

ENDOCRINE DISRUPTORS

► **Touching thermal receipts could prolong BPA body retention**

When people handle receipts printed on thermal paper containing the endocrine disruptor bisphenol A (BPA), the chemical could linger in the body for a week or more (*Environ. Sci. Technol.* 2017, DOI: 10.1021/acs.est.7b03093). Jonathan W. Martin of Stockholm University and Jiaying Liu of the University of Alberta asked six male volunteers to handle paper containing isotopically labeled BPA for five minutes. The volunteers then put on nitrile gloves, wore them for two hours, removed them, and washed their hands with soap. Afterward, the researchers measured the labeled BPA



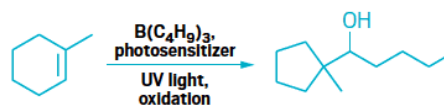
**Handling thermal receipts containing the endocrine disruptor bisphenol A could leave traces of the compound in the body for a week or more.**

and its metabolites in the volunteers' urine regularly for two days and then once again a week later. Total BPA in the urine increased linearly over the first two days, and after a week, three of the volunteers still had BPA in their urine. In contrast, after the volunteers each ate a cookie containing labeled BPA, total BPA in their urine spiked within five hours and was fully cleared within a day. Ingested BPA is rapidly metabolized in the liver and quickly excreted, Martin says. But BPA absorbed through the skin is probably metabolized much less efficiently, which could lead to a longer and more toxic exposure.—DEIRDRE LOCKWOOD, special to C&EN

SYNTHESIS

**Contracting rings with light**

Ring-contracting reactions let chemists create, for example, a five-membered ring from a six-membered ring, giving them a tool for creating complex molecular architectures. Now, chemists at the University of Texas, San Antonio, have developed a ring-contracting reaction with a bonus: It creates a side chain containing a stereocenter on the new five-membered ring (*J. Am. Chem. Soc.* 2017, DOI: 10.1021/jacs.7b07128). The reaction is a photoinduced carboboration, which uses light to convert *cis*-cyclohexenes to more reactive *trans*-cyclohexenes. These then react with organoboranes via a unique mechanism to produce substituted five-membered rings. Subsequent reactions can convert the resulting boranes to alcohols (example shown), amines, or alkenes. “The reaction offers a new shortcut to five-membered carbocycles and heterocycles from the six-membered ring precursors that are abundant among natural products or that can be easily prepared by the Diels-Alder reaction,” says Oleg V. Larionov, who spearheaded the research effort. “The reaction can also produce molecules with contiguous quaternary stereocenters that are particularly difficult to access synthetically.” The reaction’s discovery corrects work from the 1970s, when chemists first looked at the reaction of *trans*-cyclohexene and organoboranes and assumed incorrectly that the transformation produced six-membered rings.—BETHANY HALFORD

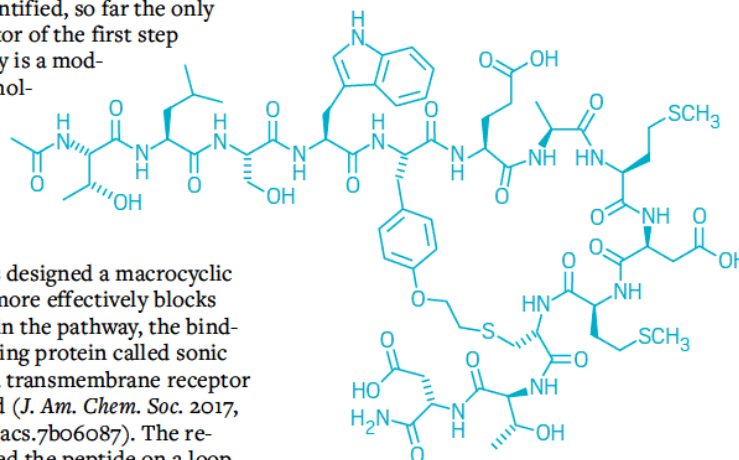


CANCER

► **Cyclic peptide blocks cancer-related pathway**

The hedgehog signaling pathway, which plays key roles during embryonic development, is involved in growth and proliferation of multiple kinds of cancer. Blocking unwanted activation of this signaling pathway is an important anti-cancer target. Although several inhibitors of downstream members of the pathway have been identified, so far the only known inhibitor of the first step in the pathway is a modestly potent molecule called robotnikinin. Now, a team led by Rudi Fasan of the University of Rochester has designed a macrocyclic peptide that more effectively blocks the first step in the pathway, the binding of a signaling protein called sonic hedgehog to a transmembrane receptor called patched (*J. Am. Chem. Soc.* 2017, DOI: 10.1021/jacs.7b06087). The researchers based the peptide on a loop in hedgehog-interacting protein, which

suppresses the signaling pathway. They swapped a leucine for a cysteine and replaced a methionine with a nonnatural amino acid that forms a thioether bridge with the cysteine. Then they made a library in which they changed five other amino acids in the 13-amino acid peptide and screened for hedgehog inhibitors. They identified a peptide that suppresses activation of the hedgehog signaling pathway in living cells with nanomolar potency. In addition, the inhibitor also blocks other hedgehog analogs.—CELIA ARNAUD



**Hedgehog inhibitor**

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MERGERS & ACQUISITIONS

# Drumroll please ... DowDuPont emerges

The next big task for the massive new firm will be to split into three

Dow Chemical and DuPont completed their merger last Thursday, Aug. 31, after the stock market closed, to form DowDuPont, the world's largest chemical company by sales. But DowDuPont won't be here for long. Managers' ultimate goal is to split the new firm into three separate companies within 18 months.

Dow and DuPont combine for nearly \$73 billion in annual sales. On the basis of recent stock prices, DowDuPont has a market capitalization approaching \$150 billion.

DowDuPont's stock began trading on the New York Stock Exchange under the ticker symbol DWDP on Sept. 1. The company replaces DuPont in the Dow Jones Industrial Average, continuing chemical industry representation in the stock index.

When the merger was first announced in December 2015, the companies expected to complete their deal in the second half of 2016, but an in-depth investigation by European Commission antitrust regulators delayed it.

Regulators worried that the combined strength of the two firms in seeds and agricultural chemicals could limit choices and drive up costs for farmers.

## DowDuPont at a glance

**Headquarters:** Midland, Mich., and Wilmington, Del.

**Sales:** \$72.8 billion<sup>a</sup>

**Operating income:** \$9.3 billion

**R&D spending:** \$3.2 billion

**Employees:** 102,000

**Future spin-offs (revenues):**

▶ **Agriculture (\$14.3 billion):** Seeds and crop protection chemicals

▶ **Materials science (\$45.1 billion):** Petrochemicals, plastics, specialty chemicals, and silicones

▶ **Specialty products (\$12.7 billion):** Electronic materials, nutrition and health, safety and protection, and industrial biosciences

<sup>a</sup> C&EN estimates based on 2016 results from Dow and DuPont. The spin-offs account for DuPont's pending asset swap with FMC.

The EC approved the deal earlier this year after DuPont agreed to sell a chunk of its pesticide business and most of its agricultural R&D to FMC. That transaction is still pending. The businesses being sold generated about \$1.4 billion in sales in 2016. In return, DowDuPont is getting \$1.6 billion in cash and FMC's health and nutrition business.

DuPont CEO Edward Breen is the CEO of the combined firm. Dow head Andrew N. Liveris will be chair until he steps down next July.

The next order of business for these executives will be splitting up the company. One of the spin-off firms will house both of the companies' agricultural businesses. It will have headquarters in Wilmington, Del., and have annual sales in excess of \$14 billion.

The largest of the firms will be the materials science company. It will reside in Midland, Mich., and have about \$45 billion in sales. It will be composed mostly of the former Dow's petrochemical, plastics, and specialty chemical businesses. It is also slated to include DuPont's polymers business and the Dow Corning silicones operation.

The smallest of the three firms will be a \$13 billion specialty products firm with headquarters in Wilmington. It will house electronic materials businesses from both firms as well as DuPont's safety and protection, nutrition and health, and industrial biosciences units.

But some investors are questioning the details of the split. Third Point, an investment fund and major Dow shareholder run by the activist investor Daniel S. Loeb, has suggested changes. For instance, Loeb

says Dow's food ingredients business is a better fit with the specialty products firm than the materials science company. He would also like to place Dow Corning into the specialty products company.

Dow and DuPont are taking the critique seriously and have hired the consulting firm McKinsey & Co. to evaluate the split plan. McKinsey's report is due out soon.



Breen (left) and Liveris shake on the deal in December 2015.

Jimmy Leppert, a principal with the management consulting firm Kotter International, says hiring McKinsey was the right move. "Being attacked by these activist investors, they are looking for objective criteria from outside," he says.

Leppert notes that Dow and DuPont managers have been refreshingly forthcoming with information about what they want to do after the deal. "With mergers of this size and complexity, it is not always that the plan going forward is laid out," he notes.

Before the split, DowDuPont will have to achieve a lot of cost savings it has promised investors. Management expects \$4 billion in annual synergies between the firms. Three-quarters of this is to come from cost-cutting and another \$1 billion from new growth. These savings are in addition to ongoing cost-cutting programs at both companies.—ALEX TULLO