PVP Derivatives

By: Robert B. Login rloginconsulting.com

Polyvinylpyrrolidone-co-Pyrrolidine:

Polylactam containing polymers especially PVP and PVCL and their copolymers can be treated with a reducing agent such as LiAlH4 or NaBH4 or H2/catalyst or their derivatives, to convert some of the lactams to tertiary cyclic amines (USP 7,956,131 claims that NaBH4 reacts with PVP to afford the hydroxy alkylamine instead of the pyrrolidine).

(57) **ABSTRACT**

Lactam polymers has been modified with sodium borohydride ($NaBH_4$) to yield lactam polymers bearing hydroxyl functional groups. These functional groups are useful for the covalent attachment of reactive groups, fluorescent probes, antimicrobial agents, bioactive factors, and drugs. The resulting as components for medical devices, specifically ophthalmic devices and more specifically contact lenses. Hydrogels based on these polymers are also useful for biomedical applications in the areas of drug delivery, tissue engineering, and implantable devices.

This patent requires that the reduction proceeds to the hydroxy alkyl amine. It mentions the pyrrolidine derivative in passing and it is not claimed. I also suggest that the key to the pyrrolidine derivative may not be NaBH4 as it is too basic a reducing agent that hydrolyses the lactam to the carboxylate and then to the alcohol.

Subsequent reaction of the pyrrolidine tertiary amine with alkylating agents especially epichlorohydrin converts said polymers to cross-linked polyquat gels.

Then the problem is to work out a synthesis of pyrrolidine containing PVP.

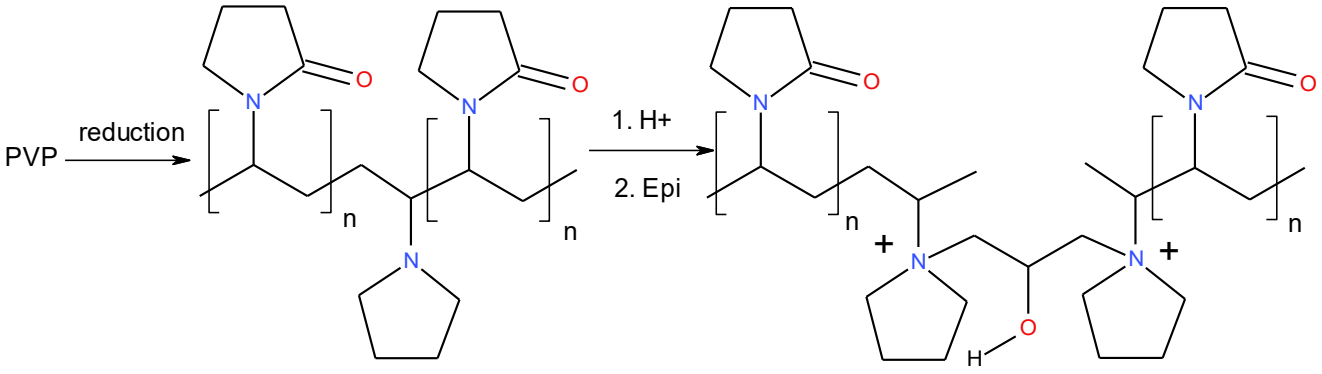


Chart 1: Partial reduction affords tertiary amines which are then half neutralized with HCl and cross-linked with epichlorohydrin.

Other cross-linkers such as dihalogen derivatives could also be used. The point is that cross-linked cationic hydrogels can be conceived of by this chemistry. Obviously mono-quats with say benzyl chloride etc. are also possible. This could afford an inexpensive route to polymeric antimicrobials, drug delivery, tissue engineering and hair conditioners, for example.

Obviously NVP could be copolymerized with tertiary amine containing monomers such as DMAEMA and cross-linked (USP 5,236,993) and this might be the simpler way; however, PVP is readily available to everyone and doesn't require preparation of a copolymer, it can simply be dissolved in a suitable solvent and treated with a reducing agent and then in the same reactor, quaternized.

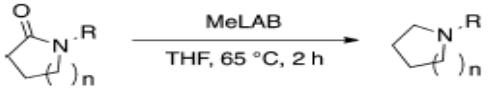
Suggested Reducing Agents:

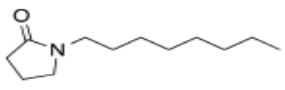
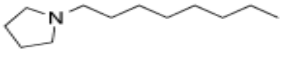
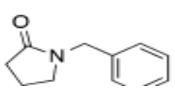
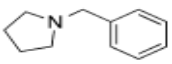
Controlled Reduction of Tertiary Amides to the Corresponding Alcohols, Aldehydes, or Amines Using Dialkylboranes and Aminoborohydride Reagents

J. Org. Chem. 2016, 81, 3619–3628

Christopher L. Bailey, Al
and Bakthan Singaram*

Table 4. Reduction of Lactams to Amines with Lithium Dimethylaminoborohydride[a]



Entry	Lactam	Amine	% Yield[b]
1			89
2			86

Reduction of Amides and Lactams to Amines by Reactions with Phosphorus Oxychloride and Sodium Borohydride[1]

M. E. Kuehne* and P. J. Shannon

J. Org. Chem., Vol. 42, No. 12, 1977

Issue in Honor of Prof. Alfred Hassner ARKIVOC 2001 (iv) 59-75

Aminoborohydrides. 13. facile reduction of *N*-alkyl lactams with 9-borabicyclo[3.3.1]nonane (9-BBN) and lithium aminoborohydrides (LAB) reagents

Christopher J. Collins† and Bakthan Singaram*

Aminoborohydrides. 11. Facile Reduction of *N*-Alkyl Lactams to the Corresponding Amines Using Lithium Aminoborohydrides

Org. Lett., Vol. 1, No. 5, 1999

John M. Flaniken, Christopher J. Collins, Marc Lanz, and Bakthan Singaram*

The only references to the reduction of PVP to secondary hydroxy alkylamines are several patents to J&J (above and also 7,473,738 and 2007/0299206 and probably others) but reduction to the tertiary amine are rare. The only one I found is JOC Vol. 24, 1404 (1959). Unusually, no one has cited this article! Therefore, this chemistry is practically unknown and has not been exploited? The J&J patents as mentioned, require the hydroxy alkylamine derivative. They are very complex and detailed patents that if you are interested in my proposal, will require close examination.

Cationic PVP hydrogels could have many valuable attributes such as; low toxicity, biocompatibility, minimum inflammatory reaction, soft and rubbery consistency. Uses include controlled delivery of biologically active agents, localized and sustained

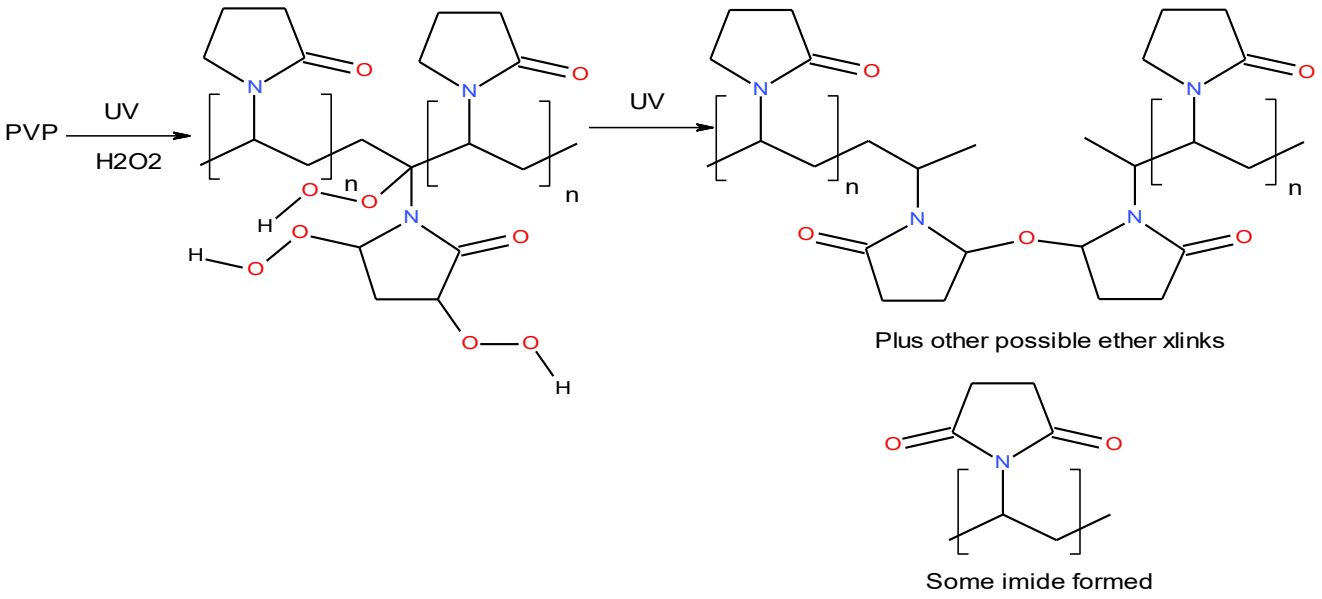
release of a drug, tissue engineering but most importantly hydrogels with these medical applications etc. (S. Budwalda et. al. Hydrogels in a historic perspective: From simple networks to smart materials, J. Controlled Release 190,(2014) 254-273).

Co- or Homopolymers of VcL can also be reduced like PVP and would also form valuable cationic hydrogels (K.M. Rao et. al., Stimuli Responsive Poly(Vinyl Caprolactam) Gels for Biomedical Applications, Gels 2016, 2,6; doi:10.3390/gels2010006.). Both of the above reviews are very informative.
Lets also consider VcL and PVP copolymers with each other and with other monomers. PolyVcL has a cloud point at body temperature which would add this characteristic to copolymers. It would afford the ability to collapse a gel after being placed in the body.

Thank you for reading this proposal. I would appreciate feedback.
Robert B. Login, rloginconsulting.com

Oxidation of PVP

Is PVP susceptible to oxidation? This could afford succinimide copolymers or upon subsequent hydrolysis primary amine derivatives; however, as an example, Zhu et. al. Polymer, V51,2010, 3054-3063 as the following chart shows, found oxidation to be more complicated. They use H2O2/UV:



Polymer V51,2010,3054-3063

The above shows all possible hydroperoxide attachment sites and an example of a resulting ether xlink.

Several additional references with similar reactions are available:

X. Zhu et. al. Polymer, V51, 2010, 3054-3063.

F. Hassouna et. al. Polymer Degradation and Stability, V94, 2009, 2257-2266.

H. Can, Radiation Physics and Chemistry, V72, 2005, 703-710.

MA. Tallon et. al., J. Appl. Polym. Sci., V107, 2007, 2776-2785.

Y. Wang & H. Wang, Radiation Physics and Chemistry, V78, 2009, 234-237.

L.Lopergolo et. al. Polymer, 44, 2003, 6217-6222.

G. Fechine et. al. Polymer, 47, 2006, 2629-2633.

J. Barros et. al., Polymer 47, 2006, 8414-8419....Fenton reaction with PVP.

The above references use their oxidation reactions to xlink with the goal of preparing hydrogels. Apparently their methods to produce PVP hydrogels by oxidation are not strong enough to oxidize PVP to the imide as the major product. So the question is how do you oxidize PVP to the a polyvinylimide copolymer?

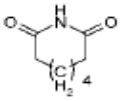
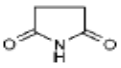
Searching the literature, I have found recent accounts of the reaction of lactams to imides in very high yields. Could these reactions based on Tempo and lacasse for example, react with PVP. (general ref. for Oxidation of Amides to Imides; Synthsis 2011(22): 3569-3580)

J. Org. Chem. **2002**, *67*, 2671−2676

Aerobic Oxidation of *N*-Alkylamides Catalyzed by *N*-Hydroxyphthalimide under Mild Conditions. Polar and Enthalpic Effects

Francesco Minisci,*,† Carlo Punta,† Francesco Recupero,† Francesca Fontana,‡ and Gian Franco Pedulli§

Table 1. Oxidation of Lactams or Acetamides of Cyclic Amines by O_2 in CH_3CN

Amide	T (°C)	t (h)	Conv. (%)	Products Selectivity (%)
	80	3	96	 (98)
	80	5	97	 (93)

Journal of Molecular Catalysis B: Enzymatic 50 (2008) 40–49

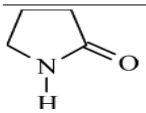
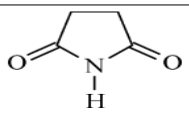
www.elsevier.com/l

Oxidation of amides by laccase-generated aminoxyl radicals

Alessandra Coniglio, Carlo Galli *, Patrizia Gentili *, Raffaella Vadalà

Dipartimento di Chimica, Università 'La Sapienza', and IMC-CNR Sezione Meccanismi di Reazione,

Table 1
Selected results of the oxidation of amides after Minisci et al. [14], by the HPI/$Co(AcO)_2$/MCBA/O_2 method in MeCN solution

Amide	*T* (°C)	*t* (h)	Product(s)	Yield (%)
	80	5		90

Metal-free aerobic oxidations mediated by *N*-hydroxyphthalimide. A concise review

Lucio Melone[1,2] and Carlo Punta*[1,2]

Beilstein J. Org. Chem. **2013**, *9*, 1296–1310.

Multi-stage Mass Spectrometry of Poly(vinyl pyrrolidone) and Its Vinyl Succinimide Copolymer Formed upon Exposure to Sodium Hypochlorite

Thierry Fouquet*, Masaki Torimura, and Hiroaki Sato*

Mass Spectrometry
DOI: 10.5702/massspectrometry.A0050

This last reference deals with the results of the reaction of sodium hypochlorite bleach with PVP. It is employed to clean membranes formed with PVP in that it removes it from interfering with the membranes application (see USP 2015/0343386 A1).

Looking back on the development of PVP-H2O2, I don't remember any concern over oxidation of PVP; however, the above references clearly illustrate the need for a energy source like UV etc. to rip off a proton from the PVP before any oxidation would take place. So no doubt that PVP is stable and simply complexes with H2O2 under mild conditions.

Applications:
The major reason in my estimation to oxidize PVP is to obtain amine copolymers. It should be possible to hydrolyze the pendant imides to the primary amines. If this turns out to be possible then how much primary amine would be required for possible applications? Some are listed below:

1. Cationic PVP for hair care and other cosmetic applications.
2. Reaction with acid containing drugs for drug delivery.
3. Cross linking through amine for coating medical devices.
4. Hydrogels through ccovalent cross linking by reaction with amines.
5. Hydrogels by cross linking with polyacids like polyacrylic acid.
6. Peptide derivatives by reaction with carboxy peptide end groups.
7. Attachment of metal ions to amines as ligands for catalyst, delivery, or removal.

I could go on and on but the real value is that PVP is safe and readily available. So

anyone could partially oxidize and hydrolyze and purify by ion exchange or precipitation etc. resulting in a relatively inexpensive primary amine copolymer. This would open up said copolymers to organizations with modest means because they would not have to deal with NVP and other monomers and their subsequent polymerization.

Thank you for reading this proposal and I would welcome feed-back.
Dr. Robert B. Login rloginconsulting.com

Thiolactam derivatives:

Several references illustrate the synthesis, and homo- and copolymerization of N-vinylthiopyrrolidone (NVTP). The claimed utility of polymers containing NVTP is as additives to motor lubricants as anti-ware antioxidants. After looking for additional information concerning other uses, none was found. This seemed rather peculiar to me as NVTP is easily prepared and readily polymerized. Surely other applications for this monomer are possible?

References:

3,519,565 and 3,666,730

OIL-SOLUBLE INTERPOLYMERS OF
N-VINYLTHIOPYRROLIDONES

L. Coleman

ABSTRACT OF THE DISCLOSURE

“N-vinylthiopyrrolidone, and its lower alkyl-substituted homologs, are interpolymerized with polymerizable alkyl (C8 or greater) carboxylates and \(optionally) other oxy gen-containing monomers to produce oil-soluble poly-

mers. These polymers are useful in lubricating oils as viscosity index improvers, dispersants and oxidation in hibitors."

COPOLYMERIZATION OF N-VINYLTHIOPYRROLIDONE WITH METHYLMETHACRYLATE AND N-VINYLPYRROLIDONE*†

S. N. Sividova, A. A. Avetisyan, G. S. Kolesnikov, F. P. Sidel'kovskaya and A. S. Tevlina

Mendeleyev Inst. of Chem. Technol., Moscow;
Org. Chem. Inst. U.S.S.R. Acad. of Sci.

* Vysokomol. soyed. 7: No. 12, 2164–2167, 1965.

This is but one of several Russian references that I have not been able to acquire; however, all of them are from the 1960's and I suspect that they were interested in these sulfur containing polymers because they could shield surfaces from radiation?

Coleman and Bork, J. Polymer Sci: Part A-1,Vol. 8, 2073-2078(1970).
They report that PVTP cannot be polymerized with peroxide initiators but only with AiBN types. This shows the antioxidant ability of PVTP or its copolymers.
They also found that the homopolymer was soluble in DMF but not in water or butanol suggesting that the thiolactam unlike the lactams of PVP is not polar enough to be soluble in polar solvents. Therefore to explain this, I have reviewed thiolactams chemistry with the goal of comparing them to the corresponding lactams.

The Dipole Moment and Structure of Thiolactams

CALVIN M. LEE AND W. D. KUMLER

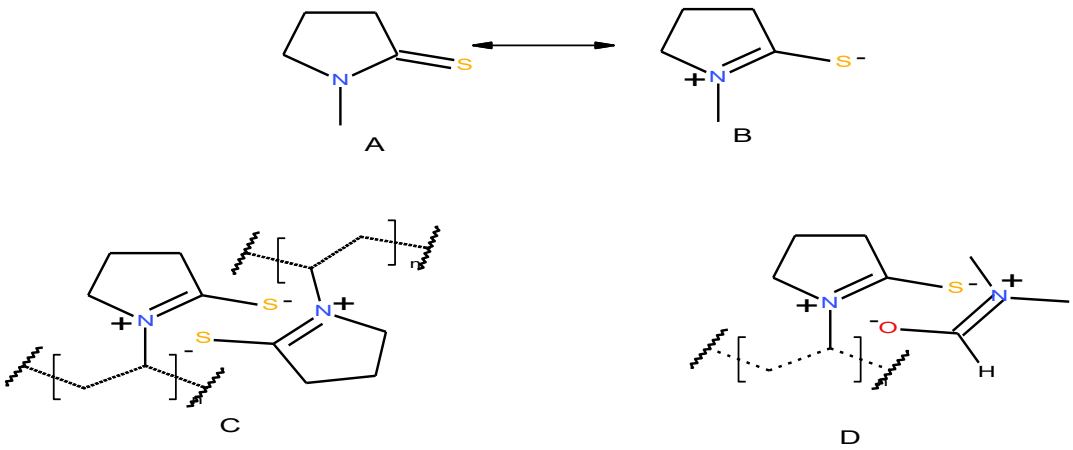
Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco Medical Center, San Francisco, Calif.

Received October 30, 1961

Measurement of the dipole moments of thiolactams in dioxane at 30° gives the following: thiopyrrolidone I, 5.07 D; thiopiperiodone II, 5.15 D, and thiocaprolactam III, 4.83 D. Comparison of the moments of I, II, and III with the moments of corresponding lactams shows that the thiolactams have dipole moments about 1.0–1.3 D. higher. This is due to the greater inherent polarization of the thiocarbonyl group which is also indicated by the lower infrared stretching frequency and the lower maxima and greater extinction in the ultraviolet. These data indicate that there is more of the ionic form $\overset{+}{C}—\overset{-}{X}$ (X = S or O) present in thiolactams than in lactams.

J. Org. Chem., **1962**, *27* (6), pp 2052–2054

The above article suggests the contrary to the solubility found by Coleman because of the higher dipole moment of thiolactams which should result in water solubility? Small monomeric thiolactams molecules are water soluble; for example, N-methylthiolactam (US 6,680,331 B2). So why is PVTL insoluble? The following chart illustrates my explanation:



Structure B, the charge separated isomer, is claimed by many references to be more inline with dipole moment measurements as indicated in the above mentioned patent which has several examples of water soluble monomeric thiolactams. Because PVTL is so highly charge, it forms ionic xlinks, only a few of these ionic xlinks are required to cause water insolubility. Solubility in DMF can be explained by disruption of those xlinks as illustrated with structure D. PVTL as can be imagined is insoluble in

several other solvents (JOURNAL OF POLYMER SCIENCE: PART A-1 VOL. 8, 2073-2078 (1970)) that you would think it would be soluble in if the insolubility in water was a result of its inherent hydrophobicity. Possibly, PVLT would be soluble in acidic solution because protonation of the sulfur would leave the polymer cationic which should now be water soluble as the ionic xlinked would be gone.

PVP is water soluble because the lactam oxygen is much more anionic than the sulfur in thiolactams and can coordinate water molecules whereas sulfur is charged but much bigger than oxygen and hence the negative charge is more diffuse and less able to coordinate water. NVTL can be readily copolymerized with a wide variety of hydrophobic comonomers. As the PVTL component is reduced, solubility is as expected in non-polar solvents.

Synthesis:
The Coleman patents employ phosphorus pentasulfide and NVP.

Expeditious Microwave-Assisted Thionation with the System $PSCl_3/H_2O/Et_3N$ under Solvent-Free Condition

J. Org. Chem. **2008**, *73*, 2890−2893
Uma Pathak,* Lokesh Kumar Pandey, and Rekha Tank

Synthetic Chemistry Division, Defence Research & Development Establishment, Gwalior- 474002, India

This reference not only shows NVTL but has a good review of the other reagents used to prepare thiolactams. A structure search(NVTL) in SciFinder produced very limited list of references and most were 1960's Russian. This is rather surprising for a polymerizable vinyl monomer.

Another possibility is to generate thiolactams by reacting PVP itself with selected thionation reagents. This would be an inexpensive method of generating random

copolymers especially if minor amounts of thiolactams are required.

Applications:
NVTL can be copolymerized with NVP to add antioxidant properties to PVP. Cationic PVP copolymers employed as hair conditioners with NVTL could prevent hair damage especially on frequently dyed hair. NVTL because thiolactams absorb UV, might also add sunscreen ability to PVP copolymers. NVTL could be grafted onto various surfaces to afford antioxidant protection. PVTL copolymers might prevent radiation from harming space craft or grafted on textiles to do the same job. Sulfur containing polymers also exhibit valuable unique optical properties.

Obviously, if NVLT adds an unpleasent odor to its polymers then this might have been the reason that its use was confined to lubricants. If this is not the case then potential new and valuable applications might be possible!

Thanks for reading this proposal.
Dr. Robert B. Login rloginconsulting.com

Polymeric Raft/MADIX Grafted initiators

The RAFT/MADIX literature is massive; however, after exhausting myself, I have not found one reference with the idea that follows. If you the reader know of a reference then please let me know.

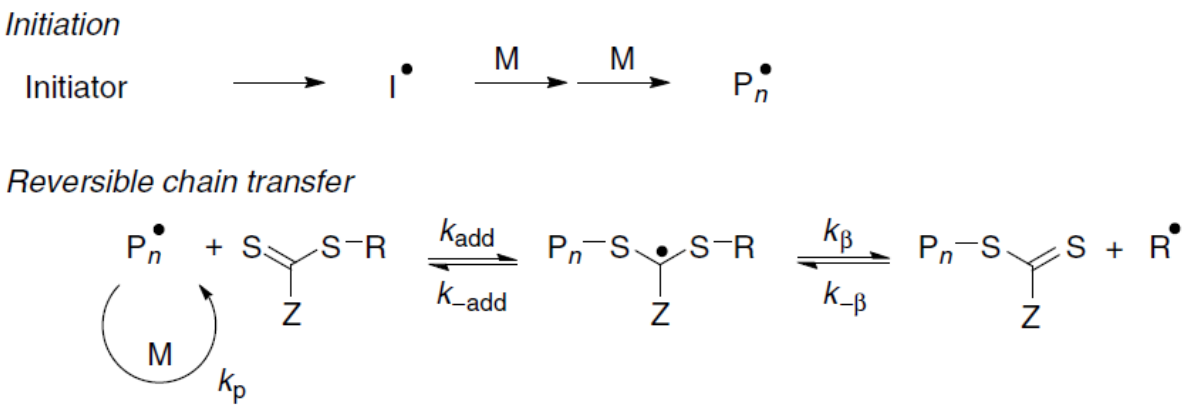
General reference:

Aust. J. Chem. **2012**, *65*, 985–1076
http://dx.doi.org/10.1071/CH12295

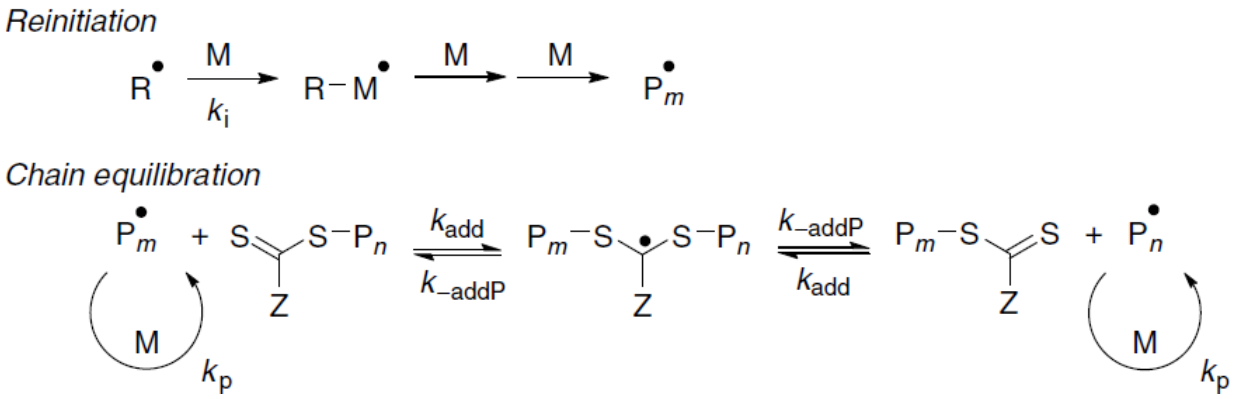
Living Radical Polymerization by the RAFT Process — A Third Update

Graeme Moad,[A,B] *Ezio Rizzardo,*[A] *and San H. Thang*[A]

RAFT/MADIX mechanism: (*reversible addition-fragmentation chain transfer) (macromolecular design via the interchange of xanthates)*



The above accepted mechanism explains initial stages of this RAFT CRP (controlled radical polymerization). It takes a small amount of added initiator to get the polymerization started. In fact in many cases there might be a significant inhibition period before the main polymerization reaction starts. This could be caused by the addition of Pn to the RAFT agent and the subsequent slow release of the R radical. The R radical must be able to add to a monomer to re-initiate and continue the polymerization.

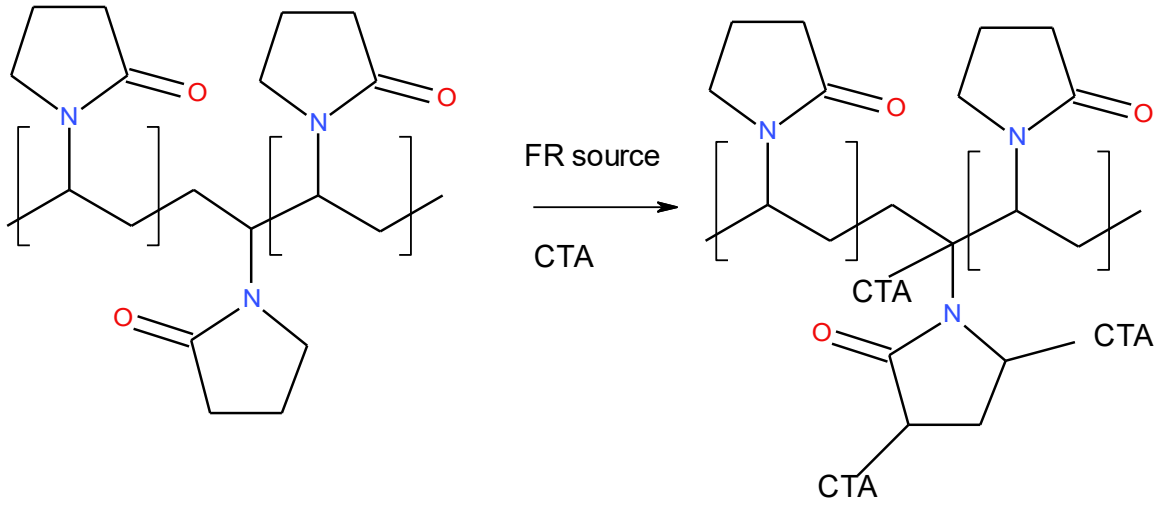


From the above, once Pm and Pn form, each can be captured by the RAFT CTA (chain transfer agent) and controlled radical polymerization can begin. After a short interval, both Pm and Pn are essentially the same. MW is determined by the amount of CTA employed. Because the growing polymer chains are quickly, reversibly captured by the CTA, side reactions are very limited and therefore the polydispersity is very low compared to conventional FR polymerization.

Besides CRP, there is a significant literature concerning the use of RAFT in organic synthesis. For example B. Quiclet-Sire and S. Z. Zard, Pure Appl. Chem., Vol. 83, No. 3, pp. 519-551, 2011 reviews numerous reactions. Their key point is that R. initially generated from the RAFT CTA must be more stable than the new radical that it generates. This is because the CTA would not fragment to form R. if it was not stable enough.

My proposal claims that selected RAFT/MADIX CTA's can react with radicals formed on pre-existing polymers. Assuming that in addition to the initiator, the R. radical is capable of abstracting a proton from a polymer resulting in the attachment of the CTA to said polymer. Lets take PVP, PCVL or other lactam polymers as examples. The patent literature shows that PVP can be cross- linked by heating an aqueous solution with a

free radical source such as persulfates (USP 2,658,045; Schildnecht/GAF 1953), redox N2H4/H2O2 (USP3,294,729; Hort & Grosser/GAF,1966), and water insoluble peroxides (USP4,330,451 and 4,33,112; Staub et. al./BASF,1982 & 1984). The BASF patents even demonstrate that PVP macro radicals will react with NVP to form more heavily xlinked polymers when the treatment (xlinking) is conducted also in the presence of the NVP monomer. This would be an example of "grafting from".



Possible CTA attachments
depending on which is the most stable

Polymer grafting and cross- linking / edited by Amit Bhattacharya, James W. Rawlins, and Paramita Ray, Wiley, 2009. This reference reviews "grafting from" but not my proposal. It however is a very good review as of 2009.

There are a large number of references concerning cross-linking of PVP with radiation to form hydrogels. Several reviews are as follows:

Review

Radiation-induced synthesis of nanogels based on poly(N-vinyl-2-pyrrolidone)—A review

Slawomir Kadlubowski *

Radiation Physics and Chemistry 102 (2014) 29–39

CHEMISTRY & CHEMICAL TECHNOLOGY

Vol. 4, No. 4, 2010 Chemistry

Iwona Gibas and Helena Janik

REVIEW: SYNTHETIC POLYMER HYDROGELS FOR BIOMEDICAL APPLICATIONS

When I was working in R&D, I thought that PVP was branched, and the following patent is an example of that.

United States Patent [19]

Login et al.

[11] **Patent Number: 5,262,171**

[45] **Date of Patent: Nov. 16, 1993**

[54] **PHARMACEUTICAL TABLET WITH PVP HAVING ENHANCED DRUG DISSOLUTION RATE**

[75] Inventors: **Robert B. Login**, Oakland, N.J.; **Mohammed Tazi**, Marietta, Ga.; **Jui-Chang Chuang**, Wayne, N.J.; **Rama K. Haldar**, Randolph, N.J.; **Dinesh Jaiswal**, Butler, N.J.; **Chi-San Wu**, Wayne, N.J.

[73] Assignee: **ISP Investments Inc.**, Wilmington, Del.

[21] Appl. No.: **796,999**

[22] Filed: **Nov. 25, 1991**

[51] **Int. Cl.**[5] **A61K 9/20**; A61K 47/32; C08F 126/10; C08F 4/34

[52] **U.S. Cl.** **424/465**; 514/772.5; 514/960; 424/485; 526/264; 526/93; 526/94; 526/218.1; 526/219.6; 526/227; 526/915; 526/936; 526/230.5

[58] **Field of Search** 424/78.24, 78.32, 78.35, 424/465, 485; 514/772.5, 960; 526/93, 94, 263, 915, 936, 216, 219, 219.1, 219.5, 219.6, 227, 230.5, 264

[56] **References Cited**

5,008,106 4/1991 Merianos et al. 424/466
5,073,614 12/1991 Shih et al. 526/258
5,082,910 1/1992 Tazi 526/227

Primary Examiner—Edward Webman
Attorney, Agent, or Firm—Walter Katz; Marilyn J. Maue; Joshua J. Ward

[57] **ABSTRACT**

A pharmaceutical tablet is provided herein having an effective dissolution rate. The tablet contains a pharmaceutically-active ingredient and a substantially linear, i.e. non-crosslinked K-30 to K-120 PVP as a binding agent. The PVP used herein is made by an initiated polymerization process in which vinyl pyrrolidone monomer is polymerized in the presence of an initiator which produces a linear PVP polymerization, i.e. is a poor hydrogen abstractor of PVP polymer backbones, which would produce a disadvantageous crosslinked PVP product. Suitable initiators include low energy peroxyester free radical initiators, such as t-amylperoxy pivalate, an azo initiator, or a redox initiator which can perform at low temperatures.

Preferably the residual initiator level in the PVP is reduced to less than 500 ppm, thereby further precluding the possibility of crosslinking of the PVP polymer during the shelf-life of the tablet.

Many articles have appeared, concerned with backbiting where a terminal radical abstracts a proton from the polymer chain, for example PolyVAc is a well known example, led me to believe this occurred with PVP. Well the patents I listed above clearly show a FR mechanism for PVP cross- linking. Where exactly is a proton removed is not mentioned but the above chart indicates three possibilities. My bet is its on the third ring carbon resonance stabilized by the carbonyl. The point is that free

radical sites can readily form on PVP, PVPVAC copolymer and PVcl and combinations as long as a suitable FR source is employed.

Grafting from PVP:
I would conduct the reaction by adding an amount of RAFT CTA to a solution of PVP, the MW of which I don't think matters but I would start with K-30. I would purge the dissolved oxygen with pure nitrogen and heat to 50-100C (depending on the initiator) with stirring to which I would then add a FR initiator or radiation source known to gel PVP such as ammonium persulfate or the Fenton reaction. Obviously one would have to experiment with conditions and all the reagents as to type and level to perfect this reaction. The PVP radical would then be equivalent to the Pn radical that would then be trapped by the CTA. The ratio of initiator to PVP would determine the number of CTA's that could attach to PVP. The R radical could be designed to undergo nonproductive side reactions or abstract a proton resulting in more FR sites, and the resulting PVP-CTA could undergo purification. The resulting PVP-CTA would then be ready for reaction with FR polymerizable monomers.

Alternatively, design of the CTA is most important as I believe the level of added FR initiator could conceivably be reduced if the CTA's R group is very capable of abstracting protons from the PVP polymer itself. Once you have a PVP/CTA macromolecular initiator which could be purified by precipitation, extraction, column chromatography etc., it can then be employed in subsequent polymerizations. This would be an example of "grafting from" because you could add other monomers to form brush like copolymers. Because PVP is soluble in a variety of solvents that would allow quite a variety of monomers to be copolymerized. In fact multiple block terpolymers could be made available, and the whole gamut of RAFT/MADIX

technology would be possible. Several methods are known that will remove the CTA if required at the end of the polymerization. The advantage of preparing “bottle brush” polymers by RAFT/MADIX is the uniformity of the polymer brushes, a key factor in their utility.

Another possibility would be to start from insoluble PPVP and add further PVP chains on its surface to improve its ability to complex. In fact PPVP-CTA could be used to graft from a variety of monomers for unique applications.

In conclusion, a similar set of reactions might be applicable to other polymers and copolymers where “grafting from” would lead to an enormous variety of new materials.

Grafting From References:

(12) **Patent Application Publication**
Wang et al.

(10) **Pub. No.: US 2016/0024234 A1**
(43) **Pub. Date: Jan. 28, 2016**

(54) **NOVEL RAFT AGENTS AND THEIR USE IN THE DEVELOPMENT OF POLYVINYLPYRROLIDONE GRAFTED NANOPARTICLES**

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(57) **ABSTRACT**

Nanoparticles having a plurality of PVP chains covalently bonded to a surface of the nanoparticle are provided, along with their methods of formation and the RAFT agents for the polymerization of the PVP chains. RAFT agents are generally provided, along with their methods of formation and use. Methods are also generally provided for grafting a PVP polymer onto a nanoparticle. In one embodiment, the method includes: polymerizing a plurality of monomers in the presence of a RAFT agent to form a polymeric chain covalently bonded to the nanoparticle.

Macromolecules 2012, 45, 9303–9311

Grafting Bimodal Polymer Brushes on Nanoparticles Using Controlled Radical Polymerization | *Macromolecules* 2012, 45, 9303–9311

Atri Rungta,[†] Bharath Natarajan,[‡] Tony Neely,[†] Douglas Dukes,[‡] Linda S. Schadler,[‡] and Brian C. Benicewicz[†,*]

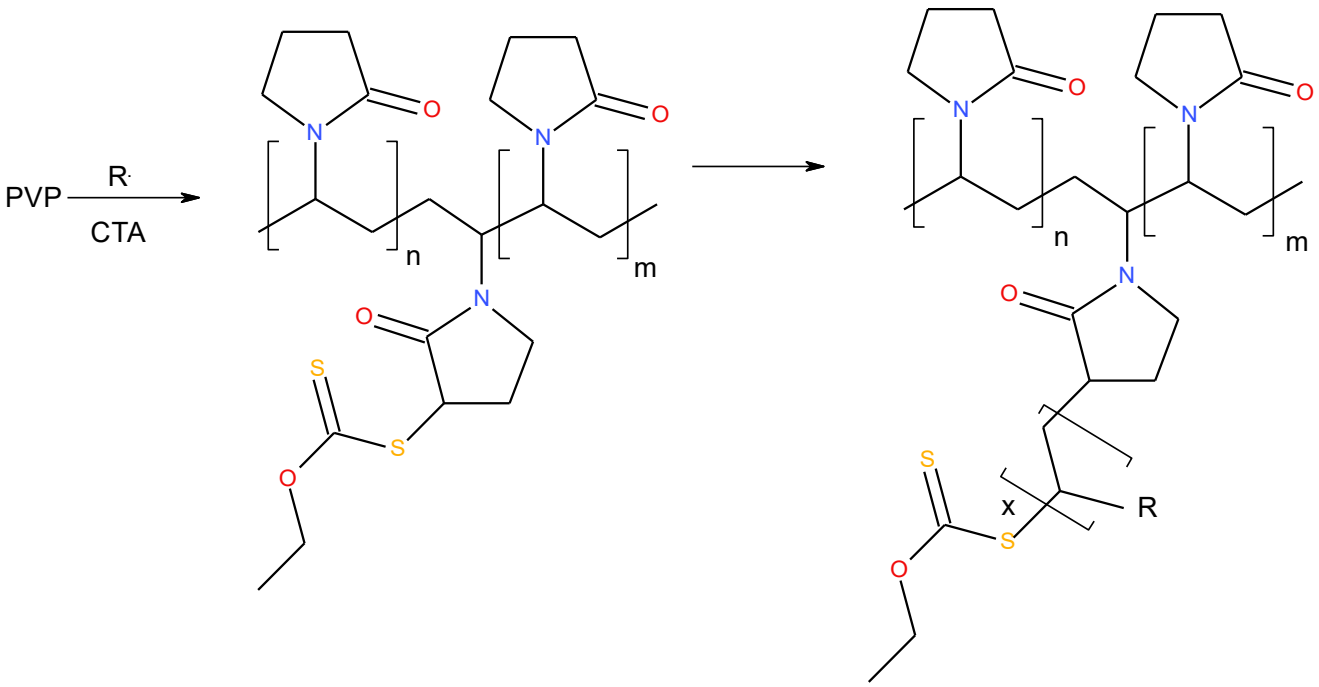
Controlled synthesis and association behavior of graft Pluronic in aqueous solutions

Y. Zhang, Y.M. Lam *

' *Journal of Colloid and Interface Science 306 (2007) 398–404*

There are many references to grafting NVP onto solid surfaces which are related to grafting from dissolved polymers but are not directly applicable to this proposal.

The following chart summarizes one example of my proposal:



Other polymers that are susceptible to formation of a radical on the backbone or a pendant group such as PVAc eta. should also be considered.

The advantage of employing a “grafting from” polymers is it would introduce another control over architecture. Should this idea work with a variety of polymers such as PVAc or acrylamides, polyethers, esters, amides etc. polymer manufacturers would avoid preparing the grafting from polymer and could convert inexpensive commodity polymers into copolymer specialties. For example look at this reference;
S. Strandman and X.X. Zhu, Progress in Polymer Science, 42,(2015), 154-176, a recent review highlighting current thinking concerning block copolymers and their applications.

Another application for this idea is to prepare tailor made copolymers that could be radiation cured to hydrogels with unique attributes for biological/medical applications.

Thank you for reading this proposal. I would welcome your feed-back.
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