM2 parameters have been augmented to work with *all* elements in the periodic table. In addition, third-party software programs for ab initio calculations, including Gaussian '90, offer access to CAChe products.

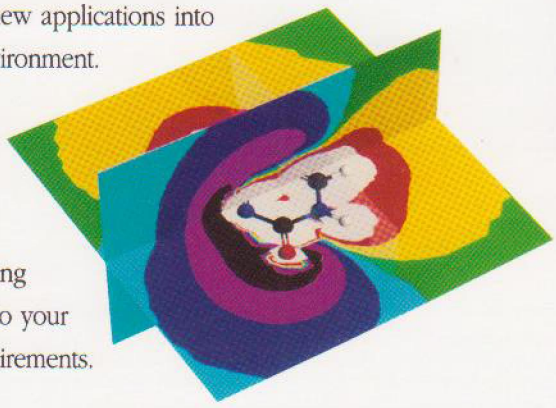


The plane slicing through phosphocreatine uses color to show the value of the electron density at points on the plane. The translucent iso-density surface is colored according to the rate of change of the electron density normal to the surface.

At the same time, the system allows you to incorporate more accurate parameters as they become available. The CAChe product family is being continuously advanced and supported by a team of experimental and theoretical chemists.

Build on the best. CAChe products feature an open architecture to aid in porting applications. A graphics and chemistry "tool kit" gives application developers a complete display-list-driven interface to CAChe 3D graphics software and chemistry libraries. The kit includes file I/O for the CAChe standard database format. In addition, "C" and Fortran compilers are available to assist advanced users and software developers in integrating new applications into their existing compute environment.

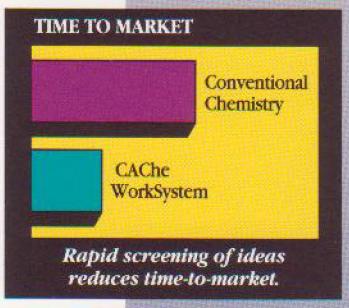
Make the CAChe connection. Let your nearest CAChe applications specialist provide expert assistance in matching our computer-aided tools to your desktop and network requirements.



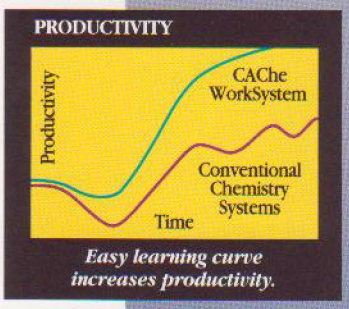
The orthogonal planes contain color contours of the electrostatic potential of cytosine.

A Record Of Success.

CAChe is easy to use — and afford. That's why it *gets* used routinely by bench chemists in leading corporations in the petrochemical, pharmaceutical, plastics, semiconductor, dyes and inks, soaps and detergents, and other industries worldwide. They depend on CAChe to hasten experimental research. As you'll discover, the time it takes to screen a series of analogs in the lab can be dramatically accelerated by first using the CAChe system to sift out the most promising few. And the insight gained from the graphical display of molecular properties and reactivity can lead to fast solutions for even the most difficult problems. Successes in predicting compound color, designing zeolites, discovering active structures and analyzing reaction mechanisms described in the examples can shave months off the time it takes to get products to market. And reduced development costs, combined with CAChe products' low entry price, means systems can pay for themselves in a matter of weeks.



Rapid screening of ideas reduces time-to-market.



Easy learning curve increases productivity.

All the elements of a safe buy and sound investment.

Learning and re-learning curves are also important productivity indicators. Unlike conventional computational chemistry software, CAChe's easy, intuitive graphical interface leads you along. There's no need to re-learn command sequences and connection procedures.

Sound chemistry, an evolving line of affordable solutions, industry-standard hardware and software and a commitment to deliver the best service and support in the business all make CAChe products a safe buy and a wise investment. And with all the competitive pressure these days to be first with the best, having a resource like CAChe isn't just practical. It's practically a necessity.

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