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INSIGHTS

# STEALING A FIELD OR RUFFLING FEATHERS?

Some complain that 'diversity-oriented synthesis' is a superfluous catchphrase

BY STU BORMAN

"Your article on diversity-oriented synthesis was the most worthless thing I've ever seen in C&E News." That was the less-than-encouraging start of a phone call I received from a prominent member of the chemistry community about my recent article on diversity-oriented synthesis, or DOS ([C&EN, Oct. 4, 2004, page 32](#)). "What have I done now?" I wondered to myself, as my insides began to knot up.

DOS is the synthesis and evaluation of libraries of small-molecule compounds with greater structural complexity, more varied core structures, and richer stereochemical variation than in traditional combinatorial libraries. A Canadian researcher had suggested C&EN cover DOS research. I adopted the suggestion because I had heard a lot about DOS, I wanted to learn more about it, and I thought readers would be interested as well.

More scientists than I had expected turned out to be working actively in this area, and I interviewed many of them. The problem was that I didn't interview people outside the DOS field. In fact, I had no idea there was opposition to it, but I soon found out otherwise.



DIGITAL VISION PHOTO

Soon after the article appeared, Anthony W. Czarnik, editor of the *Journal of Combinatorial Chemistry*, wrote a letter to the editor ([C&EN, Nov. 1, 2004, page 4](#)). Czarnik said that the blurb on the cover of that issue--"Combichem: Saved by Diversity-Oriented Synthesis?"--was the type of tagline he was more accustomed to seeing "on display near supermarket checkout counters" and that it represented "an unfortunate disservice to the many chemists engaged in this field--past, present, and future." Ouch!

In writing the blurb, I had no intention to insult the whole field of combinatorial chemistry and even its yet-unborn practitioners. I thought the blurb was provocative but well supported by the article's content. DOS researchers aim to create compound libraries that address the principal problem for which combichem has been widely criticized--that massive investments in the field have not yielded much, if anything, in the way of marketable drugs, the key goal for which it was devised. Such criticism has appeared not only in C&EN before ([Oct. 13, 2003, page 77](#), and [Oct. 27, 2003, page 45](#)) but also in the *Wall Street Journal* (Feb. 24, 2004, page A1) and other publications.

The cover blurb turned out to pique the gizzard of my phone caller as well. Okay, there's a question mark in the blurb, he said, but nobody's going to notice that question mark. The caller said he'd be surprised if I could show him any combinatorial chemists "who think they have to be grateful because DOS saved their ass." Why, he asked, had C&EN become a tool of the DOS deception?

DOS is an unnecessary redefinition of something that already exists, the caller added. Those

who had originated the DOS concept were making an unabashed attempt to steal a field--to capture credit for combichem by changing its name.

Distinctions between DOS and conventional combichem are minor at best, he said. DOS researchers may synthesize libraries with complex scaffolds and stereochemical sites, he said, but lots of traditional combichem libraries are like that. Actually, in my article's defense, it did include that point in a quoted comment.

The caller noted that another superfluous catchphrase was "chemical biology," the idea that small organic compounds can be used to perturb cellular function. Organic compounds are already used to perturb cellular function by a little thing called the pharmaceutical industry, he said, so "chemical biology" is simply an unneeded new slogan for pharmacology.

Not only was my blurb offensive, but C&EN shouldn't have covered DOS at all, he said. (When my editor-in-chief heard that, he replied that C&EN isn't in the business of not covering things.) The caller's comments reveal strong resentments in the combichem field that I believe to be unseemly but that nevertheless warrant being aired. Hence this Insights.

I sent out a draft of this piece for review and got several comments on it. One researcher noted that slowed drug pipelines have been caused by a turning away from natural products chemistry, "which has been extraordinarily successful as a route to approved drugs." A better balance between combichem and natural products chemistry is needed, he said.

Another commented that the synthesis of small, highly diverse compound libraries is a longtime practice and that the idea of creating such libraries "absolutely must not be attributed to DOS."

A third said that DOS is indeed a renamed concept. Some researchers "are known for their abilities in scientific revisionism--renaming or modifying things to put their own spin or mark on an area they did not originate," he said. "That, however, is and has been a part of science forever. In fact, it is true in all fields of human endeavor."

I believe that what a field is called is less important than what it is able to accomplish and that DOS should be given an opportunity to prove itself. An author whose works are not worthless once wrote: "What's in a name? That which we call a rose by any other name would smell as sweet."

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