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NEWS

Biocatalyst greenness

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A very interesting inquiry into the use of biocatalysts is presented to illustrate how their use in synthetic chemistry schemes complies with the tenets of green chemistry. The qualitative aspects of green chemistry are eschewed in preference for quantitative or semi-quantitative methodologies to assess the environmental footprint via simple metrics such as the *E* factor (ratio of waste mass to product mass). Considerations important to the development of a useful metric are developed in a stepwise fashion. The article considers the "greenness" using water as a solvent, the effect of reagent concentration, neat reactions/water-deficient reaction media, and multiphase reactions for their roles in the identification of an environmental footprint. The article notes that biocatalyst preparation must be evaluated in detail for its contributions to the sustainability of synthetic application of the catalyst. Many biocatalytic reactions are based on established equilibria that may lead to the use of excess amounts of reaction substrate, in situ product removal, and smart co-substrates. Cofactor regeneration is important to many biocatalytic reactions and must be assayed for its contribution to the sustainability features. Downstream processing considerations loom as important components that can derail the effectiveness of a targeted chemical synthesis using a biocatalyst in terms of green chemistry tenets. The focus of the paper is the improvement of biocatalyst applications to make chemical synthesis more environmentally benign.

ChemCatChem 2014, 6, 930–943

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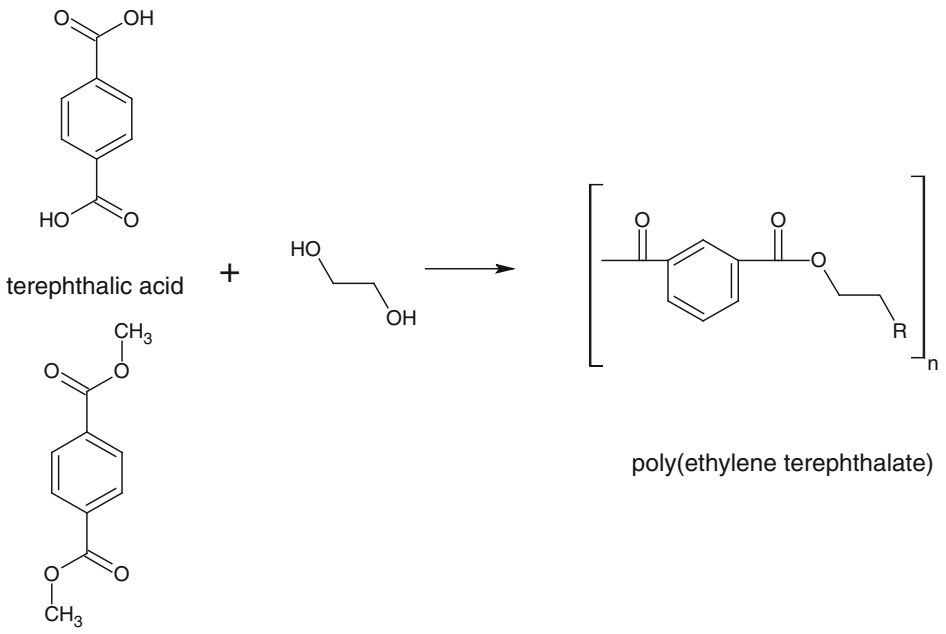
Biobased polymers and green plastics

A very interesting assessment of attempts within the macromolecular chemistry/engineering community to develop green polymer production technologies can be found in this review. The 12 principles of green chemistry are used in this article to delineate process improvements and their applications. One observation connected to the principle of atom economy can be found in the comparison of the step-growth polymerization routes to poly(ethylene terephthalate). When terephthalic acid is used as a monomer, water is formed in the condensation reaction leading to an atom efficiency of 91.26 % i.e., relatively atom inefficient. If the methyl ester is employed, the by-product is methyl alcohol which can be recycled thereby enhancing atom efficiency. Interfacial step-growth polymerization is recognized as the most atom economical. This technique, where a polymer is formed at the interface formed between two immiscible layers, is not applied widely in industry due to reactive monomer cost, solvent removal, and product recovery issues.

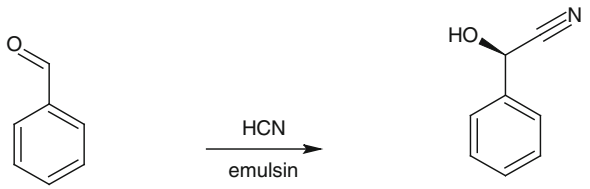


An example of the utility of catalysts to polymerization chemistry can be found with the use of polymer production catalyzed by enzymes. The in vitro catalysis of polymerization by enzymes such as oxidoreductases, transferases, and hydrolases can be used to synthesize polyphenols, polyanilines, vinyl polymers, polysaccharides, polyesters, polyamino acids, polyamides and polycarbonates. Monomers and polymers designed to degrade after use is a very important focus of these considerations. Biodegradable polymers have been made from renewable and nonrenewable sources, and the chemical composition of the polymer is important to its biodegradability. A variety of productive research directions are briefly outlined to lead to better biodegradable polymers. Finally, the review points to combinations of the green chemistry principles that can assist the transformation of polymer production and discovery to the formation of products aligned with the tenets of sustainability.

Macromol Chem Phys 2013, 214, 159–174

Biocatalytic organic chemistry

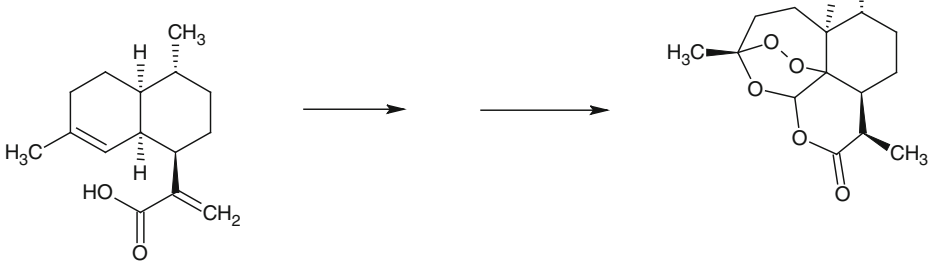
A very engaging perspective is offered on the use of enzymes as catalysts in synthetic organic chemistry. This obvious application has been thwarted during the last half century due to the inaccessibility of many enzymes in sufficient quantities to permit practical applications. The synthetic abilities of many naturally occurring enzymes also limited synthetic consideration due to narrow substrate specificities, insufficient stability under operating conditions, product inhibition, and poor regioselectivity (preference of chemical bond making or breaking in one direction in contrast to all other possibilities). Early application of the utility of enzymes can be found in the work of Ludwig Rosenthaler in 1913 which offered an example of enzyme-mediated asymmetric catalysis forming (R)-mandelonitrile from optically inactive benzaldehyde.



benzaldehyde (R)-mandelonitrile

Considerable efforts were expended to expand the utility of enzymes but protein engineering changed matters rapidly. A host of related technologies were developed, using the basic tenets of direct evolution to conduct extensive and complex searches of laboratory evolution experiments to find new desired enzymatic activities. The complexity of laboratory evolution experiments demanded that the efficacy and speed of the process be enhanced. Saturation mutagenesis has been a workhorse in this effort and has

become more efficient recently. There are still perplexing problems found when directed evolution yields a mutant library constructed along a given evolutionary pathway, failing to form an improved enzyme variant. This use of directed evolution shows that controlling the outcome is critical to the advancement of these techniques.



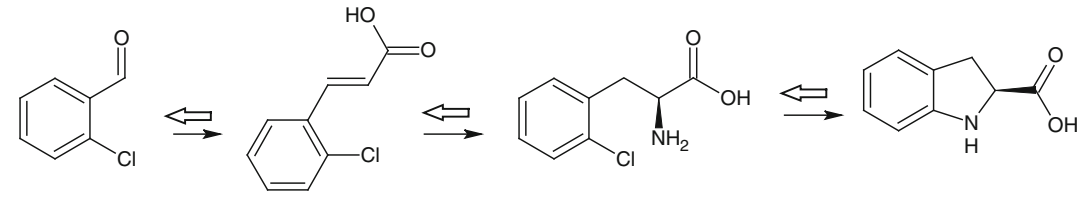
artemisinic acid artemisinin

For example, one research testing selection focuses on how to devise enzyme promiscuity. Enzymes in contrast to non-biological catalysts, such as transition metal complexes, are unable to catalyze a similar scope of reaction types. Hybrid catalysts arising from unnatural amino acid incorporation or computation-based de novo design are a few of the directions taken in this endeavor. Metabolic engineering can be utilized as a means to synthesize both simple and complex compounds. An impressive example of this strategy can be found in the synthesis of the antimalarial therapeutic drug artemisinin from artemisinic acid through the use of metabolic engineering and synthetic organic chemistry. This perspective report is highly detailed and deserves to be expanded into a separate monograph. The utility of selected enzymatic activity either directly from natural sources or through evolutionary techniques is great and clearly can be a strong contributor to future developments of sustainable chemistry.

J Amer Chem Soc 2013, 135, 12480–12496

Retrosynthetic analytics for biocatalytic conversions

The burgeoning field of biocatalysis has been applied to recent fine/pharmaceutical chemical conversions in remarkable ways. The design of chemical processes has used natural processes and materials for biomimetic and natural product synthesis. Wild-type enzymes exhibited low substrate specificity and significant limitations encountered at larger synthetic scales. Recent applications of directed evolution and protein engineering have led to a new age for the studied selection of biocatalysts. Biocatalytic methodologies employing isolated enzymes or whole cells are valuable when applied to the manufacture of diverse chemical products ranging from pharmaceuticals to biofuels. Retrosynthetic analysis of synthetic pathways has been employed by those engaged in the total synthesis of natural products since the 1960s. The inspiration of nature has been a major directional influence in past approaches to synthetic strategies. Retrosynthesis permits the development of simple building blocks or readily available starting materials through disconnection of the chemical structure of a chemical synthesis target. The disconnections are selected for structural points, where a feasible transformation exists. This process generates 'synthons' (destructural components within a target chemical related to potential synthetic blocks) via heterolytic or homolytic cleavage of the target chemical structure's C–C or C-X bonds. Functional group interconversions offer a strategy to employ the proper synthetic chemistry at each stage of disconnection. Databases of chemical conversions can be consulted to select targets of synthetic opportunity. This logical analysis can be applied to incorporate the synthetic utility of enzymes in innovative synthetic schemes. The paper highlights several examples of the utility of retrosynthetic planning as part of synthetic strategy development. The synthesis of a key side chain of atorvastatin, the ACE inhibitor perindopril, offers an elegant example of biocatalytic retrosynthesis. In this case, (*S*)-2-indoline-2-carboxylic acid is a key structural component that can be generated from 2-chlorobenzaldehyde via a Perkin condensation, a phenyl alanine lyase, followed by a copper-catalyzed ring closure.



2-chlorobenzaldehyde (S)-2-indolinecarboxylic acid

It is anticipated that the application and development of retrosynthetic analytics will assist the future use of enzyme-catalyzed reactions as part of fine and pharmaceutical synthetic applications and even biosynthetic pathways.

Nat Chem Biol 2013, 9, 285–288; 2010, 2014, 10, 392–399

Global chemical industry energy goals achievable

The 162-page International Energy Agency (IEA) report, *Energy Efficiency Indicators: Essentials for Policy Making*, offers a survey of the impact of improved energy efficiency and provides tools to develop in-depth indicators to assist the advance of energy efficiency. Policy makers will benefit from the use of such indicators to set energy efficiency goals, and to track progress. Indicators are developed for the residential, services, industry, and transport sectors. Global chemical and petrochemical industry operations are estimated to be able to reduce energy consumption by 20 % or more with a significant decrease on CO_2 emissions through implementation of the best practices in core chemical processes.

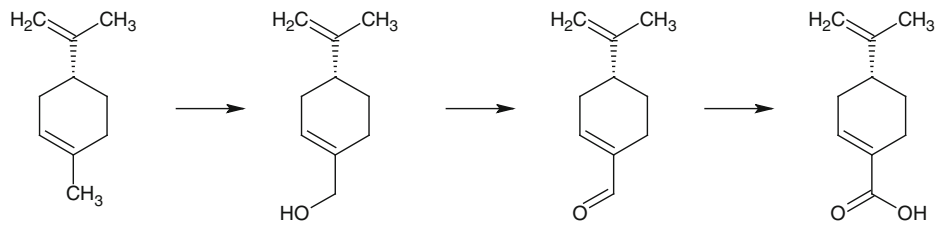
The widespread use of recycling, energy recovery, cogeneration and other measures could save even more energy and cut more carbon dioxide emissions in the short-to-medium term. Between 1990 and 2011, an overall global chemical and petrochemical sector's energy consumption was found to increase by 41 %. Energy consumption was found to exceed 107 exajoules with the associated CO_2 emissions of 10.55 gigatons in 2011. The chemical and petrochemical sectors of 10 major economies are analyzed for the potential energy savings. The U.S. chemical and petrochemical sector employed 6.3 exajoules of energy in core chemical processes for 2009. Energy use could have been reduced to 4.3 exajoules, a savings of 31.9 %, had it implemented the best practices for core chemical processes as shown by calculations of this report. Other global economies such as China could have used at least 27.3 % less energy, Japan at least 15.8 %, and Germany 14.7 % had the recommendations of the report been followed. The IEA provides statistical tools used to compile; the reports are profiled in a separate 387-page report: *Energy Efficiency Indicators: Fundamentals on Statistics* to help countries set energy efficiency and carbon dioxide reduction targets, and to track their progress.

Energy Efficiency Indicators: Essentials for Policy Making: http://www.iea.org/publications/freepublications/publication/IEA_EnergyEfficiencyIndicators_EssentialsforPolicyMaking.pdf.

Energy Efficiency Indicators: Fundamentals on Statistics: http://www.iea.org/publications/freepublications/publication/IEA_EnergyEfficiencyIndicatorsFundamentalsonStatistics.pdf.

Fine chemicals from terpenes

Secondary metabolites found in plants offer a significant source of organic substrates amenable to synthetic conversion to desirable commercial products ranging from flavor and aroma chemicals to pesticides and pharmaceuticals. There are some 55,000 terpene (terpenoids and isoprenoids) chemical structures that have been isolated from a diverse global plant universe. The composition of terpenes range from C_4 to C_{40} offering molecules that are amenable as building blocks or transformation products from cleavage. Chemical and biotechnological synthetic methodology can transform the selected terpene chemicals into commercially viable items.

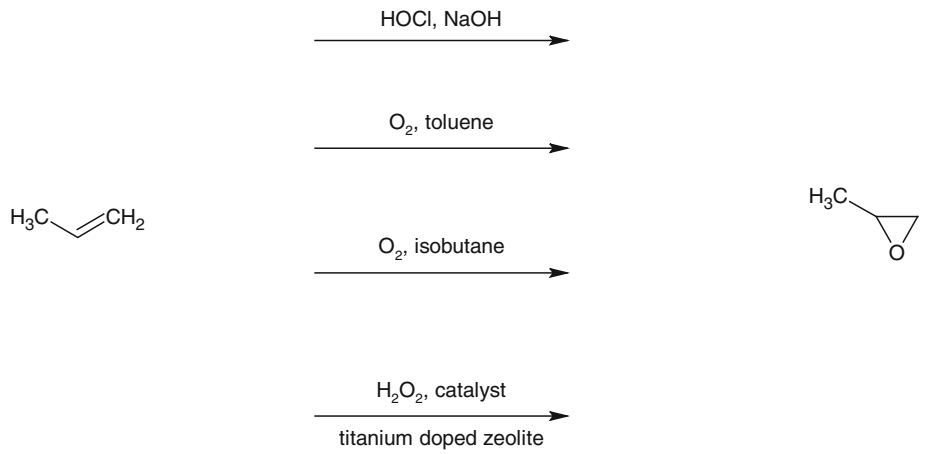


R-(+)-limonene
$4/kg

R-(+)-perillic acid
$400-800/kg

One example of this methodology is the conversion of the flavor and antimicrobial, R-(+)-limonene, which is available from citrus oil to the desirable product preservative R-(+)-perillic acid. This highly efficient conversion uses the abilities of a solvent-tolerant Gram-negative bacterium *Pseudomonas putida* to oxidize limonene to perillic acid at a 100 kg scale. As a class of natural products, terpenes have been utilized as novel and valuable starting materials for the industrial production of fragrances, perfumes, flavors/aromas, and pharmaceuticals.

Eur J Lipid Sci Technol 2013, 115, 3–8



Clean propylene oxide synthesis

Propylene oxide is an important commodity chemical to the production of organic chemicals and polymers. The chemical production sector has been called upon to use cleaner and sustainable production technology. Propylene oxide is a commodity chemical having significant demand. In 2010, there was a total demand of about 7 Mt with a production capacity of 8 Mt. Market analysis showed that demand could reach 9–10 Mt/year by 2015. Propylene oxide can be made from propylene or propane via a chlorohydrin process and indirect oxidation processes while there has been a phase-out of the chlorohydrin process in preference for a different technology. Most existing plants continue to use the chlorohydrin technology infrastructure. A new methodology offers the promise of coproduct elimination.

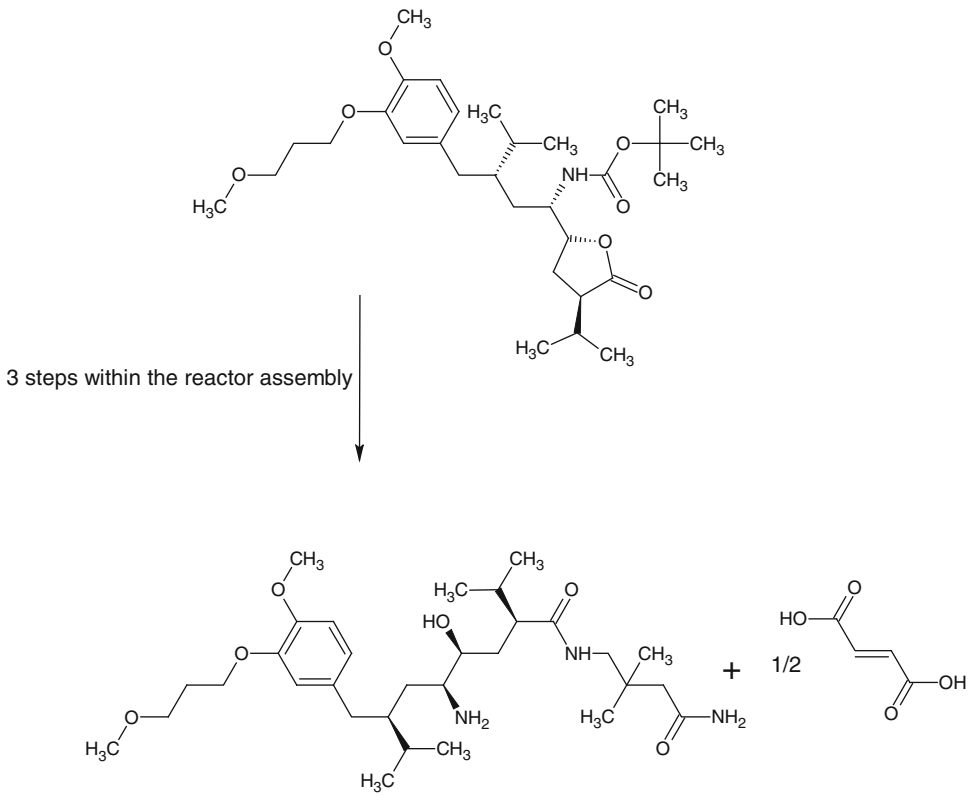
The formation of propylene oxide from propylene has an activation energy of 26 kJ/mol which is substantially high. Reaction temperatures range from 0 to 60 °C. Epoxidation is an exothermic reaction leading to high reaction temperatures. Propylene oxide has a heat of formation of −123 kJ/mol. The promising technology designed to

synthesize propylene oxide employs a titanium silicate-1 zeolite with framework type of MFI. The reaction pressure is critical to the reaction rate of propylene to propylene oxide. The reaction system is expected to be gas–liquid–solid or liquid–liquid–solid phase system. The oxidant of this new system is hydrogen peroxide. The reaction mixture also contains a solvent which is recycled after dewatering. The new process is claimed to be a state-of-the-art technology that forms no coproduct and has only water as a waste product.

Chem Oggi 2014, 32(2), 31–35

Continuous process chemistry developments

Process chemistry is a challenge in the development new synthetic pathways important to fine and pharmaceutical chemistry. The traditional approach to larger scale synthesis was to accomplish conversions leading to the desired chemical in a stepwise fashion. Clearly, reducing the total number of steps is desirable for several reasons including reduced reactor use, less waste generation, shorter equipment time commitment, and improved process economics. Continuous-flow reactors generally have a smaller footprint than start-and-stop batch production methodology. When coupled with real-time monitoring, end-to-end chemistry offers the possibility for enhanced product quality due to better control of product variability. Advantages of end-to-end processing such as reduced space requirements, lower capital investment, processing time reduction, safety considerations, new possible chemistries, and facilitation of scale-up are attractive for a variety of considerations. Clearly, competition with existing infrastructure investment, new development demands, mind-set shift changes, and other limitations should be considered for their impact. End-to-end processing has not yet attained mainstream status for fine and pharmaceutical chemical production. Fine chemical and pharmaceutical production firms are engaged in a slow adoption of these new techniques. A number of research centers have been established to assist in the development of different aspects of continuous process production such as crystallization and downstream product formulation.



aliskiren fumarate

To illustrate the utility of this new technology, an initial example of end-to-end synthetic process was developed for the target pharmaceutical, aliskiren fumarate. The compact synthesis plant, with a footprint of 17.5 m^2, could be adjusted for throughput setpoints of 20 and 100 g/h. The throughput of the plant was selected as 45 g/h. The three-step synthesis scheme from a preformed intermediate was optimized through the adjustment of residence times and other reaction parameters. The end-to-end process plant required a 10-day startup period. This plant operation shows the conversion of a chemical intermediate to targeted product progressing through intermediate reactions, separations, crystallizations, drying, and product formulation. With the anticipated changes in the fine and pharmaceutical chemical industry, the use of end-to-end continuous processing could become a major component in the manufacturing arsenal showing significant green chemistry/engineering features.

Chem Eng News 2014, 92, 21, 13–21; Angew Chem Internat Ed 2013, 52, 12359–12363; http://www.pharmoutsourcing.com/Featured-Articles/146709-Continuous-Processing-to-Enable-More-Efficient-Synthetic-Routes-and-Improved-Process-Safety/.

Contaminated land remediation sustainability

An estimated 294,000 contaminated US sites and potentially more than 300,000 ha of UK land demonstrate quite prominently the challenge that land contamination has become in modern society. Recently, the concept of sustainable remediation has been supported by industry and government for the United States and Europe. The sustainability focus calls for consideration of environmental appropriateness of the proposed remedial solutions. The standardized method of LCA as specified by the International Organization for Standardization requires much information input, is time consuming, and may not be affordable for many remediation projects. A generalized framework to address the practicability of the sustainable remediation concept has been constructed to assist the selection of the most environmentally sustainable remediation technology for various contaminated site conditions. Pump and treat, enhanced in situ bioremediation, permeable reactive barrier, and in situ chemical reduction were the remediation technologies selected for evaluation under the proposed framework. Depending on the technology, the results show the importance of site characteristics in the evaluation of the life cycle impact of the various remedial technologies. Site remedy selection can be greatly assisted through the use of this type of analysis, hopefully leading the selection the most environmentally sustainable remedy.

Environ Sci Policy 2014, 39, 25–34; J Environ Plan Manag 2014, 57, 1083–1100.

Renewables cap and trade program claimed more effective

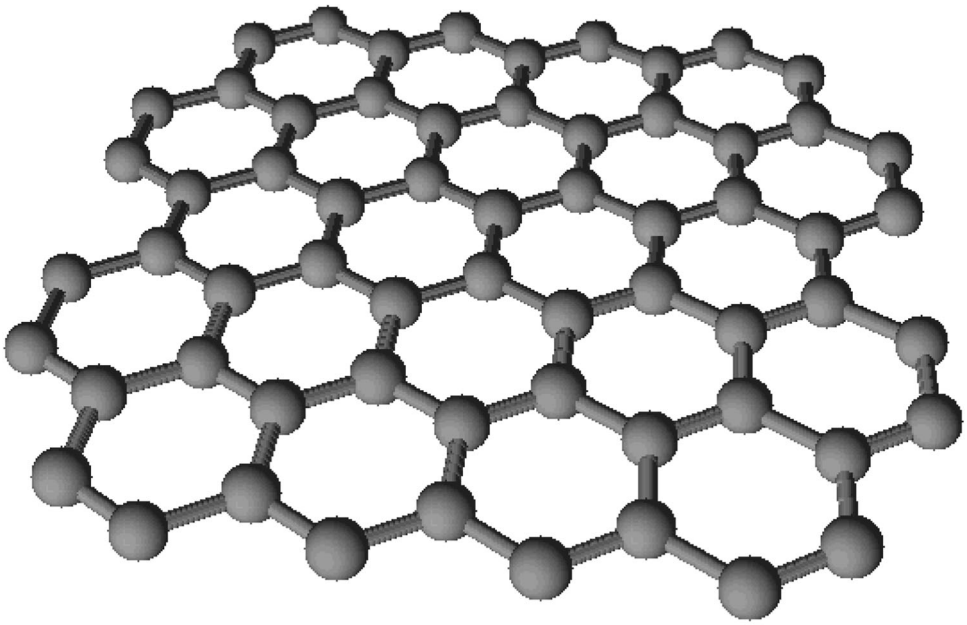
A 16-page Institute for Policy Integration report *Shifting Gears: A New Approach to Reducing Greenhouse Gas Emissions from the Transportation Sector* offers analysis of options for GHG emission control for the United States. Reductions of GHG emissions from the transportation sector could be accomplished through the development of a cap-and-trade program for renewable fuels. Market forces associated with a cap-and-trade program for renewable fuels would determine the most cost-effective means of reducing greenhouse gas emissions according to the report's analysis. The report asserts that the Clean Air Act supports the use of a trading program for renewable fuels. A cap-and-trade program for renewable fuels is expected to be more predictable and effective than command and control regulations. In 2012, the GHG emissions of the US transportation sector amounted to 28 % of the US total.

The report interprets the term "control" to connote a sufficiently broad meaning which can support cap-and-trade program implementation. The report expects cap-and-trade program for greenhouse gas emissions from both vehicles and stationary sources to achieve the desired carbon pollution reduction.

http://policyintegrity.org/files/publications/Shifting_Gears.pdf.

Graphene sheet roll up

Carbon nanotubes (CNTs) as cylindrical graphene layers have exceptional electronic, thermal, and mechanical properties that can react with biological entities (membranes, biomolecules, and cells) in a variety of exciting ways. Efficient synthetic strategies are sought in response to the growing demand for CNTs.



Graphene

CNTs have been produced at large scale through stochastic synthetic processes including arc discharge, laser ablation, and chemical vapor deposition leading to mixtures of CDTs having various sizes (differences in diameter and length). Different CNT properties can arise from these differing sizes. The separation of the CNT mixtures is not a trivial task. CNTs are easily envisioned as long nanoscale cylinders formed from rolled up graphene structures. Exfoliation of graphite followed by the functionalization of graphene sheets with dangling carbon bonds with the sheets rolled into cylinders without affecting the electronic structure is the conceptual understanding of the process. The ultrasonication of graphite forms graphene fragment through exfoliation. When the fragments are treated with ferrocene aldehyde in dimethylformamide, it forms a nanoscroll. This simple reaction sequence can be conducted within the confines of a single reaction vessel. The facile availability of CNTs is expected to lead to new forms having different geometric dimensions and open investigations into many applications.

ChemPhysChem 2013,14, 3447–3453

Investor perception of climate change risk

Climate risks are becoming significant components to investment decisions and are reported to influence pension funds asset selection. A 52-page report, *Global Investor Survey on Climate Change*, was released by an investor group composed of The European Institutional Investors Group on Climate Change, the North American Investor Network on Climate Risk, the Australia/New Zealand Investor Group on Climate Change, and the Asia Investor Group on Climate Change, which offers an analysis of investment practices of asset managers and owners related to climate change. The report notes that a majority of investors recognize that climate change is a material risk and consequently appear to have changed their commitment to climate change within their investment activities. Among the top climate risk factors identified by asset owners and managers in the survey were regulatory changes related to greenhouse gas emissions, government support schemes, physical impacts, and corporate governance policies for climate change. Climate risks were found to be evaluated within asset classes and for particular investments outside the portfolio level. As an example, assessments for real estate and infrastructure portfolios emphasized the importance of potential physical impacts and GHG emissions for specific assets. Surprisingly, more than half of the asset owners and asset managers declared low-carbon investments. In recent years, investor attention to the importance of climate change effects has steadily increased across the globe.

http://www.ceres.org/resources/reports/global-investor-survey-on-climate-change-2013.

Embodied GHG emissions from electronic products

Computers and electronics have been found to be significant contributors to household electricity consumption. Information and communications technology (ICT) devices are sources of embodied GHG emissions. A process-sum life cycle assessment (LCA) approach was used to evaluate the embodied GHG emissions of 11 ICT devices/products such as laptop personal computers, LCD monitor, mobile devices (Apple iPad, iPod Touch, and Amazon Kindle), rack servers, and network switches. Complete lists of materials involved in the device assemblage were developed through disassembly and weighing. Processes contained in the ecoinvent v2.2 database were used to produce impact estimates for all the materials. Results were analyzed to develop simplified impact estimation models using linear regressions based on product characteristics. Mass and embodied emissions were found to be correlated as a simple and robust relationship. When display mass, battery mass, and circuit board mass are used to parameterize a more complicated model, the correlation was improved slightly. Newer products were found to be 50–60 % lower in embodied GHG emissions than older products with similar functionality. Decreased material usage in the form of integrated circuit content reductions was identified as the major contributor to these differences. These modeling efforts are expected to be useful in practice and to support decisions related to the environmental impact of modern electronic and computing products.

Environ Sci Technol 2013, 47, 3997–4003

Sustainable biorefineries

The design of production processes using different sources of biomass are reviewed covering the first, second, and third generation of biofuels and including bioethanol, biodiesel, hydrogen, and FT-diesel. Using mathematical programming techniques, these processes were reviewed to systematically evaluate alternative technologies. These processes were identified by incorporating use of raw material, energy, and water to evaluate the process for its economics and sustainability. The future biorefineries are expected to exploit synergies available to the processes and enhance them through integration to reduce production cost. The processes considered in this analysis begin with corn- and sugar-based bioethanol as a 1st-generation process. The lignocellulosic biofuels processes considered are 2nd-generation bioethanol, biochemical conversion, hydrogen conversion, and biooil and fuel gases via fast pyrolysis. Oil-based biofuels included vegetable oils, 1st-generation biodiesel, production process of biodiesel from oil, and glycerol as a valuable by-product. A final process area is algae-based biofuels. Conceptual design has been traditionally augmented with mathematical optimization techniques in the petrochemical industry to improve the performance of processes. These same techniques were used to scope the processes under evaluation to optimize and design biorefineries of the future in terms of operational economics and sustainability.

Ind. Eng. Chem. Res. 2013, 52, 3044–3064

New publication

Sustainable Chemical Processes is a peer-reviewed open-access journal covering both scientific and engineering aspects of sustainable approaches in chemistry. The broad scope includes, but is not necessarily limited to Green routes to isolation, purification and synthesis of organic, inorganic, or organometallic compounds and materials, all aspects of catalysis (including use of nanosized materials) and biocatalysis that lead to sustainable processes. The latter includes biocatalysis in various reaction media. It also includes bioseparation, stabilization, and engineering aspects; biomass conversion and use of renewable resources (including valorization of agricultural and industrial waste), biofuels, biorefineries, and other alternative sources of energy (such as H_2 generation and storage, solar cells, fuel cells, and photovoltaic cells); process intensification including flow chemistry, green metrics, and sustainability assessment of products and processes (including LCA methods); microwave- and ultrasonic-assisted reactions in chemistry, biochemistry, and material science; nanotechnology that enhances the sustainability aspects of processes, green electronics and sensors; approaches to reduce water consumption in chemical processes; and CO_2 capture processes.

http://www.sustainablechemicalprocesses.com/.