Biotechnology and Polymer Chemistry: A Growing Relationship

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SUMMARY: DuPont is using biotechnology to make chemical compounds and materials, especially polymers and polymer intermediates - demonstrating that biotechnology can lead to more effective and productive manufacturing processes for traditional chemical businesses as well as pharmaceuticals, agricultural products, and new products for improved nutrition and health.

Introduction

Significant changes have taken place in the chemical industry, driven by a powerful combination of global economic and scientific forces. One change: a number of chemical firms including Monsanto, Dow, Hoechst and Novartis have left their traditional chemical businesses behind and headed for businesses based on what is termed the "life sciences".

Similar changes have taken place in DuPont which bought out Merck's portion of a pharmaceutical joint venture, sold off Conoco, purchased Protein Technologies International, and acquired Pioneer Hi-Bred International with its research on the genetic modification of corn, soybeans, and other oil seeds.

DuPont, however, is not counting solely on the life sciences or biological sciences to transform the company. Scientific advances being made in the material, biological, and information sciences will all be important. For DuPont life sciences including biotechnology will be linked to the chemical and materials businesses - a different strategy than that being followed by most others.

Biotechnology, defined as techniques that use living organisms to make products, modify plants, animals, or other organisms to carry desired traits, can also be taken in a broader sense - to mean the application of scientific and engineering principles to create materials by biological processes.

In fact, we have seen glimpses of biotechnology-based products going back to the nineteenth century when Louis Pasteur insisted that each fermentation process can be traced to a specific

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living organism. This inspired changes in brewing practice to assure healthy conditions for the growth of the critical microorganisms.

The biotechnology industry today itself is unusual in that it is defined not by a set of products but rather by a set of enabling technologies. These are used by a broad array of companies applying DNA sequence data and engineering the metabolism of microorganisms or green plants to create new products and processes.

Biotechnology: On the Technology Agenda

One of the important items on DuPont's technology agenda is the strengthening of the biotechnology platform extending it across a number of businesses - pharmaceuticals, agricultural products, materials businesses, and nutrition and health products. Building this technology platform will help achieve other objectives on that agenda - improving capital productivity of manufacturing processes, developing all new products and new businesses, developing several new polymer platforms, and driving discovery research. [1,2)]

DuPont's agenda and strategy rest on the belief in the convergence of technology. Life sciences used to be mainly a matter of classical biology, biochemistry, and genetics. Material science was strictly a matter of chemistry and engineering. But biotechnology today is potentially useful in both life sciences and polymer science. In the future DuPont believes the marketplace will reward companies that have diverse, interdisciplinary skill sets, because they will be able to supply products and functionality that single-focus companies just cannot.

While major effort is underway in DuPont applying biotechnology to crop input and output traits, DNA diagnostics, crop protection chemicals, pharmaceuticals and environmental remediation, the focus here is on work using biotechnology to find new routes to important polymers and polymer intermediates.

The potential is great for biotechnology to replace petroleum-based chemical and engineering routes to polymers and polymer intermediates. Processes based on transgenic plants and/or microorganisms can be cheaper, less capital intensive, and much more environmental friendly.

Engineering Challenges

The engineering challenges however are significant. Product separations and process control can be difficult. Many of the processes will not be continuous, and using a biocatalyst introduces issues of changing kinetics, need for sterile conditions, and questions on the reuse and disposal of the catalyst.

In the final analysis, the ability to meet the engineering challenges in bioprocessing will depend on the skills of people. Bioprocessing will have to be integrated into the complex infrastructure of the chemical industry. Product development and technical marketing skills will also be needed, because bio-derived materials will not necessarily be drop-in replacements for petroleum based products. This is a broader skill set than is going to be possessed by a life sciences company that is geared to only agriculture and food or pharmaceuticals. DuPont's strategy is leading to development of these skills across a broad front.

Three Approaches for Bioprocessing

Using microbes or biocatalysts, DuPont is actively developing a number of biological processes to make monomers or polymers. Three general approaches are being used: (1) inserting genes into seeds, growing the plants, and then isolating the monomer or polymer, (2) inserting genes into microbes which then process a feed source producing the desired polymer intermediate, and (3) using recombinant DNA technology to prepare protein-based polymers via bacteria.

Using the second approach, a process for an intermediate for nylon 6,12, and for a new polyester have been developed.

Dodecanedioic acid, the diacid in 6,12 nylon, has been made in four steps by conventional chemical means. DuPont scientists have now genetically engineered a new and novel biocatalyst which makes DDDA from dodecane in one reactor. The power of biotechnology is apparent in that such a transformation should cut capital investment in half, and reduce manufacturing costs by two-thirds.

1,3 propanediol (3G), is the key intermediate used in the manufacture of polypropylene terephthalate (PPT or 3GT), a polyester closely related chemically to polyethylene terephthalate (PET).

PPT is a unique polymer which combines the resilience of nylon with inherent stain and static protection and potentially polyester-like economics, but today is very expensive to manufacture by traditional chemical routes. DuPont has now developed a bioprocess for 3G.

Pathways have existed in natural organisms to convert glucose to glycerol and then in other pathways to convert glycerol to 1,3 propanediol. In partnership with Genencor International, DuPont has genetically engineered and patented organisms which are capable of catalyzing the entire process for the first time - and with high conversions and high yields.[3)]

This bioprocess when scaled-up should give a competitively superior route to 3G when biochemical engineers meet some challenges. After the microbes catalyze sugar and water into 3G, the microbes must be removed and the 3G separated from the reaction liquid. One recognized challenge in applying biotechnology in such processes is the concern that product concentrations will be so low that boiling off or removing water will dominate the entire process economics. Biochemical engineers have now increased the concentrations of 3G in the reactor to the point that concentrations now exceed the performance of large scale fermentations or chemical routes. Further improvement is expected.

Work at DuPont now seeks to isolate and characterize additional microbes that can make known materials and also completely new products. Recently for example scientists were able to isolate a microbe that can convert para xylene to terephthalic acid (the T in 3GT).[4)]

Protein-Based Polymers

Biotechnology also offers a route to protein based polymers with enhanced structural properties.[5)] Fibers and biocomposites in nature have attained remarkable levels of performance through evolutionary selection. The biosynthetic process is uniquely adapted to making such materials because it allows precise specification of hierarchical order at four levels:

Primary: based on sequence and composition

Secondary: based on conformation

Tertiary: based on supermolecular helices and sheets

Quarternary: based on folding patterns and relative placement to other components in a composite structure

The current processes by which common engineering polymers are prepared generally allow good control of only primary and secondary structure. The precision with which living systems manage all levels of materials organization accounts for the extraordinary diverse functions of protein polymers which in structural and chemical terms can be thought of as nature’s nylons. This diversity is even more striking when it is considered that proteins are constructed from a comparatively small set of monomers - the twenty naturally occurring amino acids.

The silk filaments produced by orb weaving spiders and silkmoths are among nature's most highly engineered structural materials, achieving in some cases combinations of strength and toughness not found in today's manmade materials. The dragline filaments produced by orb weaving spiders have been the focus of numerous recent investigations because they are among the strongest known protein fibers. Recombinant DNA techniques allow insertion of specific genes into host bacterium for protein-based polymers that have been carefully designed. The protein polymer is first designed and the design is translated into a DNA sequence. This sequence is then cloned and inserted into a plasmid vector for incorporation into a suitable host bacterium, typically E. coli. At DuPont the strategy for constructing dragline silk analogs involved the selection of a sequence containing certain hard segment and soft functional groups; the type and position of which were specified at the design stage. The practicality of this approach is based on two factors: First recombinant DNA technology provides the methodology that allows functional units to be coupled in a precise fashion to produce high molecular weight protein polymers. Second and of equal importance the required sequences and compositions of the functional groups can be estimated with a high level of confidence by drawing from a large database of natural protein sequence and structural information. The next steps will involve not only looking at how variations in amino acid sequence and chain length affect properties, but also investigating other aspects of fiber property development downstream from protein manufacture.

As has been seen is being seeing again, game changing innovations usually occur at the interfaces between often apparently disparate scientific disciplines. Analysis of the historical development of many breakthroughs such as xerography, the heart pacemaker, or oral contraception demonstrate this. The dramatic growth in polymer science and technology in fact was fueled by interdisciplinary developments using organic and analytical chemistry, material science, as well as engineering. Today exciting developments are taking place at the interface of biotechnology and polymer science. This will certainly be a lasting and growing relationship.[6)]

Personal Reflections

As we do this work on bioprocessing along with the related work on pharmaceuticals, nutrition and health, and agricultural products, we have three beliefs:

(1) Biotechnology will lead to more effective and productive manufacturing processes in traditional chemical businesses.

(2) Biological solutions will lend themselves to the systems approach essentially increasing expectations for sustainability.

(3) Only a few companies will have the financial capability, technological know-how - especially in the enabling technologies - and critical mass necessary to succeed in this transformation.

These three beliefs will sustain our efforts.

As we speak of lasting relationships; the DuPont Company has been born or re-born three times in its history as it transformed its businesses - and developed new or evolving technology platforms upon which to base these businesses. As we look back we see where DuPont faced the challenges of employing emerging sciences and technologies to produce these platforms and the chemicals and polymers that make DuPont what it is today. Now looking forward we face the similar challenges of employing the emerging sciences and technologies related to the biotechnology. How well we take this science and technology to the marketplace will determine the extent to which this transformation is successful. We are counting on success.

References

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