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NESACS Member Interviews

Marc Bazin - President of HeptoChem

President Marc Bazin (r) and Project manager Ryan Buzdygon photographed in HepatoChem's Beverly laboratory.

HepatoChem (http://www.hepatochem.com/) is a company co-founded in 2008 by Marc Bazin, formerly of Pfizer, and Professor John T. Groves, holder of the Hugh Stott Taylor Chair of Chemistry at Princeton University. HepatoChem was started in the Groves lab at Princeton, but in August 2011 moved to the Biotech InnoVenture Center in Beverly, MA. My interest in Hepa- toChem was piqued by Business Development Manager Shelly Amster at a recent NESACS Monthly Meeting. A subsequent interview was arranged with HepatoChem President, Marc Bazin, at their Beverly facility.

HepatoChem uses technology based on many years of metalloporphyrin research conducted at Princeton in the Groves laboratory. A variety of metalloporphyrins (Fig. 1) are used to simulate liver metabolism and oxidatively convert drug candidates in vitro to metabolites in milligram to gram quantities.

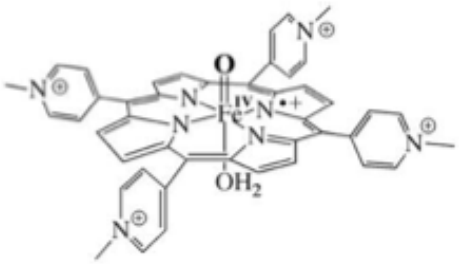

Fig. 1: A Synthetic Metalloporphyrin

This is in stark contrast to the nanogram quantities available by in vitro or in vivo biological methods. Easy access to large quantities of metabolites allows structure determination and additional evaluation and testing, which would not be possible without the larger quantities available from HepatoChem's biomimetic methods. "The technology we developed at HepatoChem can produce not only metabolites but also new analogues of lead candidates that could have better biological properties than the original drug. This positions it as an important tool for drug discovery." Initial screening is done in 96-well plates loaded with the test molecule. A series of test reactions are then con- ducted in which the metalloporphyrin, the oxidant, and the solvent are varied. These experiments are then analyzed by LC-MSMS to identify a profile of metabolites and allows rapid selection of conditions to produce the targeted metabolite.

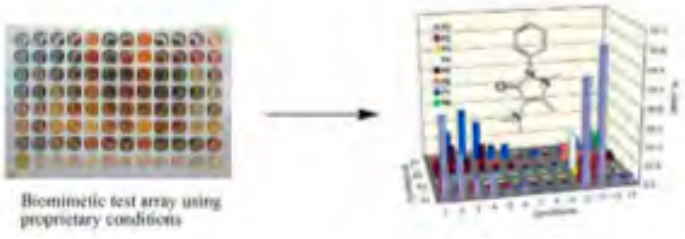

Fig. 2. Graphical illustration of metabolites formed by the oxidation of aminopyrine with HepatoChem's technology.

A second round of experiments allows optimization and larger scale production of any or all of the metabolites generated in the screen.

Examples of reactions which can be achieved with metalloporphyrin oxidation are hydroxylation, imine and enamine formation, halogenation, carbene insertion, amine formation and dealkylation. Tolbutamide is an example which illustrates aliphatic hydroxylation and dealkylation (Fig 3).

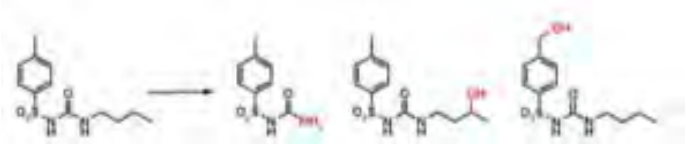

Fig. 3: Metabolites formed by biomimetic oxidation of Tolbutamide.

HepatoChem has also partnered with Princeton-based Novatia, http://www.enovatia.com/, a capillary NMR contract laboratory, to do structure elucidation of metabolites with small amounts of material (0.1-0.5 mg).

Although only a four-person company at this stage, HepatoChem already has numerous clients ranging from start-ups to big Pharma. “Our clients are very satisfied with the quality and speed of our service.” Dr. Bazin stated that the business in liver metabolites is $100 million per year and their business is expected to grow rapidly for a number of years. “This is very exciting to see our company growing in this economy.”

Interview by Michael Filosa