

Applications of Microwave in Organic Synthesis Symposium

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University of Connecticut, CT, USA

New Avenues for Microwave Promoted Chemistry

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University of Texas at El Paso, TX, USA

Microwave-Assisted Carbocyclizations on Solid Support

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Merrimack College, North Andover, MA, USA

Clean, Fast Organic Chemistry for the Undergraduate Laboratory: Examples of Microwave-Assisted Synthetic Procedures

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Universidad Autónoma de Coahuila, Saltillo, Coah., México

Making Waves in the lab: Application of Microwave Assisted Synthesis in Organic and Macromolecular Chemistry

ICOS-MOS-6 **Jonathan Collins**
CEM Microwave Technology

New Advances in Microwave Technology Assisted Solid Phase Peptide Synthesis

New avenues for microwave promoted chemistry

ICOS-MOS-1

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The use of microwave heating in synthetic chemistry is a fast growing area. As well as being able to reduce reaction times and increase product yields, chemists are finding that by using microwave heating it is possible to open up new avenues for synthesis. Results from our laboratories using a range of different commercially available scientific microwave systems will be presented. This will include examples of chemistry at high temperature, low temperature, under pressure, open vessel, larger scale batch and continuous flow.

Microwave-Assisted Carbocyclizations on Solid Support

ICOS-MOS-2

Luis Martinez, *Department of Chemistry, University of Texas at El Paso, 500 W. University Ave., El Paso, TX 79968-0513*

Solid-phase synthesis techniques have been the primary method utilized in combinatorial chemistry efforts. However, very few carbon-carbon bond forming strategies provide structures that are privileged by biological receptors. Transition metal-mediated carbocyclizations that take advantage of the high dilution conditions inherent on solid support are a viable approach for the synthesis of pharmacologically active small molecules on solid support. This presentation will highlight our current efforts in the development of microwave-assisted methods for the synthesis of differentially substituted aromatic, heteroaromatic, and phenolic scaffolds privileged by biological receptors for combinatorial/solid phase organic chemistry

Clean, Fast Organic Chemistry for the Undergraduate Laboratory: Examples of Microwave-Assisted Synthetic Procedures **ICOS-MOS-3**

Cynthia B. McGowan, *Professor of Chemistry*
Merrimack College, North Andover, MA, USA

In preparation for both the industrial and academic worlds, the undergraduate chemistry major of today must gain proficiency with state-of-the-art reaction equipment, synthetic techniques, and analytical instrumentation. Reactions covered in undergraduate organic chemistry laboratory typically require lengthy reflux periods, leaving limited time for characterization, purification or repeating a procedure. Microwave heating can offer a rapid and efficient alternative to conventional oil-bath, sand-bath, or steam-bath technology.

We have converted a number of undergraduate laboratory experimental procedures for use with microwave heating. Shortened laboratory reaction times can gain students more time to design, optimize, characterize and analyze reaction processes and products. Additionally, microwave-assisted reactions can often be run neat or in aqueous solutions, minimizing the need for organic solvents, simplifying work-up procedures, and providing more environmentally friendly reaction conditions. We will describe classical organic reactions such as elimination, addition, esterification, Diels-Alder cycloaddition, and aldol condensations that now require minutes to perform. In addition, a multi-step synthesis will also be presented in which microwave heating is used in each step.

Microwave-Assisted Organic Synthesis: a) Thermal vs. Microwave Studies on 2,4-Dialkylaminoquinolines and b) Real-Time *in Situ* Raman Analysis

ICOS-MOS-4

James R. Empfield, Scott R. Throner* and Don E. Pivonka

The application of microwaves in organic synthesis has become increasingly common over the past few years. This technology has been employed to advance numerous drug discovery programs within AstraZeneca. Our interest in microwave-assisted organic synthesis has prompted us to investigate further the parameters that influence the efficiencies that have been observed with this technology. This presentation will highlight two areas of investigation. First, we will present our findings, within a series of 2,4-dialkylaminoquinolines, on thermal versus microwave reaction rates, and describe the effects of a variety of parameters such as solvent/reaction media, microwave power, and microwave pulsing. Secondly, we will illustrate the use of real-time *in situ* Raman analysis of microwave-assisted organic reactions.

Making waves in the lab: application of microwave assisted synthesis in organic and macromolecular chemistry**ICOS-MOS-5**

Catalina M. Pérez Berumen, *Departamento de Química Orgánica, Universidad Autónoma de Coahuila, Facultad de Ciencias Químicas, Blvd. V. Carranza y J. Cárdenas, 25265 Saltillo, Coah. México. Phone [+52] 844 416 9213, 844 415 5752 Fax [+52] 844 439 0511, 844 415 5752, catalina@usquim.uadec.mx*

Over the last years, research in chemical synthesis has been oriented to the design of “specific processes for the production of special products”. Now, the chemists have a new challenge because their main objective has been modified, focusing on obtaining new highly-specific compounds or materials, but contemplating all the detrimental consequences to the human health and to the environment that these processes and products could imply.

The present work arose from the main interest of our research group to incorporate the principles of green chemistry to the organic and macromolecular synthesis. The goal is to develop new routes of synthesis of small organic molecules that will be used in order to obtain original macromolecular architectures with specific properties.

In this presentation, we discuss the effect of the use of focused microwave radiation on the synthesis of linear and cross-linked polysiloxanes. Both types of polymers were obtained based on the Diels-Alder cycloaddition reaction. This reaction represents a useful “green” tool because of its high atomic efficiency, and mainly, because of its thermally reversible character, that permits to shift the equilibrium to the reagents by increasing temperature. This characteristic allows recovering the raw matter from the polymers once ended the life-cycle of the plastic article.

In order to explore the performance of the microwave assisted synthesis (MAS) on these systems, we first carried out model reactions with small organic molecules. Thus, we started with the synthesis of linear polymers involving two different monomers with diene and dienophile functionalities. These monomers were then polymerized by a Diels-Alder polycondensation. The cross-linked polymers were achieved by chemical modification under microwave radiation of commercially available polysiloxanes bearing pendant functionalities. The cross-linking of the dienophile polymers were carried out with two different multifunctional dienes acting as cross-linkers. All the monomers and polymers were characterized and the thermal-reversible character of the polymers was confirmed.

The strategy presented here represents a convenient green method to achieve original macromolecular structures with inherent green attributes. Work is in progress to investigate the MAS Wittig-type polymerizations, expecting to obtain highly conjugated polymers by a green method.

New Advances in Microwave Technology Assisted Solid Phase Peptide Synthesis

ICOS-MOS-6

Jonathan Collins

CEM Microwave Technology

Microwave enhanced SPPS has been growing in popularity because of its ability to synthesize high purity peptides with routine 20-25 minute cycle times. In this study we investigated side reactions of all twenty amino acids using the following peptide.

“VYWTSPFMKLIHEQCNRADG-NH₂”.

Synthesis of all peptides was performed on an automated microwave peptide synthesizer, Liberty (CEM Corp., Matthews, N.C.), while racemization was measured by a GC-MS method involving hydrolysis and derivatization using deuterated reagents (C.A.T. GmbH & C.O.). Optimized methods allowed for the efficient synthesis of longer peptides including the ¹⁻⁴²β-amyloid protein (19 hours; 68.8% purity) and the 68mer SDF-1a chemokine protein (35 hours; 50% purity).