

Mechanochemical organic synthesis

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Recently, mechanical milling using a mixer mill or planetary mill has been fruitfully utilized in organic synthesis under solvent-free conditions. This review article provides a comprehensive overview of various solvent-free mechanochemical organic reactions, including metal-mediated or -catalyzed reactions, condensation reactions, nucleophilic additions, cascade reactions, Diels–Alder reactions, oxidations, reductions, halogenation/aminohalogenation, etc. The ball milling technique has also been applied to the synthesis of calixarenes, rotaxanes and cage compounds, asymmetric synthesis as well as the transformation of biologically active compounds.

DE ANIVERSARIO: “QUÍMICA VERDE”

Irradiación infrarroja: una alternativa para la activación de reacciones y su contribución a la química verde

René Miranda,¹ Olivia Noguez,¹ Benjamín Velasco,¹ Gabriel Arroyo,¹ Guillermo Penieres,¹ Joel Omar Martínez¹ y Francisco Delgado²

ABSTRACT (Infrared irradiation: An alternative for reaction activation and its contribution to Green Chemistry) In this work, we present a review covering reactions activated by means of infrared irradiation, with the following features of the reaction: solvent-less conditions, the employment of a bentonitic clay as either catalyst or reaction medium; furthermore, since multicomponent reactions are considered as green approaches, several of them are also discussed. Almost all the reactions included, correspond to a decade of work of our research group, and they are offered as a contribution to Green Chemistry.

KEYWORDS: Green Chemistry, infrared irradiation, multicomponent reactions, catalysis, bentonitic clay

http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0187-893X2009000400005

QUÍMICA VERDE

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¿Qué tan verde es un experimento?

Marina L. Morales Galicia,¹ Joel O. Martínez,¹ Laura Bertha Reyes-Sánchez,¹ Osnieski Martín Hernández,² Gabriel A. Arroyo Razo,¹ Adolfo Obaya Valdivia¹ y René Miranda Ruvalcaba¹

ABSTRACT (How green an experiment is?)

There are many publications pretending to belong to the green chemistry protocol; however, only few papers ask questions and make suggestions in order to obtain an appropriate evaluation about the green approach of a particular experiment. Thus, in this paper a contribution for an educative change is offered, searching for sustainability; the goal is to establish a model, in a critical way and under the green chemistry protocol: how green is a chemical experiment?

KEYWORDS: education, green approach, criteria, evaluation

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Aporte de la química verde a la construcción de una ciencia socialmente responsable

Laura Bertha Reyes-Sánchez*

ABSTRACT (Green Chemistry's contribution in the construction of socially responsible science)

Between teachers and scientists the sustainable and supportable development are neither consensual nor conscientious concepts in Latin America; on the contrary, they are indeed an essential part of a conceptual argument which is necessary to approach from the educational ambit in order to be decanted to the citizenship. The lack of clearness at this respect allows us to consider the Green Chemistry as a supportable one, but at the same time, it is also designated sustainable — in agreement to the sustainable development concept affixed by the UN in 1987. However, beyond the simple language, a sustainable system is not conceptually the same than a supportable one, and they do not mean the same neither socially nor economically for the development of the region; on the other hand, they do affect all of the aspects of the life, including the educational and scientific development. The objective of this work is to analyze in a critical way the philosophy of the Green Chemistry with respect to the sustainability concept, in order to elucidate how to advance toward a chemical science that is able to contribute with a true development: a chemistry socially responsible whose paradigm is still pending to be established.

KEYWORDS: science, social responsibility, sustainability, green chemistry, education

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Mechanochemistry of inorganic and organic systems: what is similar, what is different?

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Mechanochemistry of inorganic solids is a well-established field. In the last decade mechanical treatment has become increasingly popular as a method for achieving selective and “greener” syntheses also in organic systems. New groups and researchers enter the field of mechanochemistry, often re-discovering many of the previously known facts and effects, while at the same time neglecting other important concepts. The author of this contribution has long been involved in mechanochemical research in both inorganic and organic systems. The aim of this contribution is to provide an overview of the basic concepts of mechanochemistry in relation to inorganic and organic systems.

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APUNTES

Educación y Desarrollo Post-2015



Oficina de Santiago
Oficina Regional de Educación
para América Latina y el Caribe

Educación para el Desarrollo Sostenible y el Cambio Climático

Liliana Morawietz

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Heredera de una tradición fundada en la educación ambiental, la educación para el desarrollo sostenible se implementa en América Latina y el Caribe a través de iniciativas de diversa índole, que van desde el desarrollo de políticas nacionales hasta la ejecución de proyectos por parte de la sociedad civil. Esta proliferación de acciones, impulsada en gran parte la implementación del Decenio de la Educación para el Desarrollo Sostenible (DEDS, 2005-2014), contrasta con la ausencia de mecanismos que permitan evaluar su incidencia e impacto.

Si bien la educación para el desarrollo sostenible no aparece en la declaración de Dakar, ni es uno de los objetivos —expresamente indicados— del movimiento de Educación para Todos, desarrollarla e implementarla será un imperativo de la agenda educativa posterior a 2015.

Química verde: Un tema de presente y futuro para la educación de la química*

María del Carmen Doria Serrano¹ y René Miranda Ruvalcaba²

ABSTRACT (Green Chemistry: A topic for the present and future of chemistry education)

This special issue on Green Chemistry focuses on one of its most important goals, which is the diffusion of its principles, advances and challenges to the general public, chemistry students and professionals. This text gives an overview of the contents of the papers included in the issue, which were written by experts in education from several countries. The reader will appreciate how education of Green Chemistry is an expanding endeavor in various regions of the world.

KEYWORDS: Sustainability, Green Chemistry, Chemistry Education

ÁREAS EMERGENTES DE LA EDUCACIÓN QUÍMICA [QUÍMICA VERDE]

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Química Sostenible: Naturaleza, fines y ámbito

Ramon Meñes¹

ABSTRACT [Green and Sustainable Chemistry: Nature, Aims and Scope]

Green Chemistry entails a philosophy which is summarized in the twelve principles enunciated by Anastas and Warner, and whose aim is an industrial chemical process based on clean and safe reactions. This philosophy applies as well to other industries and activities which are based on chemical conversions, or on use of chemicals. Study of the industrial chemical process allows the visualization of convenient strategies for its greening, which are to be accomplished by related research or development fields, such as use of renewable source materials, substitution of traditional organic solvents, use of catalytic and biocatalytic procedures, or selective activation of reacting molecules. Previous to the industrial process, although with much later effects on the environment, new chemicals must be designed to fulfill conveniently their function and to be easily recycled or degraded at the end of their use.

KEYWORDS: green chemistry, sustainable chemistry, catalysis, biocatalysis, solvents, selective activation

EMERGENT TOPICS ON CHEMISTRY EDUCATION [GREEN CHEMISTRY]

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Green Chemistry for Postgraduates

Louise Summerton, Andrew J. Hunt and James H. Clark¹

ABSTRACT (Química verde para posgraduados)

The multidisciplinary nature of Green Chemistry is recognised worldwide as a route to the development of chemical products and processes with lower environmental impact. Green chemistry and sustainability have had a profound effect on the way industry wish to be perceived. To promote uptake of green and sustainable methodologies amongst the chemical and chemical-using industries requires the exemplification of green chemistry in education and training material to influence and inspire the next generation of scientists. Herein, we examine important aspect of successful graduate green chemistry courses and how the skills gained from such studies can open doors to careers in a wide cross section of chemistry related industries.

KEYWORDS: Green Chemistry, graduate, multidisciplinary, career, transferrable skills, courses

Reacciones asimétricas organocatalizadas en ausencia de disolvente: una estrategia para hacer más “verde” la organocatálisis

José G. Hernández¹ y Eusebio Juaristi¹

ABSTRACT (Solvent-free asymmetric organocatalyzed reactions: a strategy towards a greener organocatalysis)

According with the principles of “green” chemistry, asymmetric organocatalysis aims to become a sustainable strategy to catalyze a wide range of chemical transformations. Furthermore, during the last decade the application of solvent-free methodologies has transformed asymmetric organocatalysis into an even “greener” alternative, avoiding the use of volatile, toxic and expensive reaction media. In this article, we review some recent salient examples of solvent-free strategies that have converted asymmetric organocatalysis into a more sustainable synthetic methodology.

KEYWORDS: Asymmetric organocatalysis, green chemistry, solvent-free reactions, ball-milling

JOC Article
pubs.acs.org/joc

Green Synthesis of α,β - and β,β -Dipeptides under Solvent-Free Conditions

José G. Hernández and Eusebio Juaristi*

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The reactivity of *N*-tert-butyloxycarbonyl-*N*-carboxyanhydrides derived from β -alanine, (*S*)- β^3 -homophenylglycine, and (*S*)- β^3 -carboxyhomoglycine with different α - and β -amino ester hydrochlorides was examined under ball-milling activation. In particular, good to excellent yields of several relevant α,β - and β,β -dipeptides were obtained. An illustrative application of this methodology consisted in the high-yield synthesis of the mammalian α,β -dipeptide *N*-Boc-L-carnosine-OMe.

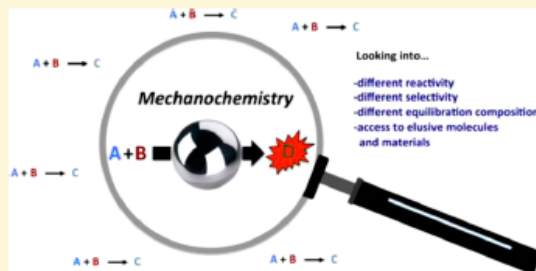
DOI: 10.1021/jo101159a

Altering Product Selectivity by Mechanochemistry

José G. Hernández* and Carsten Bolm*

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ABSTRACT: Mechanochemical activation achieved by grinding, shearing, pulling, or milling opens unique opportunities in synthetic organic chemistry. Common features are that mechanochemistry facilitates reactions with insoluble reactants, enables high-yielding solvent-free synthetic procedures, and shortens reaction times, among others. However, mechanochemical techniques can also alter chemical reactivity and selectivity compared to the analogous solution-based protocols. As a consequence, solvent-free milling can lead to different product compositions or equilibration mixtures than in solution. Reactions by milling have also allowed the trapping and characterization of elusive intermediates and materials. In this Perspective we highlight a few selected examples that illustrate the value of mechanochemistry in uncovering interesting chemical reactivity, which is often masked in typical liquid-phase synthesis.



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Fuentes alternativas de materia prima

Rolando A. Spanevello,¹ Alejandra G. Suárez y Ariel M. Sarotti

ABSTRACT (Alternative sources of starting materials)

Biomass is the source of renewable carbon that will allow to achieve the future development of our society. With the prospect of the fossil resources depletion, it is necessary to find new alternative sources of energy and raw materials. Chemistry will play a key role to design new materials from biomass which will reshape our way of living and consumption.

KEYWORDS: biomass, cellulose, levoglucosenone, waste materials

EMERGENT TOPICS ON CHEMISTRY EDUCATION [GREEN CHEMISTRY]

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Pierre-Jean Robiquet

Jaime Wisniak¹

ABSTRACT

Pierre-Jean Robiquet (1780-1840), a French pharmacist, made important contributions in the areas of mineral chemistry, mineral and vegetable pigments, and extractive and analytical chemistry. Alone, or with his collaborators he discovered asparagine (with Vauquelin), alizarin and purpurin in madder (with Colin), orcin, and orcein in lichens, glycyrrhizin in licorice, cantharidin in cantharides, amygdaline in bitter almonds (with Boutron-Charlard), caffeine (independently of Pelletier, Caventou, Runge) and narcotine and codeine in opium.

KEYWORDS: vegetable dyes, alizarin, purpurin, orcin, glycyrrhizin, cantharidin, amygdalin, alkaloids, caffeine, opium, morphine, codeine



Review

Infrared Irradiation: Toward Green Chemistry, a Review

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Abstract: This review provides a comprehensive overview of where infrared irradiation has been employed, mainly as regards activating green mode for natural products extractions, as well as to favor a reaction, highlighting its actual importance. It is also underlined that infrared irradiation heating has been around for a long time; however, only in the last eighteen years have many of its advantages been applied to satisfy a wide range of chemical processes, natural products extractions, and for the promotion of many kinds of reactions. In addition, it is brought to light that near infrared irradiation is more efficient than middle and far infrared irradiations, being easily controllable and with the quality of a fast responding heat source. Thus, the main objective of this review is to offer infrared irradiation as an alternative clean energy source to activate reactions, in addition to favor the selective extraction of natural products, all of which is within the Green Chemistry protocol. Some recent results from our laboratory are also included.

Keywords: catalytic clay; clean energy; green chemistry; infrared irradiation; natural products extraction; reaction activation

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Organic electrosynthesis: a promising green methodology in organic chemistry†

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Over the last decade, organic electrosynthesis has become recognized as one of the methodologies that can fulfill several important criteria that are needed if society is to develop environmentally compatible processes. It can be used to replace toxic or dangerous oxidizing or reducing reagents, reduce energy consumption, and can be used for the *in situ* production of unstable and hazardous reagents. These are just a few of the most important attributes that render electrochemistry environmentally useful. In this review the main characteristics of electrochemistry as a promising green methodology for organic synthesis are described and exemplified. Herein we provide basic information concerning the nature of electrosynthetic processes, paired electrochemical reactions, electrocatalytic reactions, reactions carried out in ionic liquids, electrogeneration of reactants, electrochemical reactions that use renewable starting materials (biomass), green organic electrosynthesis in micro- and nano-emulsions, the synthesis of complex molecules using an electrosynthetic key step, and conclude with some insights concerning the future. Throughout the review the “green aspects” of these topics are highlighted and their relationship with the twelve green chemistry principles is described.

Comparative study of the *N*-isobutyl-(2*E*,6*Z*)-dodecadienamide chemical and electrochemical syntheses†

Agustín Palma, Jorge Cárdenas and Bernardo A. Frontana-Uribe*

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In order to show the advantages and limitations of organic electrosynthesis in the total synthesis of a natural product, one of the promising green chemistry techniques in organic chemistry, the synthesis of *N*-isobutyl-(2*E*,6*Z*)-dodecadienamide (**3**) was undertaken. Chemical and electrochemical routes that use the same intermediates were used to carry out the syntheses. Four reactions were compared from a green chemistry point of view in the synthesis of **3**: (a) alcohol to aldehyde oxidation, (b) the Horner–Emmons reaction, (c) carboxylic acid amidation with triphenylphosphonium ions and (d) the Wittig reaction. All the electrolyses were carried out in non-divided cells at a constant current. The electrochemical method in the oxidation reaction of alcohols and the carboxylic acid amidation gave better yields (95% and 67%, respectively) than the corresponding chemical reactions. The Horner–Emmons reaction gave the same yields in both techniques (80–85%); however, the electrochemical method was more environmentally friendly, due to the fact that the base used was electrogenerated, avoiding corrosive and sensitive base manipulation. Finally, the electrochemical Wittig reaction was unsuccessful in the different experimental conditions attempted, and only the chemical method produced the target product. This study demonstrated that organic electrochemistry can be a reliable method for the synthesis of important intermediates, but not all electrochemical reactions can compete with the already well-established methods of organic chemistry.

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Mechanochemistry

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Stuart L. James^a and Tomislav Friščić^{a,b}

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It is our pleasure to present this themed issue of *Chemical Society Reviews* dedicated to mechanochemistry. Over the past decade, the application of mechanical force to chemical systems, either in the form of mechanical grinding and milling, or in the form of ultrasound has resulted in a number of exciting

developments and a practical re-discovery of the field.¹ While some of the recent excitement surrounding mechanochemistry is strongly related to its application in relatively young areas of green² and supramolecular chemistry,³ pharmaceutical co-crystals⁴ and metal-organic frameworks,⁵ its applications in more traditional areas of organic synthesis,⁶ catalysis⁷ and inorganic chemistry⁷ are just as exciting and innovative. This diverse and innovative spirit of modern mechanochemical research is well illustrated in the recent web themed issue of *Chemical Communications*,⁸ which features developments in the mechanochemistry of metal hydrides,⁹

oxides¹⁰ and intermetallic compounds,¹¹ pharmaceutical materials,¹² regioselective and solvent-free organic synthesis,¹³ supramolecular synthesis¹⁴ and catalysis in mechanochemistry.¹⁵

The current collection of review articles, we believe, manages very successfully to simultaneously address this diversity of contemporary mechanochemistry, as well as capture the breadth and fundamentals of the well-established discipline. A historical introduction into the topic has been provided by Laszlo Takacs¹⁶ whose account of *The historical development of mechanochemistry* (DOI: 10.1039/c3cs35442j) leads us from ancient times to the modern day, and

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Catalysis as a foundational pillar of green chemistry

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Abstract

Catalysis is one of the fundamental pillars of green chemistry, the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. The design and application of new catalysts and catalytic systems are simultaneously achieving the dual goals of environmental protection and economic benefit.

No subject so pervades modern chemistry as that of catalysis. (Ron Breslow, *Chemistry Today and Tomorrow: The Central, Useful, and Creative Science*)

Green chemistry, the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances, is an overarching approach that is applicable to all aspects of chemistry. From feedstocks to solvents, to synthesis and processing, green chemistry actively seeks ways to produce materials in a way that is more benign to human health and the environment. The current emphasis on green chemistry reflects a shift away from the historic “command-and-control” approach to environmental problems that mandated waste treatment and control and clean up through regulation, and toward preventing pollution at its source. Rather than accepting waste generation and disposal as unavoidable, green chemistry seeks new technologies that are cleaner and economically competitive. Utilizing green chemistry for pollution prevention demonstrates the power and beauty of chemistry: through careful design, society can enjoy the products on which we depend while benefiting the environment.

The economic benefits of green chemistry are central drivers in its advancement. Industry is adopting green chemistry methodologies because they improve the corporate bottom line. A wide array of operating costs are decreased through the use of green chemistry. When less waste is generated, environmental compliance costs go down. Treatment and disposal become unnecessary when waste is eliminated. Decreased solvent usage and fewer processing steps lessen the material and energy costs of manufacturing and increase material efficiency. The environmental, human health, and the economic advantages realized through green chemistry are serving as a strong incentive to industry to adopt greener technologies.

Developing green chemistry methodologies is a challenge that may be viewed through the framework of the “Twelve Principles of Green Chemistry” [1]. These principles identify catalysis as one of the most important tools for implementing green chemistry. Catalysis offers numerous green chemistry benefits including lower energy requirements, catalytic versus stoichiometric amounts of materials, increased selectivity, and decreased use of processing and separation agents, and allows for the use of less toxic materials. Heterogeneous catalysis, in particular, addresses the goals of green chemistry by providing the ease of separation of product and catalyst, thereby eliminating the need for separation through distillation or extraction. In addition, environmentally benign catalysts such as clays and zeolites, may replace more hazardous catalysts currently in use. This paper highlights a variety of ways in which catalysis may be used as a pollution prevention tool in green

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On the mechanochemical activation by ultrasound

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Chemists have discovered, and recently actively exploited, the fact that subjecting certain molecules to ultrasound waves can bring about transformations that give insight into the correlation between classical tribological processes and the mechanical action caused by collapsing microbubbles when sonic waves propagate through a liquid medium. Chemical transformations induced by ultrasound take place in solution via mechanisms that are markedly different from those associated with molecular activation in the solid state. Both fields, however, share some striking similarities and numerous sonochemical reactions can be rationalized in purely mechanical terms. This tutorial review examines the tribochemical interpretation of sonochemical reactivity and how the multifaceted action of cavitation phenomena determines molecular evolution. A series of case studies involving solids, crystals, and polymers illustrate the mechanical properties of sound waves.

Key learning points

- (1) Think of acoustic cavitation as mechanochemical energy capable of driving chemical transformations.
- (2) Surface acoustic waves (SAWs) predicated cavitation and remain a useful tool in separation technologies and chip-based applications.
- (3) Consider the mechanical effects caused by ultrasound waves on solid surfaces, which enhance their reactivity and enable further functionalization.
- (4) Sonocrystallization, by virtue of cavitation effects on nucleation and growth, is a promising domain in pharmaceutical manufacturing.
- (5) Ultrasound-assisted mechanophore activation proves that sonication enables chemistry which one just cannot do any other way.

Mechanochemical preparation of co-crystals

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Dario Braga,^{*} Lucia Maini and Fabrizia Grepioni

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The preparation of co-crystals via mechanochemistry combines the quest for clean and green processes with the investigation of multicomponent new materials, among the currently most fashionable systems in the crystal engineering field: the physico-chemical properties of the components add, merge or transform when co-crystals are formed, giving rise to potentially improved performance in "old" solid-state chemistry fields, as in the pharmaceutical industry field, where they represent a way to obtain new formulations and to improve the properties (solubility, thermal stability, compressibility, etc.) of both new and existing drugs.

Introduction

This review deals with the crossing of two roads. The road of mechanochemistry, which is an ancient one and has been recently rediscovered to meet the demand for clean processes and environmentally friendly, solvent-free reactions,¹ and the road of co-crystals, which has become popular after discovering that most of the fundamental concepts of crystal engineering can be applied to the making of these multicomponent new materials often of pharmaceutical interest.² Undoubtedly, the impetus to the investigation of co-crystals has come mainly from their potential impact on the pharmaceutical field, as a way to improve the properties of existing drugs or as a route to new drugs. Co-crystallization can, in fact, be used to change

relevant properties such as dissolution rate, solubility, thermal and hydration stability or compressibility, etc.,³ or to develop entirely new drugs with enhanced/combined properties.⁴

Pharmaceutical co-crystals generally consist of an API and one or more ancillary molecules called co-crystal formers or "co-formers". Clearly, a co-former needs to be a GRAS (Generally Recognized As Safe) compound, i.e. accepted by the general pharmacopeia.⁵

Typically, co-crystals are prepared by slow solvent evaporation, the limitation being the solubility of the components in a given solvent or solvent mixture, but also the solubility of the co-crystal with respect to that of the single components.^{4b} Direct mixing, whether with the intermediacy of small quantities of solvent (see below), or *via* mechanical grinding of the molecular materials, has revealed itself as a more direct and cost effective (no solvent being required) way to prepare molecular and ionic co-crystals. Mechanical mixing works well with active pharmaceutical

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The historical development of mechanochemistry

Laszlo Takacs*

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This paper reviews the history of mechanochemistry. It begins with prehistoric times, when reactions could be initiated during grinding and rubbing accidentally, and follows the main developments until recent results and current trends. There are very few records on mechanochemistry until the first systematic investigations by Spring and Lea at the end of the 19th century. For the next decades, mechanochemistry developed slowly; minerals, inorganic compounds, and polymers were the main subjects of investigation. The area became more organized in the 1960s, when several large groups were established and the first dedicated conferences were held. Mechanical alloying was invented in 1966 independently and it became a subject of intense research. Interaction between the two topics was established in the 1990s. In recent years, the mechanochemical synthesis of organic compounds was added to the main subjects and the invention of the atomic force microscope provided new ways to manipulate atoms and molecules by direct mechanical action. The theoretical explanation of mechanochemical phenomena is difficult, as the mechanism is system specific and several length and time scales are involved. Thiesen proposed the first theory, the magma-plasma model, in 1967, and deeper insight is being obtained by computer modelling combined with empirical work. Practical applications have been an important motivation throughout the history of mechanochemistry. It is used alone or in combination with other steps in an increasing number of technologies.

Application of heterogeneous catalysts prepared by mechanochemical synthesis

Kathryn Ralphs, Christopher Hardacre* and Stuart L. James*

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Mechanochemical synthesis has the potential to provide more sustainable preparative routes to catalysts than the current multistep solvent-based routes. In this review, the mechanochemical synthesis of catalysts is discussed, with emphasis placed on catalysts for environmental, energy and chemical synthesis applications. This includes the formation of mixed-metal oxides as well as the process of dispersing metals onto solid supports. In most cases the process involves no solvent. Encouragingly, there are several examples where the process is advantageous compared with the more normal solvent-based methods. This can be because of process cost or simplicity, or, notably, where it provides more active/selective catalysts than those made by conventional wet chemical methods. The need for greater, and more systematic, exploration of this currently unconventional approach to catalyst synthesis is highlighted.

1. Introduction

In mechanochemical synthesis, chemical reactions are induced through the input of mechanical energy, often with little or no added solvent.¹ In practical terms it can be as simple as grinding two solids together using a pestle and mortar, but also extends

to high-energy milling equipment such as ball mills of various kinds. There are wide-ranging applications of this technique, many of which are yet to be thoroughly explored. It brings with it potential advantages over synthesis done under more conventional solvent-based conditions such as increased reaction rates, lower reaction temperatures, overall simplicity and cost.² Current environmental concerns over the use of solvents make it now particularly timely to investigate mechanochemical synthesis more extensively than has previously been done. Historically, mechanochemical synthesis has been widely applied to the synthesis of inherently insoluble inorganic materials.

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