

## rROP of Lactam Derivatives

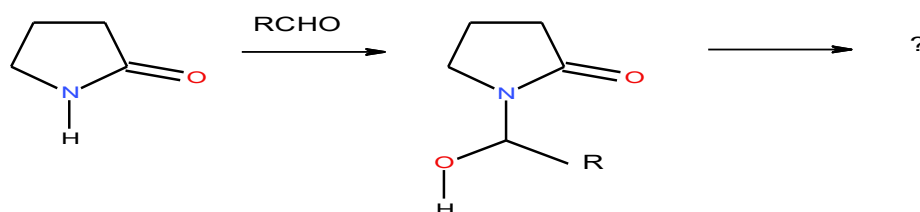
By: Robert B. Login (rloginconsulting.com)

A recent excellent detailed review has renewed my interest in radical ring opening polymerization (rROP). I previously presented several ideas concerning monomers (<http://rloginconsulting.com/joomla/images/SiteFiles/Patents/RROP%20monmers.odt2.pdf>) for this type of polymerization. However, now I would like to present new ideas based on lactam derivatives, especially those based on pyrrolidone. Obviously these ideas can also apply to most if not all lactams.

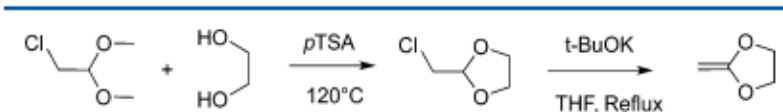
Tardy, Antoine, et al. "Radical Ring-Opening Polymerization: Scope, Limitations, and Application to (Bio) Degradable Materials." *Chemical reviews*, 117.3 (2017): 1319-1406.

My first point is that the reaction of pyrrolidone with aldehydes forms stable N-hydroxymethyl derivatives from which additional reactions can take place involving the hydroxyl group.

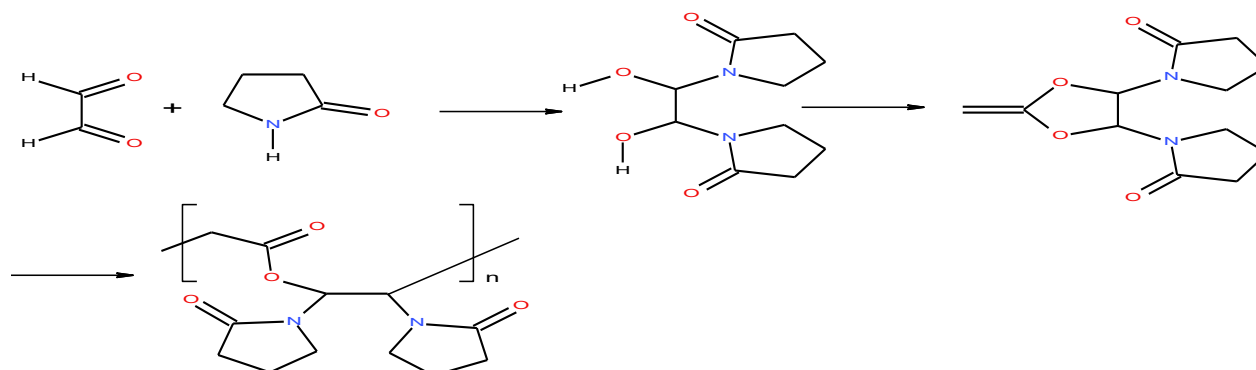
Yuri E. Kirsh. "Water soluble poly-N-vinylamides: synthesis and physicochemical properties." Wiley (1998).



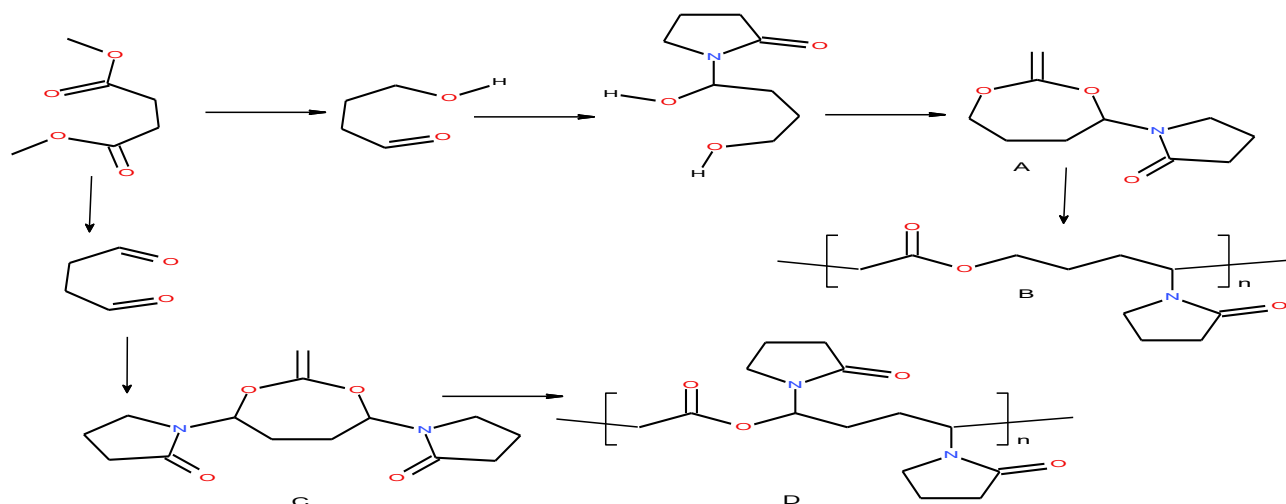
These reactions must be performed in non-aqueous solvents or neat if that's possible.



**Figure 60.** Synthesis of CKA via the transacetalization and dehydrochloration reaction.



Scheme 1: Also look at Scheme 2



Scheme 2

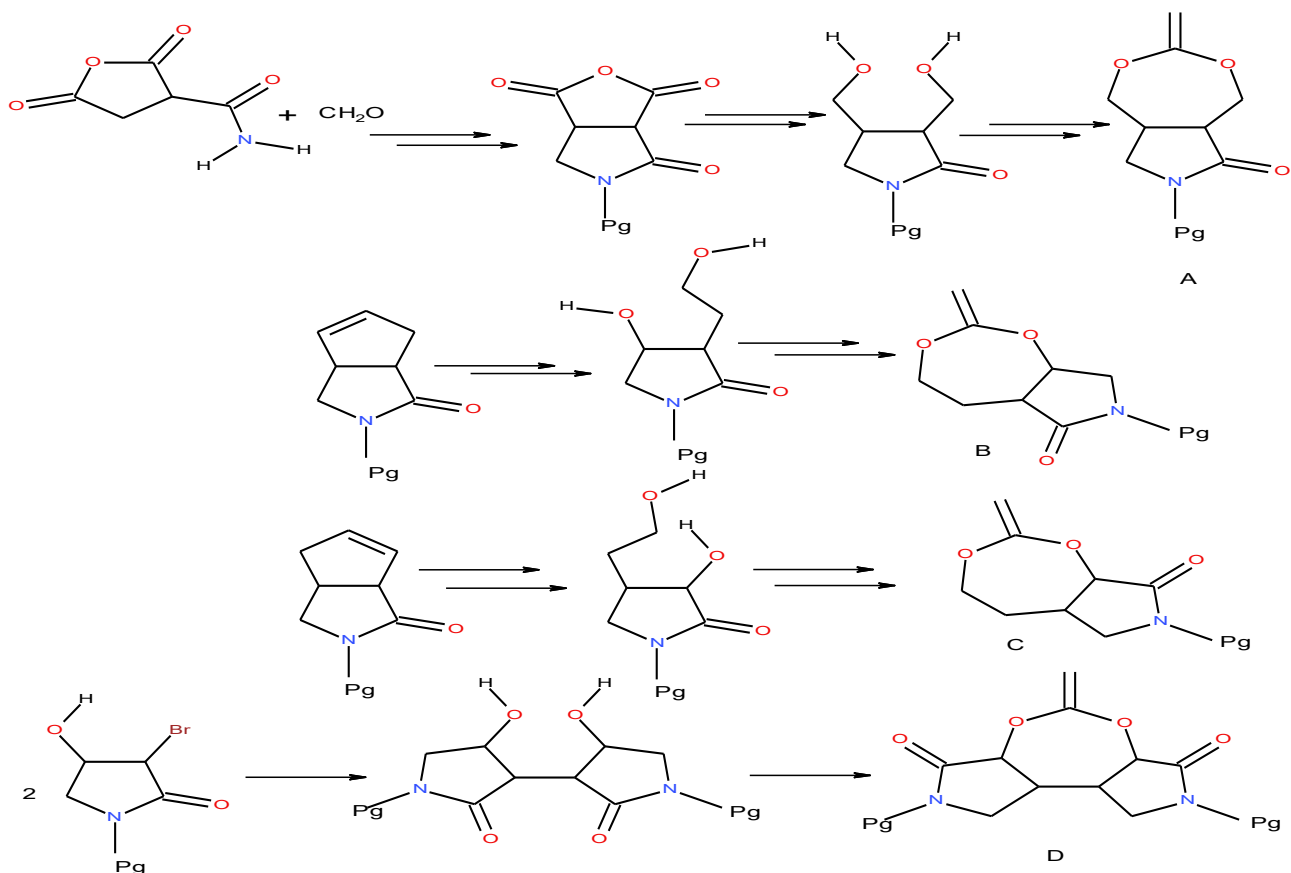
The above monomers stabilize the forming radical exactly the same as with NVP polymerization. These ideas are the closest to PVP with the benefit of degradable ester backbone groups. Scheme 2 is the same chemistry as scheme 1 but prepared from succinic anhydride, a renewable RM.

Copolymerization of scheme 1 and 2 monomers with cationic (meth)acrylate would afford hair care polymers that could be claimed to be biodegradable...a significant selling point. Copolymers of all types can be visualized affording degradable polymers; for example as, antibiotics, for drug delivery, contrast agents, skin adhesives, cell scaffolds, synthetic blood plasma expanders and so forth.

I'm suggesting that the diol is stable enough to undergo transacetalization and halogen elimination to form the rROP monomer. Polymerization of these monomers results in a polyester with two pendant pyrrolidones as the repeat unit. Such a polymer or copolymer would be hydrolyzable to potentially biodegradable fragments. In-vivo such fragments might result in easily excreted moieties. Thinking about PVP, such a copolymer with NVP would not dilute its pyrrolidone chemistry while affording degradable functionality. A major complaint about high MW PVP for in-vivo use is that it is hard or impossible to excrete.

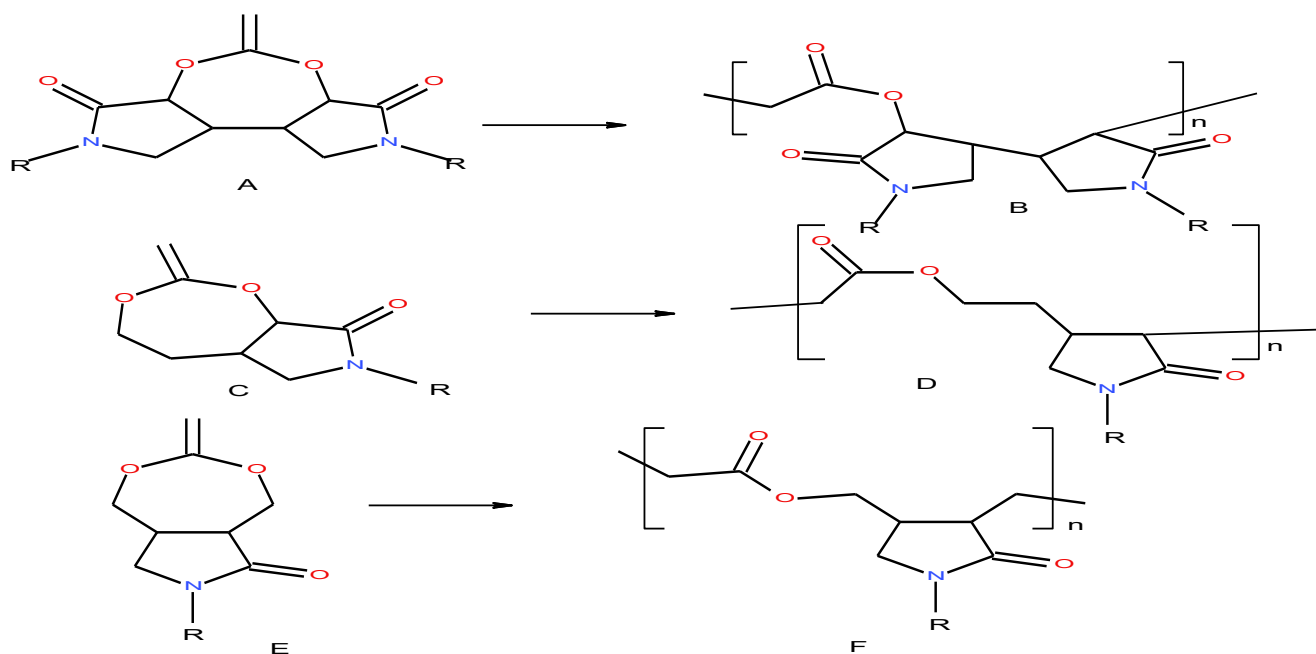
Tardy, Antoine, et al. "Radical Ring-Opening Polymerization: Scope, Limitations, and Application to (Bio) Degradable Materials." *Chemical reviews*, 117.3 (2017): 1319-1406.

Other monomers are conceivable:



Scheme 3

Several starting compounds are suggested but other approaches are possible. My point is that many pyrrolidone containing monomers are conceivable. The best rROD monomers stabilize the forming radical, in the above cases the radical is stabilized alpha to the pyrrolidone carbonyl much like acrylates (B above does not do this and maybe a poorer rDOP monomer).



Scheme 4

#### “2.9. Cyclic Ketene Acetals

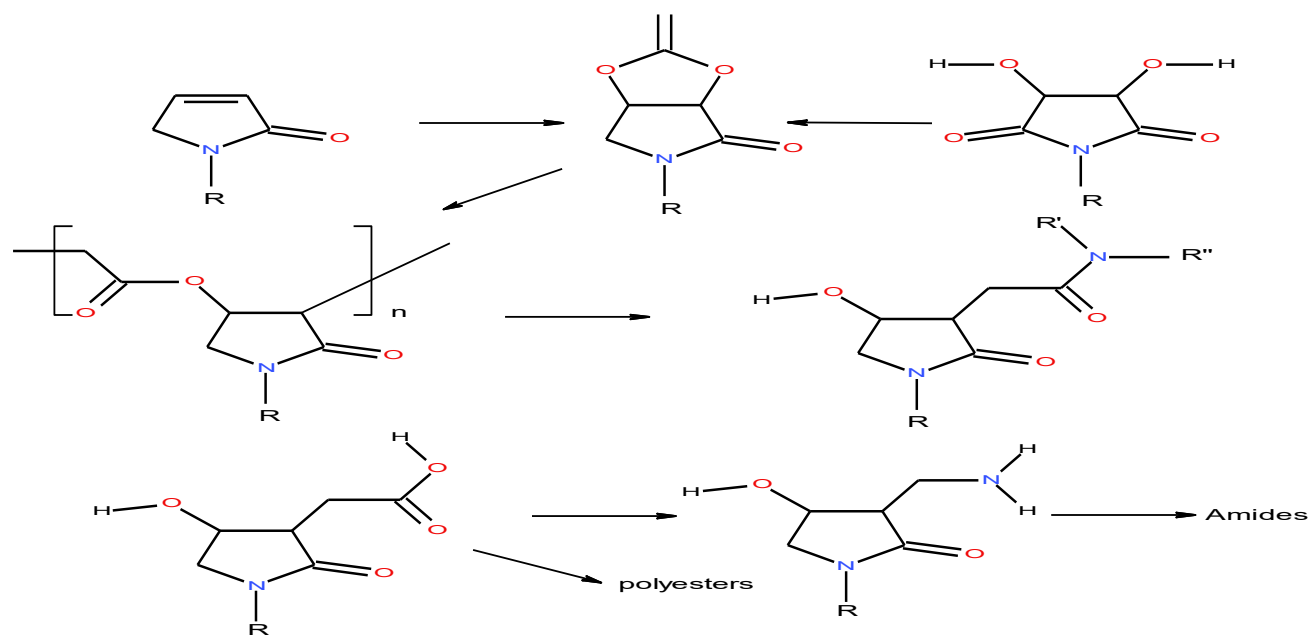
Contrary to the majority of monomers described previously, when the polymerization is performed in appropriated conditions, CKAs present the advantage of producing mainly aliphatic polyesters ( $p = 0$ , Figure 42), whose structures are similar to those of well-known (bio)degradable polyesters (e.g., PLA, PGA, and PCL). The properties of such polyesters and their potential applications have already been studied and thus the interest to prepare polyester by a radical pathway explained why CKA has been widely studied during the past decades. Another attractive feature of the cyclic ketene acetals is their relative ease of synthesis compared to other monomers used in radical ring-opening polymerization (see subsection 4.1).”

Tardy, Antoine, et al. "Radical Ring-Opening Polymerization: Scope, Limitations, and Application to (Bio) Degradable Materials." *Chemical reviews*, 117.3 (2017): 1319-1406.

Of course I've glossed over the problems one would face if attempting the above or similar chemistry such as the potential problem of radical back biting to form branching or the possibility that copolymerization with certain co-monomers might be difficult. The recent Chem. Rev. article goes into significant detail concerning the various problems of rROP and should be consulted.

#### Polymer Derivatives:

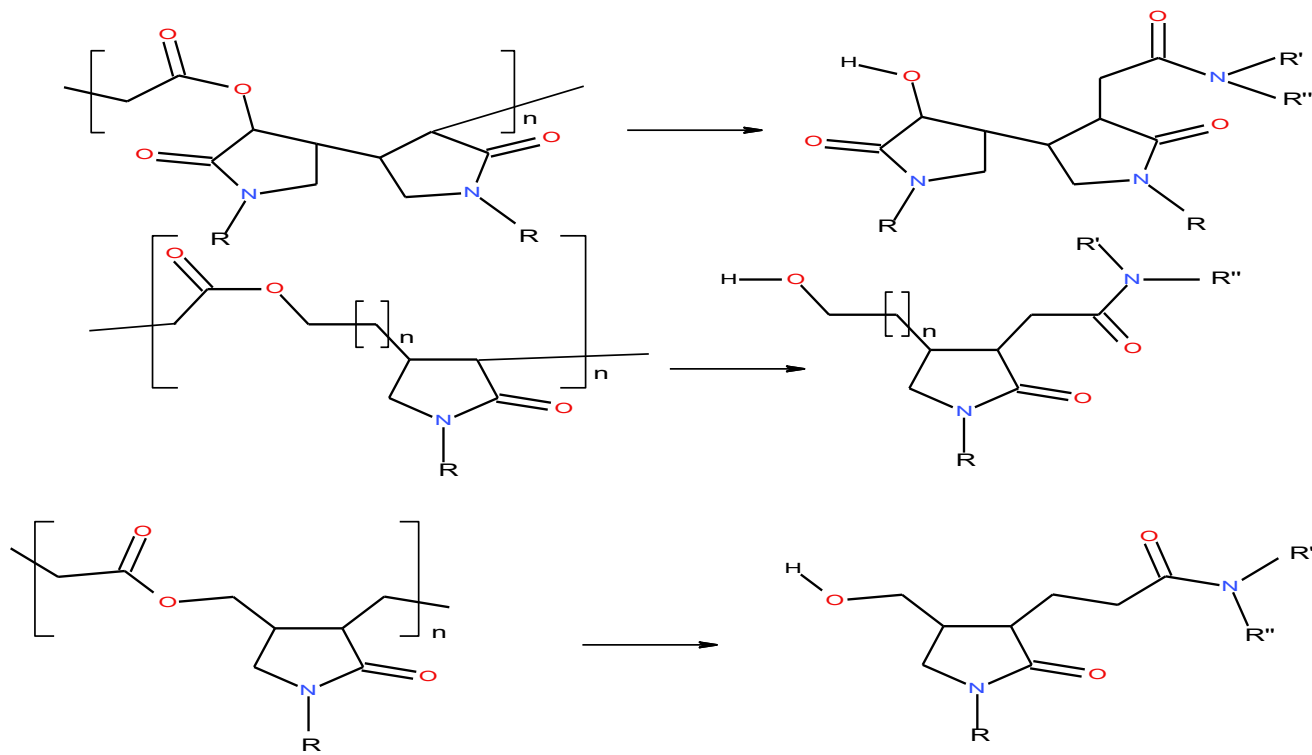
Thinking about these polyesters, I started to see additional potential for them. Treating them post CKA polymerization with fatty amines or fatty alcohols would result in new surfactants or a variety of useful intermediates by taking advantage of their ester chemistry.



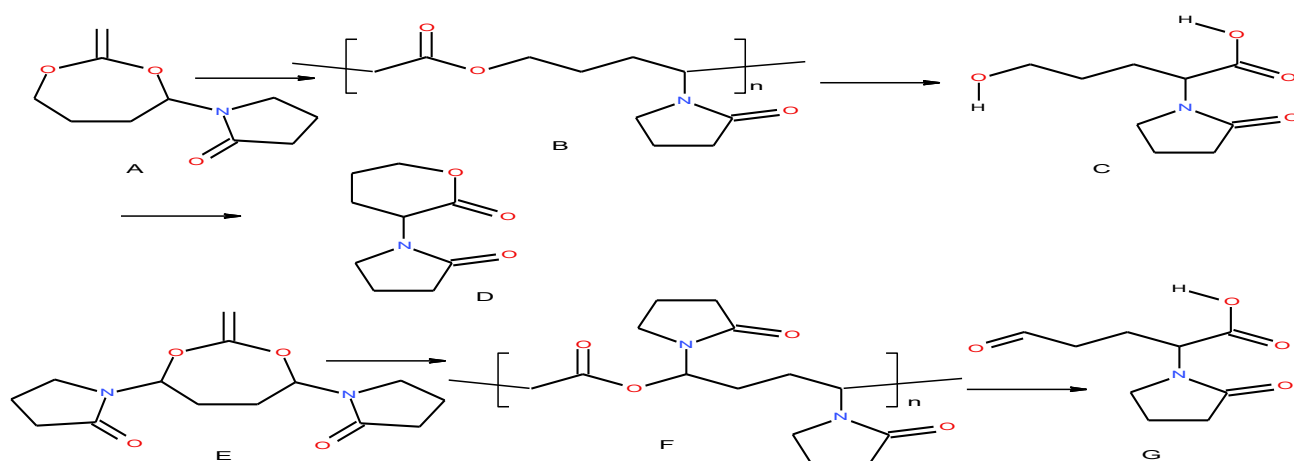
Scheme 5:

The derivatives obtained in scheme 5 are potentially very valuable as they could be a method of synthesizing unique Racetam candidates or surfactants.

Similar derivatives can be obtained from the polymers from the other schemes:

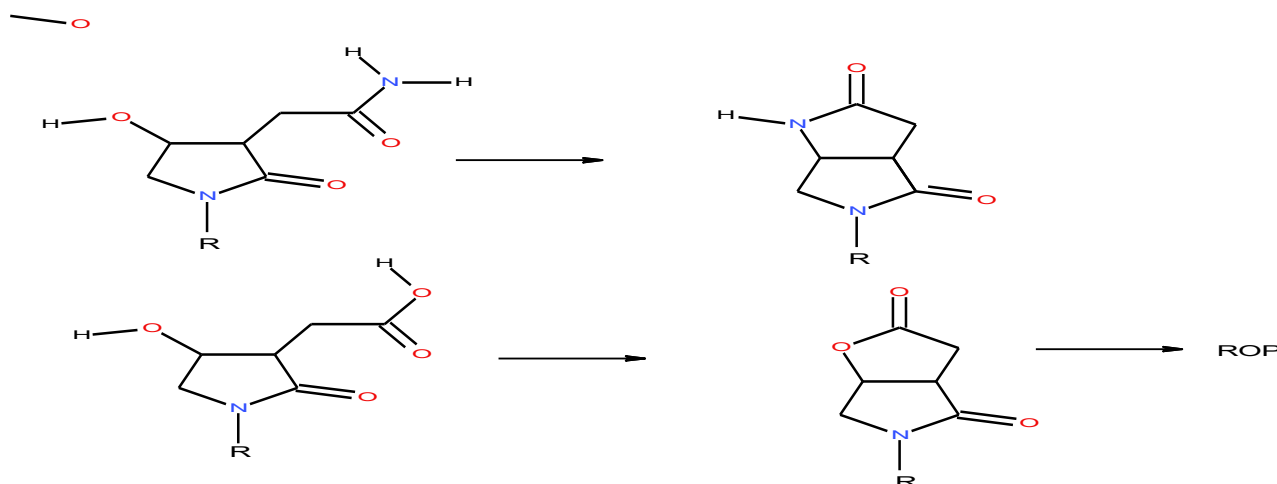


Scheme 6: Amide derivatives as potential surfactants.



Scheme 7: “Racetam type derivatives.” or components of Ugi and other MCR reactions.

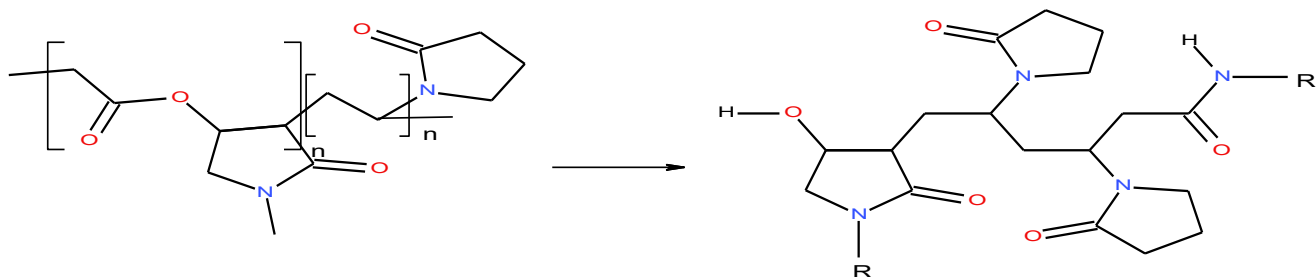
Racetam candidates continue to garner intense interest because of their nootropic effects reducing epileptic seizures, improving cognitive ability of Alzheimer sufferers. Said Racetam derivatives are unique N-substituted pyrrolidones with special R groups and said R derivatives of the above schemes could also be candidates.



Scheme 8: Conversion of Cyclic Ketene Acetals into carboxylic derivatives

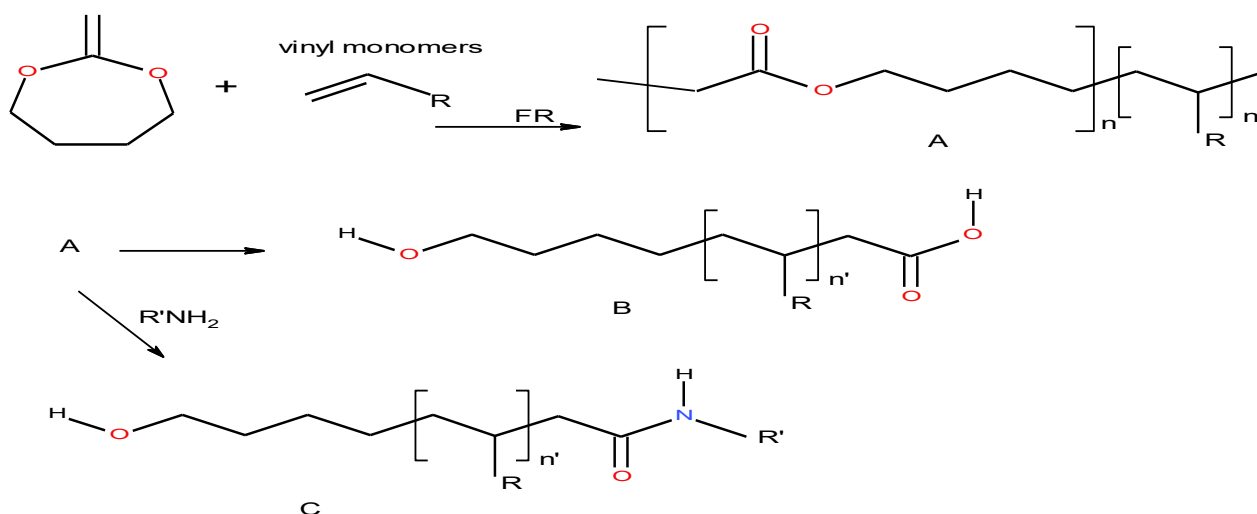
## Copolymerization

The idea of post polymerization reactions to synthesize derivatives can be further pursued in copolymerization with NVP so that these compounds can now contain several NVP units.



Scheme 9: Illustrating copolymerization with two NVP's but more can be added.

With several pyrrolidones in the surfactant head group, said surfactants could have very interesting properties such as the ability to complex compounds similar to PVP. This may depend on how many pyrrolidones are in the resulting head group. Surfactant versions of PVP-Iodine or hydrogen peroxide with low surface tension would be very valuable. This idea can be viewed generally. For example:



Scheme 10: An example of a general use of vinyl monomers to prepare hydrolyzed derivatives.

For example, vinyl acetate would result in a polymer in which the acetate can be hydrolyzed along with the polyesters to eventually synthesize surfactants with several hydroxyl groups in the head group. Obviously, a wide variety of monomer and monomer types can be copolymerized depending on the planned end use of the degraded(hydrolyzed) copolymer.

Thank you for reading these proposals. I would appreciate comments or suggestions.

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