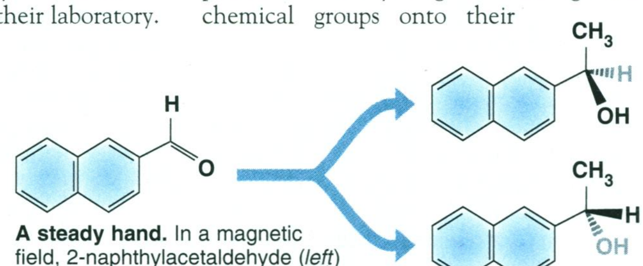
ORGANIC CHEMISTRY

A New Twist in the Tale of Nature's Asymmetry

One of the enduring mysteries of nature is why plants and animals that have two possible mirror-image forms consistently opt for one and not the other. Spiraling seashells of the same species always twist one way, honeysuckle stems corkscrew around each other in one direction only, and mammals normally have their hearts on their left. This bias for a single "handedness" extends into the realm of molecules. Amino acids, the building blocks of proteins, are chiral: They can exist in two mirror-image forms, or enantiomers, known as D and L. Nature, however, mostly uses the L form. Similarly, DNA's double helix could corkscrew to the left or right, but in nature it always makes a right turn. Now German synthetic chemists are reporting a new clue to the origin of this molecular handedness.

The right stuff. Only the right-handed DNA helix (*left*) exists in nature.

Earlier theories had ascribed it to everything from a primordial legacy of oriented molecules borne by interstellar dust to a bias in the fundamental forces of physics, but there has been little evidence for any of these scenarios. Now Eberhard Breitmaier and his colleagues at the Institute for Organic Chemistry and Biochemistry at the University Gerhard-Domagk-Strasse in Bonn and at the chemical company Bruker Analytical in Rheinsletten think they may have seen another possibility at work in their laboratory. Trying to coax chemical reactions that normally produce a mixture of enantiomers into making just one of the two, they found a remarkably simple solution: Apply a magnetic field, and the product is virtually pure single enantiomer.



A steady hand. In a magnetic field, 2-naphthylacetaldehyde (*left*) reacts to produce just one of the two mirror-image forms of 2-napthylethanol.

The work, published earlier this year in *Angewandte Chemie*, barely caused a ripple at the time, but it is now drawing increasing attention. To organic chemist Philip Kocienski of the University of Southampton in England, the possibility that Earth's magnetic field might have exerted a similar effect in the evolution of organic molecules makes the German discovery "the single most important finding since chemists discovered the chiral carbon atom itself." Tony Barrett of London's Imperial College is more circumspect, saying "it seems just too good to be true."

But if it is true, says Roger Newton, director of the research and development arm of Glaxo, there will be another reason for enthusiasm: the possibility of synthesizing just one enantiomer of a drug or other compound simply by applying a magnetic field. "This is an extremely exciting finding," he says, "that could prove very useful in large-scale synthesis."

An interest in industrial synthesis, in fact, was what motivated the German work in the first place. For industrial chemists, devising a single-enantiomer synthesis technique is a long-sought goal, because chiral chemicals often interact with our bodies in very different ways depending on whether they are left-handed or right-handed. One enantiomer of the compound limonene smells of oranges, the other of lemons. One form of the pain-killer ibuprofen is three times stronger than the other. And, tragically, while one thalidomide enantiomer quells morning sickness, the other interferes with fetal growth.

But most chemical syntheses produce equal amounts of both enantiomers. To skew the results, chemists have tried all sorts of procedures—everything from tacking chiral chemical groups onto their starting materials to using chiral enzymes and catalysts to manipulate the reaction (*Science*, 15 May 1992, p. 964)—with varying degrees of success. The German team adopted a new tack in its work on aldehyde alkylations and ketone reductions, processes used to add small functional chemical groups onto larger molecules to build precursor compounds for drugs and agrochemicals. They applied a magnetic field of between 1.2 and 2.1 teslas to the reaction solution—and found that 98% of the product, which normally contains both enantiomers, consisted of a single mirror-image form. What's more, they found that they could choose which enantiomer dominated the product by adding a tiny amount of the desired enantiomer to the starting materials.

Breitmaier and his team have no idea why the magnetic technique works. But Kocienski points out that the large starting molecules in these reactions are dipolar, with more negative charge at one end than the other. This polarity might allow the magnetic field to align all these molecules in the same direction, somehow biasing the outcome toward one chiral form. Newton thinks an additional clue lies in the fact that the reaction can be persuaded to follow the route to one particular enantiomer simply by adding a small amount of desired product. This "seed" might form weak bonds with molecules of the starting material; the complex might then be held in a certain position by the magnetic field so that a copy of the seed molecule is formed. "Without this added ingredient, it is almost like flipping a coin," he says. Beyond these speculations, however, chemists are pretty much in the dark.

But if the technique proves to work with reactions on other polar molecules, says Breitmaier, it could offer a cheaper, simpler, and more environmentally benign alternative to other means of single-enantiomer synthesis. Agrees Newton, "One could imagine a production synthesis using a continuous flow [of reactants] passing through the magnetic field."

Something analogous may have happened on the early Earth, Kocienski points out. "The Earth's magnetic field could have influenced the outcome of reactions that led to life, so that one form of essential molecules was favored over the other," he says. The German group found that the proportions of enantiomers in the final reaction products were related to magnetic field strength. Earth's extremely feeble magnetic field, about 10,000 times weaker than the field used in the experiments, would therefore only tip the scales very slightly in favor of one enantiomer.

But Kocienski believes that this imbalance, exerted over a very long time, could have been enough to create the one-sided biology we see today. The possibility is certainly worth following up, says organic chemist Andrew Holmes of Cambridge University. "The discovery is likely to stimulate a lot of interest and will promote a whole new area of research in which reactions are carried out in a magnetic field."

–**David Bradley**

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