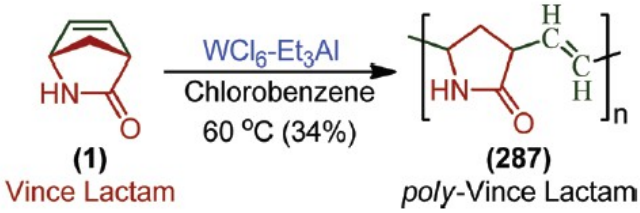
# "Vince Lactam" ROMP

by: Robert B. Login  rloginconsulting.com

While reading the interesting Chem. Rev. article by Prof. R. Vince, I found the brief mention of the use of ROMP to prepare a polymer, for example:

**Scheme 43. Transition Metal-Catalyzed Ring-Opening Metathesis Polymerization (ROMP) of Vince Lactam**



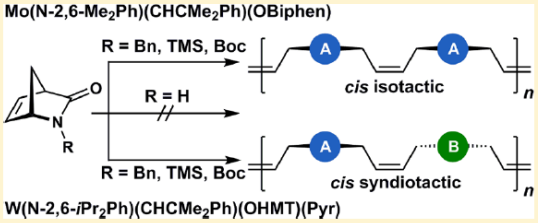

Singh, R., & Vince, R. (2012). 2-Azabicyclo [2.2. 1] hept-5-en-3-one: chemical profile of a versatile synthetic building block and its impact on the development of therapeutics. *Chemical reviews*, *112*(8), 4642-4686.

Obviously seeing the pyrrolidone ring got my attention because I think the resulting pyrrolidone polymer would be of value. I wrote a pdf' describing various synthetic routes and subsequent uses for such backbone polymers as compared to PVP.

http://rloginconsulting.com/joomla/images/SiteFiles/Patents/pyrrolidone%20backbone%20polymers.pdf

I searched for additional references to this ROMP and found a more recent account.

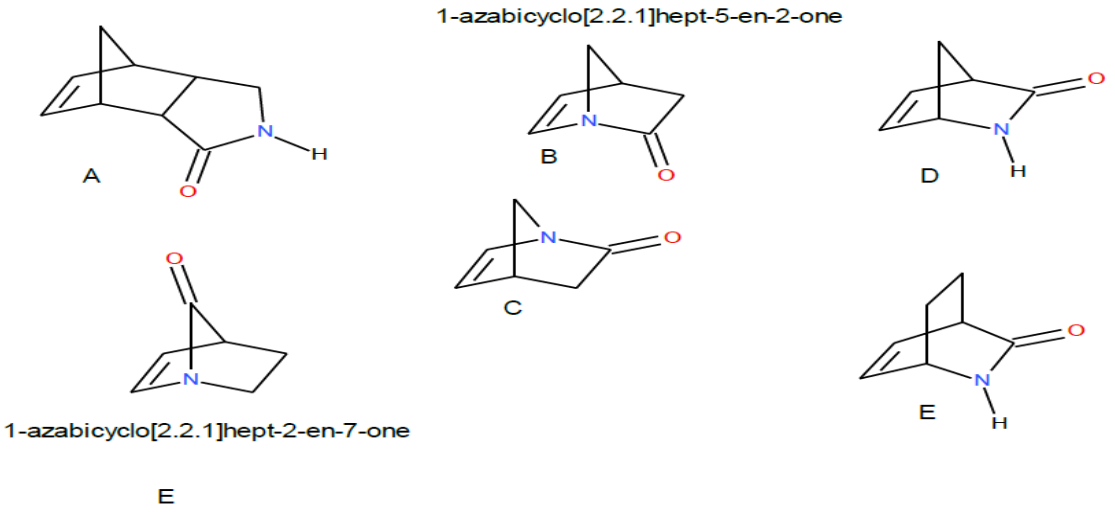
**ABSTRACT:** The ring-opening metathesis polymerization (ROMP) of (+)-Vince lactam [(*S*)-azabicyclo[2.2.1]hept-5-en-3-one] (**1**) and its *N*-benzyl, *N*-trimethylsilyl (TMS), and *N*-*tert*-butoxycarbonyl (Boc) derivatives (**2a**–**c**) is reported. Highly *cis-syndiotactic* (*st*) poly(Vince lactam) was readily accessible by using the cyclometalated ruthenium complex Ru[CH(2-OiPr-Ph)](Piv)(1-mesityl-3-$C_4H_8$-imidazol-2-ylidene) (Piv =2,2-dimethylpropanoate) (**4**); however, small amounts of *trans* double bonds (ca. 5%) formed. Highly *cis-st* (>98%) polymers were accessible by the action of the monoaryloxide pyrrolide (MAP) type complexes W(N-2,6-$i$Pr$_2$C$_6$H$_3$)(CHCMe$_2$Ph)(Pyr)(HMTO) (Pyr = pyrrolide, HMTO = 2,6-(2,4,6-Me$_3$C$_6$H$_2$)$_2$C$_6$H$_3$O) (**7**) and W(O)(CHCMe$_2$Ph)(PMe$_2$Ph)(Me$_2$Pyr)(TPPO) (TPPO = 2,3,5,6-tetraphenylphenolate) (**8**). Complementary, *cis*-isotactic (>98% *cis-it*) polymers were prepared by the action of Mo(N-2,6-Me$_2$C$_6$H$_3$)(CHCMe$_2$Ph)(OBiphen) (OBiphen = 3,3′-di-*tert*-butyl-5,5′,6,6′-tetramethyl-1,1′-biphenyl-2,2′-diolate) (**5**) and its tungsten analogue W(N-2,6-Me$_2$C$_6$H$_3$)(CHCMe$_2$Ph)-(OBiphen) (**6**). Notably, none of these Mo- and W-based initiators polymerize unprotected Vince lactam. Deprotection of poly(*N*-TMS Vince lactam) and poly(*N*-Boc Vince lactam) with neat trifluoroacetic acid allowed for the isolation of *all-cis* highly tactic poly(Vince lactam).




**Properties of Poly(Vince lactam).** One dominant and somewhat inconvenient property of all poly(Vince lactam) samples is their insolubilities in essentially all solvents short of organic acids. This was found for all polymers independent of tacticity. The hydrogenation of deprotected poly(Vince lactam)

Benedikter, M. J., Frater, G., & Buchmeiser, M. R. (2018). Regio-and Stereoselective Ring-Opening Metathesis Polymerization of Enantiomerically Pure Vince Lactam. *Macromolecules*, *51*(6), 2276-2282.

After reading the above excellent reference, I was of course interested in other ways of synthesizing pyrrolidone backbone polymers, but could the Vince lactam have related structures that would also polymerize by ROMP? I thought that unsaturated bicyclic lactams isomeric to the Vince lactam could work?




Scheme 1: "A" I believe I already suggested in one of my previous pdf's. "B&C" are mirror images and seem like I should have found references using them for ROMP! So the same for "E and F(not E) and D is Vince Lactam. Why could I not find references to their ROMP? Obviously many other structures could have been suggested with longer carbon chain bridges.

These are all bridge lactams which were reviewed by Szostak, M., & Aube, J. (2013). Chemistry of bridged lactams and related heterocycles. *Chemical reviews*,*113*(8), 5701-5765. Although this is a detailed review, it didn't illustrate any of the above proposed examples. However, it did suggest that many similar bridged lactams are very easily hydrolyzed or very unstable. This is even without the complication of unsaturation. So at this point I'm thinking that these compounds are either to unstable to synthesize or if synthesized are too unstable and don't last very long. They are refered to as twisted amides because of this twisting they are not resonant with the carbonyl making them very unstable and reactive.

Also:

Szostak, R., & Szostak, M. (2019). Chemistry of bridged lactams: Recent developments. *Molecules*, *24*(2), 274.

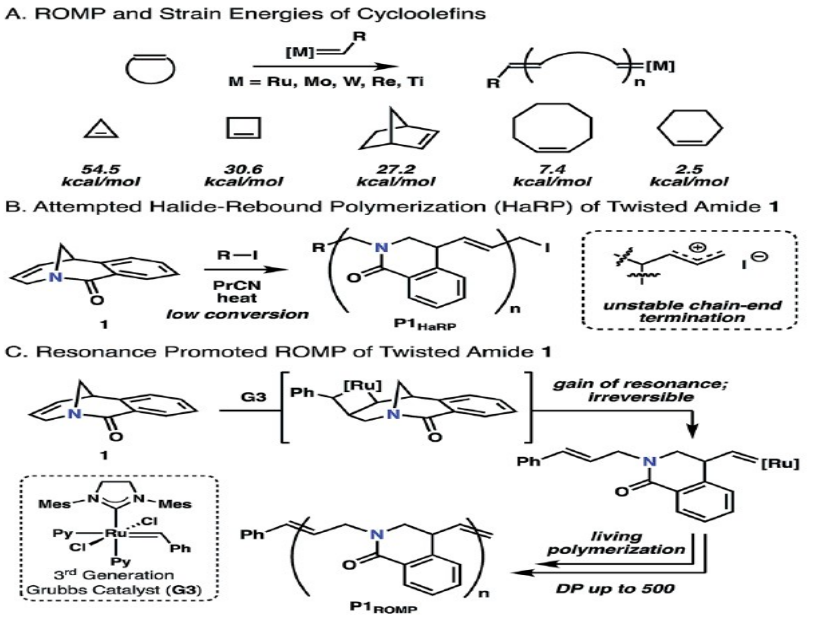



Fig. 1 (A) Typical ROMP and cycloolefin monomers. (B) Halide-rebound polymerization of twisted amide 1. (C) Resonance promoted ROMP of 1.

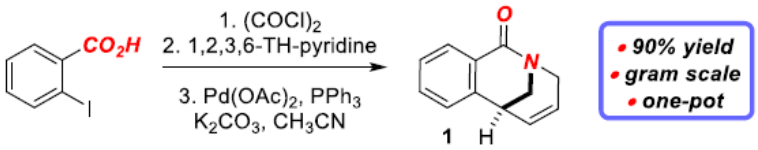
Abstract of the above reference:

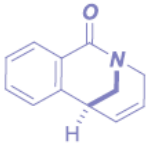
The living ring-opening metathesis polymerization (ROMP) of an unsaturated twisted amide using the third-generation Grubbs initiator is described. Unlike prior examples of ROMP monomers that rely on angular or steric strain for propagation, this system is driven by resonance destabilization of the amide that arises from geometric constraints of the bicyclic framework. Upon ring-opening, the amide can rotate and rehybridize to give a stabilized and planar conjugated system that promotes living propagation. The absence of other strain elements in the twisted amide is supported by the inability of a carbon analogue of the monomer to polymerize and computational studies that find resonance destabilization accounts for 11.3 kcal $mol^{-1}$ of the overall 12.0 kcal $mol^{-1}$ ring strain. The twisted amide polymerization is capable of preparing high molecular weight polymers rapidly at room temperature, and post-polymerization modification combined with 2D NMR spectroscopy confirms a regioirregular polymer microstructure.

Xu, M., Bullard, K. K., Nicely, A. M., & Gutekunst, W. R. (2019). Resonance promoted ring-opening metathesis polymerization of twisted amides. *Chemical science*, *10*(42), 9729-9734.

Although not an example from my scheme 1, compound 1 above has all the essentials but is a 3:3:1 bicyclic with a benzene ring. Are these critical factors? Can you use a 2:2:1 analog or a 3:2:1 type? Is benzene critical? I must say that these clever workers might already be exploring these questions? A similar reference to this type of chemistry also appeared.

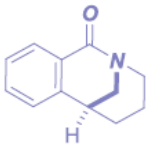
**Scheme 1. Facile Synthesis of Twisted Amide 1**[a]




**1**

*14.2 kcal/mol*




**7**

*13.7 kcal/mol*

**ABSTRACT:** Selective C=C bond cleavage in twisted amides by ring-opening olefin metathesis (ROM) has been accomplished. The reaction represents the third mechanism for ring opening of non-planar amide bonds discovered to date. Adding to the facile hydrolytic cleavage of non-planar N–C(O) amide bonds and σ N–C bond scission reactions, this reaction manifold engages a peripheral reactivity principle that hinges upon ring strain energy enforced by the twisted amide bond. Considering the wide utility of ring-opening olefin metathesis reactions in various aspects of chemistry, we anticipate that this ring opening methodology will be of broad interest and could lead to the development of ROM reactions of twisted amides as a powerful synthetic tool.

**KEYWORDS:** *twisted amides, olefin metathesis, amide bonds, ring opening, ring-opening metathesis, ROMP*

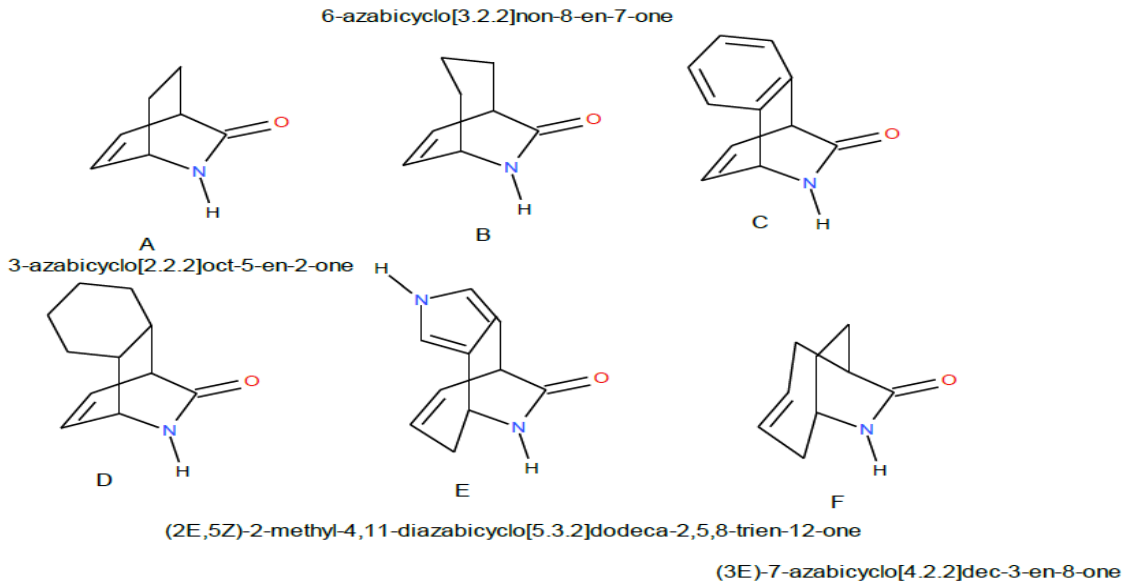
Zhao, Q., Lalancette, R., Szostak, R., & Szostak, M. (2019). Ring-Opening Olefin Metathesis of Twisted Amides: Activation of Amide Bonds by C═ C Cleavage. *ACS Catalysis*, *10*(1), 737-742.

Polymeric pyrrolidone backbone polymers, if they could be prepared by ROMP from scheme 1 or similar monomers, would be very interesting polymers.

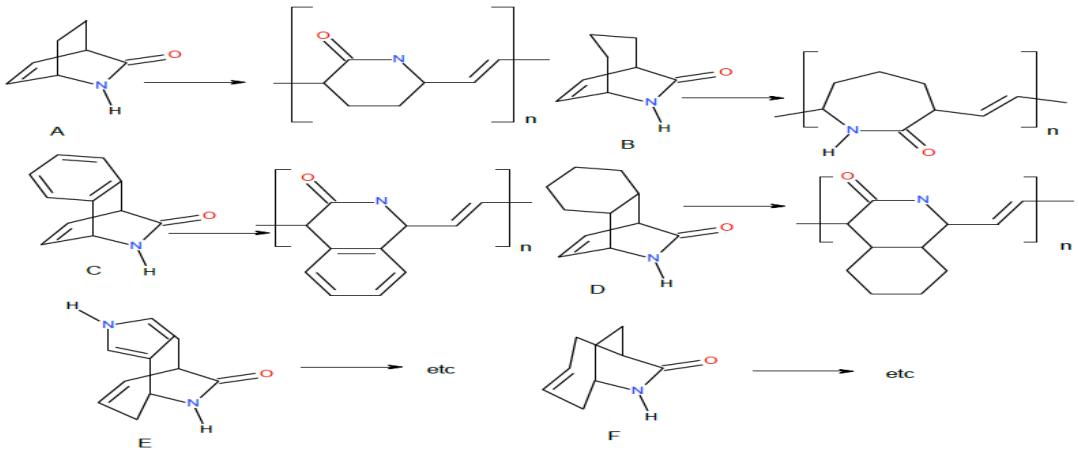
## Vince Lactam Isomers or related structures:

Since the bridge-head nitrogen types are not in the literature as stable compounds, I

thought why not just build on F in scheme 1! Several non-bridgeheads can be proposed:




Scheme 2: Several possible Vince Lactam types. The idea is that this type of related lactam should be ROMP polymerizable. They should produce six or larger membered lactam copolymers. I could conceive of many other structures but I think the above make my point.



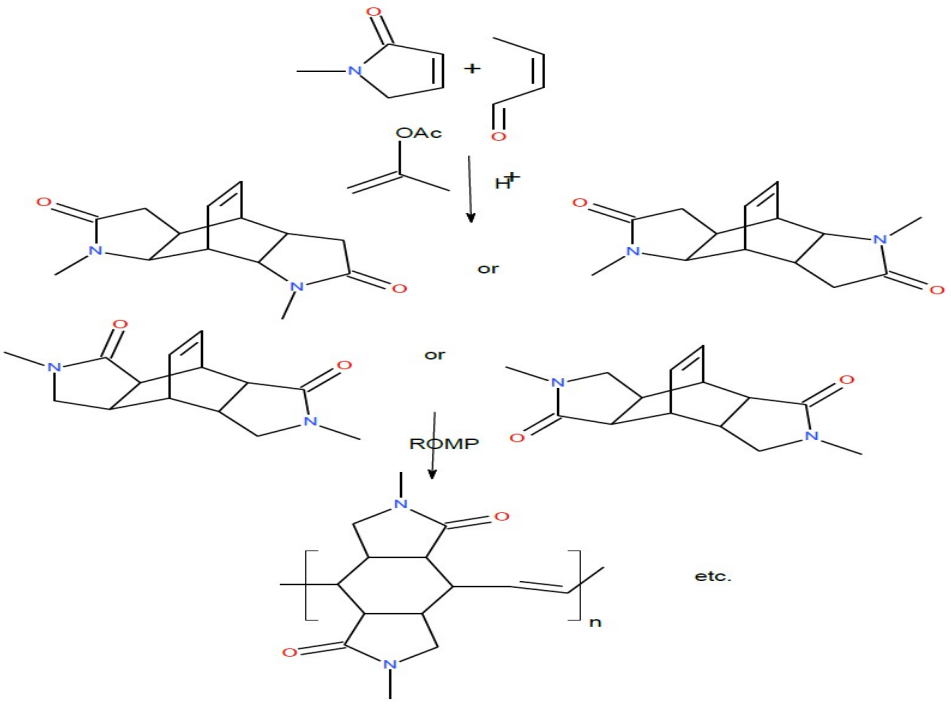

Scheme 3: Examples of the polymers.

Malpass, J. R., Belkacemi, D., Griffith, G. A., & Robertson, M. D. (2002). Cycloaddition of phenyl azide to

unsymmetrical azabicyclic alkenes. *Arkivoc*, *6*, 164-174.

Khan, M. F., Levi, M. S., Clark, C. R., Ablordeppey, S. Y., Law, S. J., Wilson, N. H., & Borne, R. F. (2008). Isoquinuclidines: A review of chemical and pharmacological properties. *Studies in natural products chemistry*, *34*, 753-787.

I looked with Sci-Finder for more related structures but it revealed only a few related structures, mostly similar to the above. This area of bicyclics seems to be of little interest?




Scheme 3: Instead of maleic anhydride that I used in the cited paper, the above dienophile might do a reaction similar to one I did for my thesis. I'm suggesting a similar reaction can be performed as above.

I suggest all four possibilities because I cannot predict which are possible.

Wolinsky, J., & Login, R. B. (1972). Novel route to bicyclo [2.2. 2] octenetetracarboxylic acid dianhydrides. *The Journal of Organic Chemistry*, *37*(1), 121-125.

Thank you for your interest!

Dr. Robert B. Login rloginconsulting.com