

Selective Synthesis of Hyperbranched Polyesters under Wet-Dry Cycling Conditions

Irena Mamajanov¹

¹Earth-Life Science Institute, Tokyo Institute for Technology,
Tokyo 152-8550, Japan
irena.mamajanov@elsi.jp

Abstract

Origin of life research can be coarsely categorized into opposing two principles, sometimes called heterotrophic and autotrophic origins. Autotrophic origin assumes that life started with a sparse chemical system that later evolved into the biochemical network, whereas heterotrophic origin follows the transformation of the initial complex chemical system. The fact that many experiments modeling prebiotically plausible conditions result in complex “messy” systems – a diverse, dynamic array of small molecule and polymeric products formed by a wide range of chemical processes – supports the idea of heterotrophic origin. The principles of selectivity and organization in these messy systems are not well understood, as the mixtures present an analytical challenge. Herein we offer a study of the selective synthesis of hyperbranched polyesters undergoing wetting-drying cycles, a simplified model messy chemical system.

Introduction

The classical approach towards the origins of life usually concentrates on studies of isolated reactions and pure chemical synthesis systems. However, it has been long noted that chemistry in prebiotically plausible scenarios, in fact, generates an intractable heterogeneous mixture of compounds. The appearance of tarry polymers was recorded in the Miller-Urey experiment (Miller, 1953), subsequently studied hydrogen cyanide (HCN) polymers (Matthews and Minard, 2006; Mamajanov and Herzfeld, 2011) and formaldehyde condensation (Breslow, 1959; Richardo et al., 2006). We are interested in a new approach to the origin of life, so-called “messy chemistry” that studies the properties of these complex mixtures that give rise to life-like systems. Messy chemistry hypothesizes that life started with complex reaction network that are common to prebiotic chemistry, evolved as a complex reaction network into biochemistry that constitutes a complex reaction network. Aspects of the messy chemistry research involve the study of the functionality of prebiotically plausible messy polymers, development of better analytical methods suitable for messy chemistries, including functional measurements experimental and theoretical modeling of the processes occurring in complex chemical systems. The ultimate goal of the “messy chemistry” is to understand the transition between messy, marginally controlled, prebiotic systems into well-orchestrated life-like chemical networks, or the origin of life.

Herein we report on the selective synthesis of highly or hyperbranched polyesters (HBPE) undergoing wet-dry cycles.

The HBPE system is somewhat more straightforward than the mentioned above tarry polymers. The Miller-Urey and HCN polymer are products of multiple chemical processes, as such, each polymeric specimen is composed of chemically diverse units, as well as distinct domains of branching and cross-linking. The present system of HBPE is uniform chemically but features multiple architectures varied in their degree of branching. The HBPE system is, therefore, more accessible to analysis and modeling, which makes it more suitable for a pilot study.

HBPEs as possible precursors for proteins

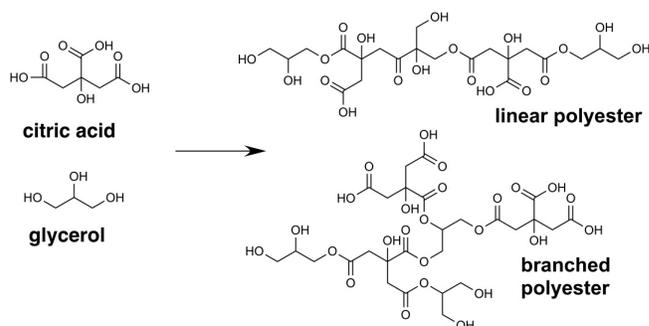
Ester bonds are common in modern biochemistry predominantly in the form of triesters of glycerol and fatty acids in lipids. Ester formation has the slightly negative bond energy (~1 kcal/mol under physiological conditions) making this functional group's synthesis facile. Polyesters have been hypothesized to have preceded peptides due to their ease of formation, and this notion is perhaps supported by the demonstrated ability of the ribosome to catalyze α -hydroxy acid coupling (Fahnestock and Rich, 1971). HBPE are of particular interest to the origin of life studies due to their ability to mimic the structure and functionality of globular proteins (Mamajanov et al., 2015). Specifically, we have previously probed the ability of HBPEs to form enzyme-mimicking catalysts. Our results showed that tertiary amine-bearing hyperbranched polyesters to form hydrophobic pockets as a reaction-promoting medium for the Kemp elimination reaction (Mamajanov et al., 2017).

Selection in HBPE systems

We have previously shown that HBPEs can be synthesized by subjecting multifunctional organic acids and alcohol mixtures to mild heating under solventless conditions (Mamajanov et al., 2015). This method, however, produces a multitude of polymeric products varied in size and shape. One possible way of selecting for the desired HBP shape and function is to investigate further the concept of far-from-equilibrium polymerization. We have established (Mamajanov et al., 2014) that linear oligoesters can be synthesized and persist under non-equilibrium conditions driven by repeated, cyclic changes in hydration and temperature that are associated with day-night cycles on the early Earth. Period of heating the open vessel stimulates esterification. Even though periodic sample

rehydration promotes hydrolysis, successive iterations of wet-dry cycles result in polymer yields, and molecular weight distributions in excess of that observed after heating alone. Products less prone to hydrolysis would tend to persist in the system at the expense of the rest. The hydrolysis patterns of HBPEs differs from linear polymer ones. The globular nature of HBPEs prevents or delays the water intrusion into the core, slowing down the hydrolysis process and resulting in macromolecular surface erosion rather than breakdown. When day-night cycling applied to HPBE condensation, the first drying phase will result in a mixture of linear, branched and mixed polymers. During the hydrated periods, linear portions of the polymer would be more susceptible to hydrolysis than their branched counterparts. Therefore it is reasonable to assume that after some cycles the makeup of the polymer would consist predominantly of branched structures. Based on size exclusion chromatography (SEC) and nuclear magnetic resonance (NMR) analyses we have concluded that as HBPE system is exposed to wetting and drying samples, the composition of polymers indeed differs from samples

A



B

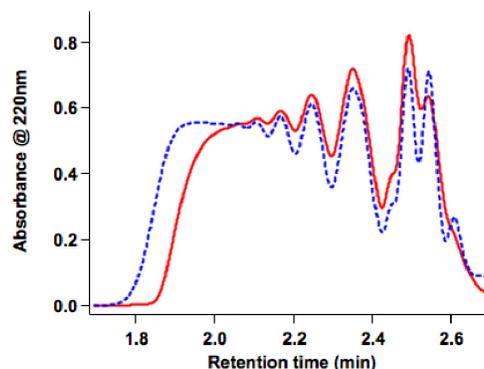


Figure 1. A) Schematic representation of citric acid and glycerol polyesterification featuring a linear and a branched product. B) Size-exclusion chromatography analysis of the polyester prepared by continuous drying (solid) and cycled wetting and drying periods (dotted). The “cycled” polymer features product with higher hydrodynamic volume.

References

- Breslow, R. (1959). On the mechanism of the formose reaction. *Tetrahedron Lett.* 1:22–26.
- Fahnestock, S. and Rich, A. (1971). Ribosome-Catalyzed Polyester Formation. *Science* 173:340-343.
- Mamajanov, I. and Herzfeld, J. (2009). HCN polymers characterized by solid state NMR: chains and sheets formed in the neat liquid. *J. Chem. Phys.*, 130:134503.
- Mamajanov, I. and Herzfeld, J. (2011). HCN Polymer. In *Encyclopedia of Astrobiology*, editors Gargaud, M., Cernicharo, J., Viso, M., Cleaves II, H. J., Pinti, D., Amils, R., and Kobayashi, K.) 730–732 Springer, New York, NY.
- Mamajanov, I.; McDonald, P. J.; Duncanson, D. M.; Jingya, Y.; Walker, C. A.; Grover, M. A.; Hud, N. V.; Schork F. J. (2014). Ester Formation and Hydrolysis during Wet–Dry Cycles: Generation of Far-from-Equilibrium Polymers in a Model Prebiotic Reaction. *Macromolecules* 47:1334-43.
- Mamajanov, I.; Callahan, M. P.; Dworkin, J. P.; Cody, G. D. (2015). Prebiotic Alternatives to Proteins: Structure and Function of Hyperbranched Polyesters. *Origins Life Evol. Biosph.* 45:123-37.
- Mamajanov, I.; Cody, G. D. (2017). Protoenzymes: The Case of Hyperbranched Polyesters. *Phil. Trans. A* 375(2109):20160357
- Matthews, C. N. & Minard, R. D. (2006). Hydrogen cyanide polymers, comets and the origin of life. *Faraday Discuss.* 133, 393-401-452.
- Miller, S. L. (1953). A Production of Amino Acids Under Possible Primitive Earth Conditions. *Science* 117:528–529.
- Ricardo, A., Frye F., Carrigan, M. A., Tipton, J. D., Powell D. H., Benner S. A. (2006). 2-Hydroxymethylboronate as a Reagent To Detect Carbohydrates: Application to the Analysis of the Formose Reaction. *J. Org. Chem.* 71:9503–9505.

synthesized by continuous drying. While continuously dried samples form insoluble glassy materials, the cycled samples feature high molecular weight but water-soluble species with a higher degree of esterification and branching. This proof-of-principle experiment can be expanded into other potential selective pressures. For example, we have already shown that citric acid/glycerol HBPs have different composition when prepared with and without divalent cations (Mamajanov et al., 2015). Furthermore, the wet/dry dynamic HBPE polymerization system is an attractive model to consider the origin of the peptide-based catalyst.

Acknowledgements

This work is supported by Kakenhi Kiban C grant # 17K01943, MEXT, Japan and World Premier International Research Center Initiative(WPI), MEXT, Japan.