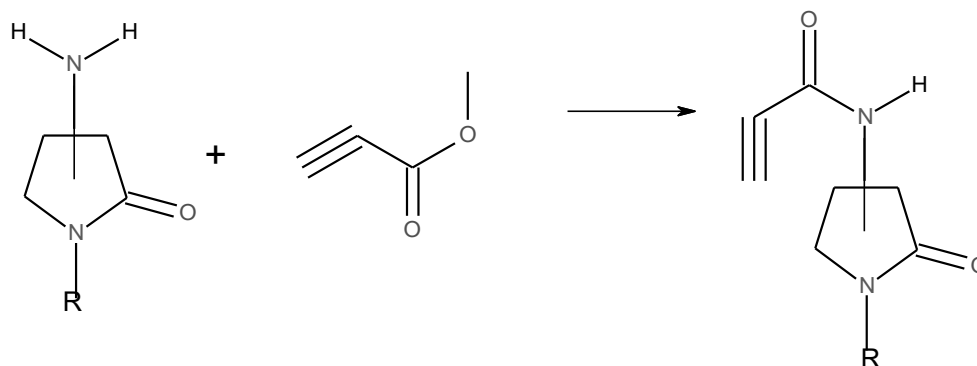
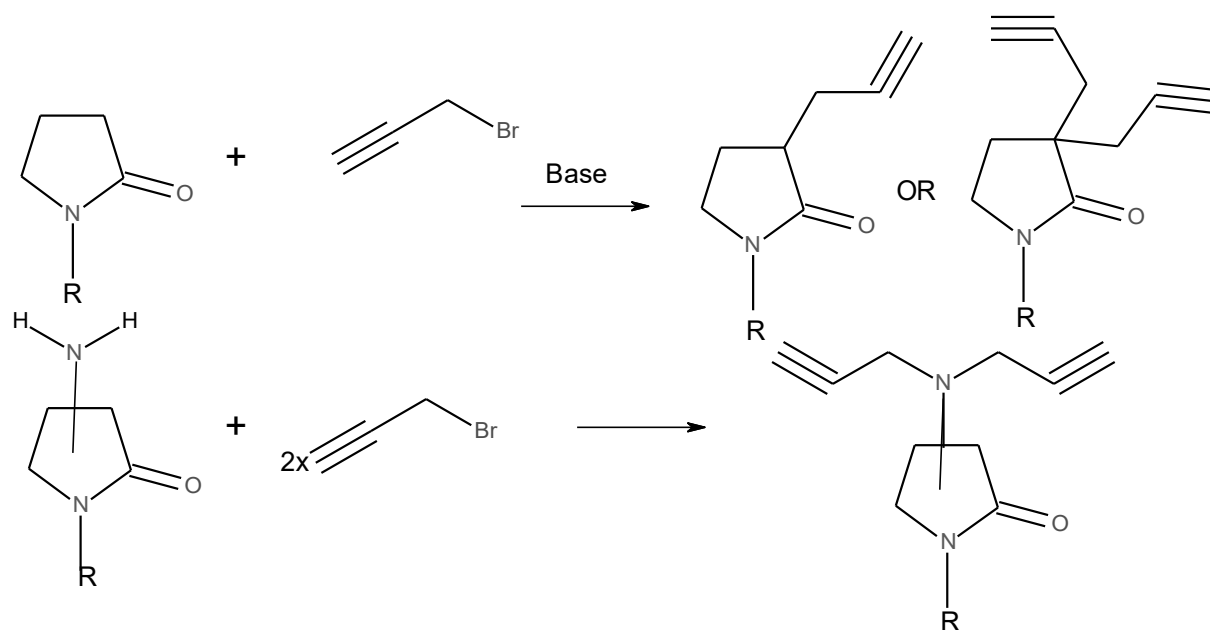
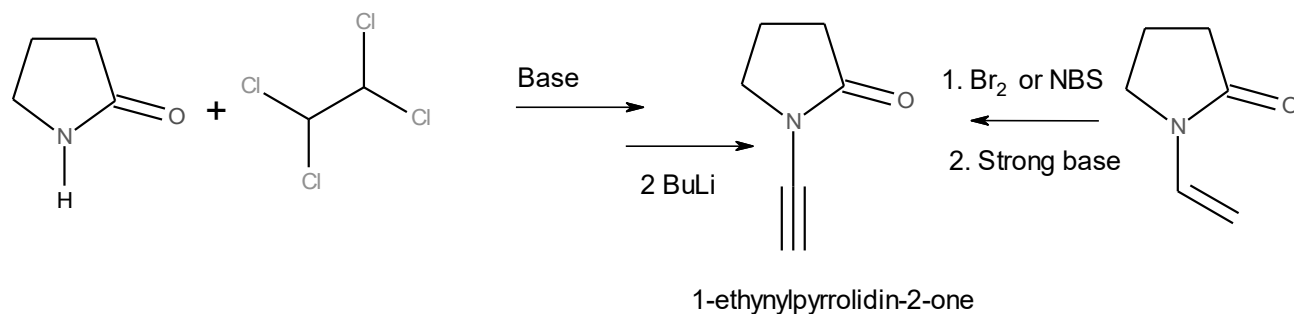


The Chemistry of Acetylenic Derivatives of Pyrrolidone

by: Robert B Login

The most obvious pyrrolidone acetylenic derivative is N-vinyl pyrrolidone; however, I am not talking about vinyl but actual acetylenic moieties attached somehow to the pyrrolidone ring. For example:

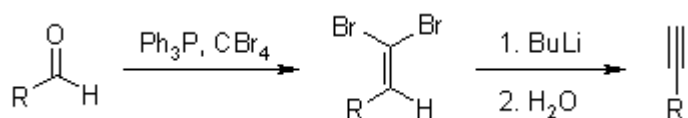


R groups can be alkyne derivatives if diynes are to be considered.

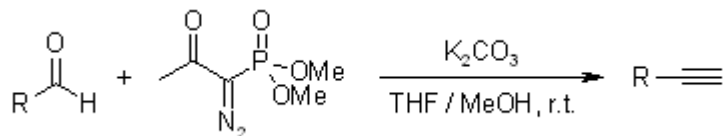
Chart 1 General acetylenic pyrrolidone derivatives (Not to be considered exhaustive).

Other methods going from aldehydes to alkynes are possible.

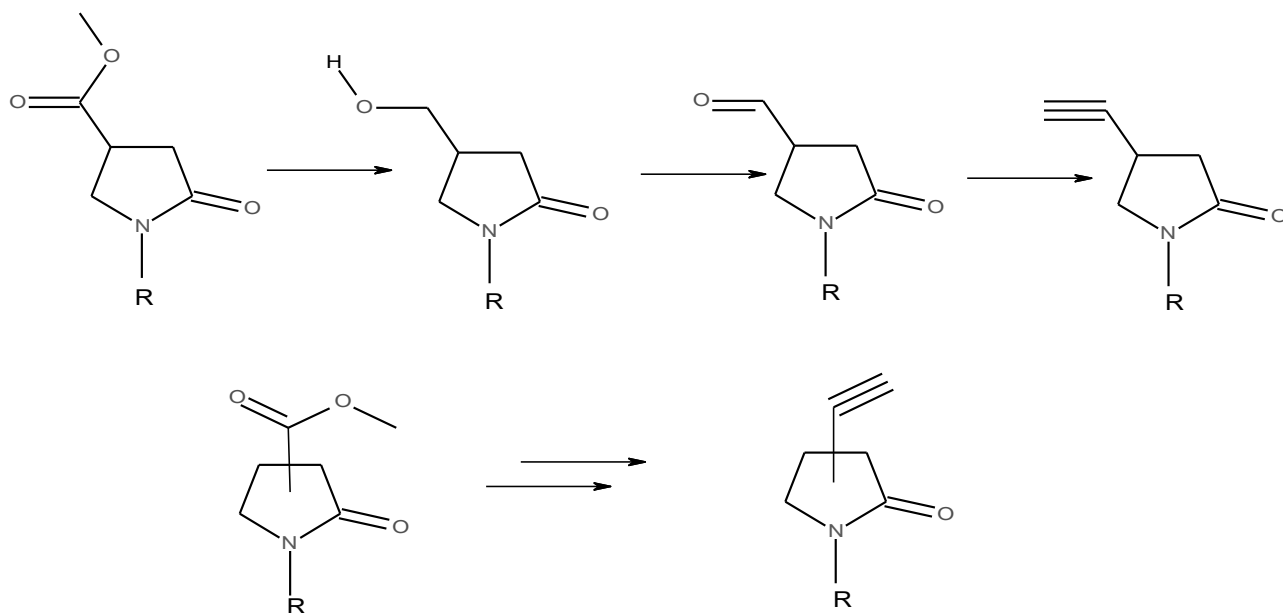
For example the **Corey-Fuchs Reaction**:



“The **Seyferth-Gilbert Homologation** is the base-promoted reaction of dimethyl (diazomethyl)phosphonate with aldehydes and aryl ketones at low temperatures, and provides a synthesis of alkynes. The **Ohira-Bestmann modification** using dimethyl 1-diazo-2-oxopropylphosphonate allows the conversion of base-labile substrates such as enolizable aldehydes, which would tend to undergo **aldol condensation** under the Seyferth-Gilbert conditions. Therefore wherever an aldehyde or its primary alcohol starting compound, attached to the pyrrolidone ring, can be converted by these reactions to an alkyne derivative.”

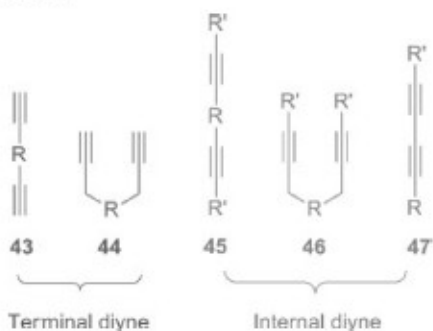


For example:



The next chart shows the many ways that alkyne monomers can be constructed.

Chart 2. General Structures of Terminal and Internal Diyne Monomers



Acetylenic Polymers: Syntheses, Structures, and Functions

Scheme 2. Examples of Linear Alkyne Polymerizations

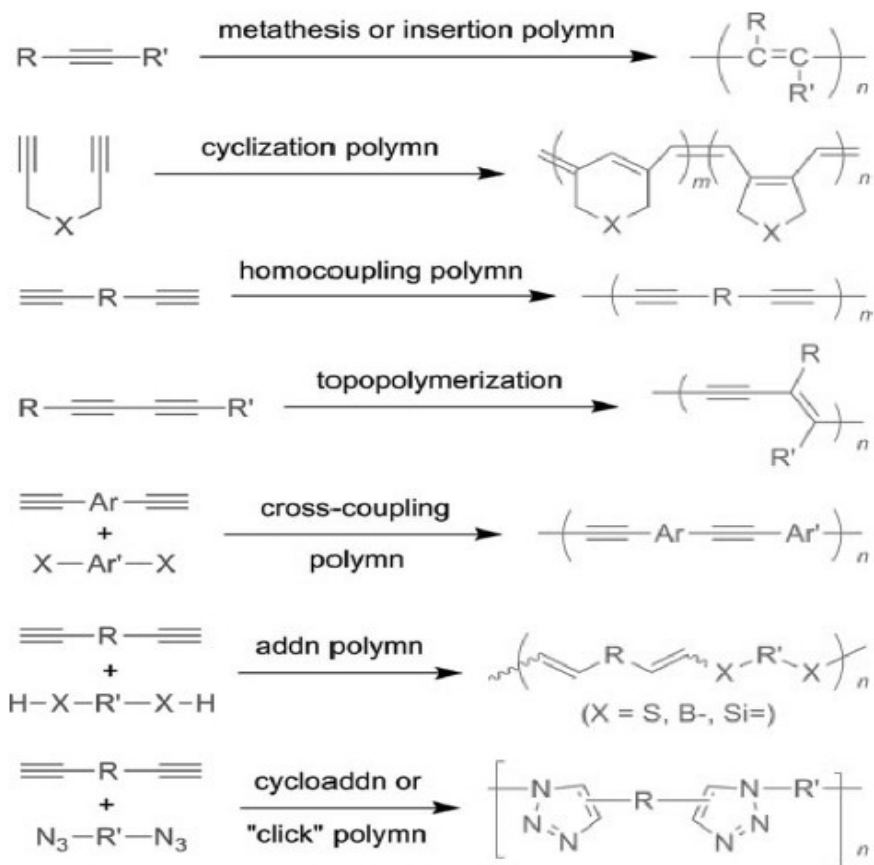


Chart 2 shows the many ways that alkynes can be polymerized.

I will not discuss the click polymerization which can be reviewed in numerous references especially *Macromolecules* 2010, 43, 5538–5543.

Chart 3 illustrates a few possibilities for pyrrolidone acetylenic monomers and polymers.

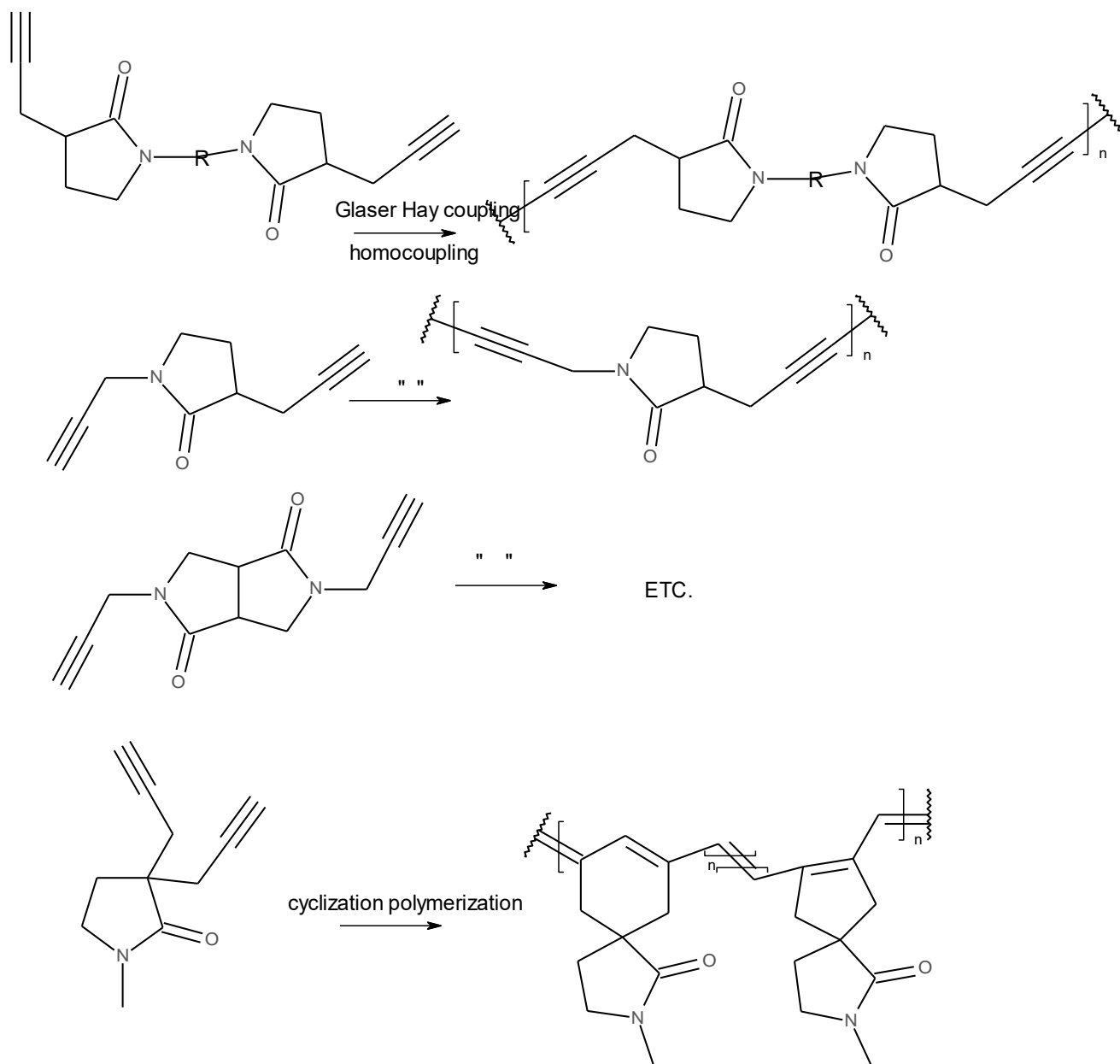
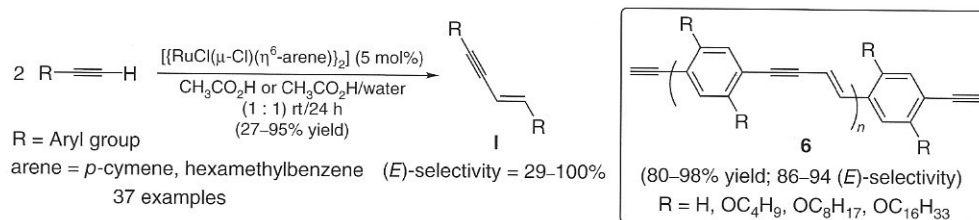


Chart 3 Examples of pyrrolidone alkyne based monomers and polymers.

Obviously many other monomers and polymers could be displayed and chart 3 is not meant to be limiting. For example:

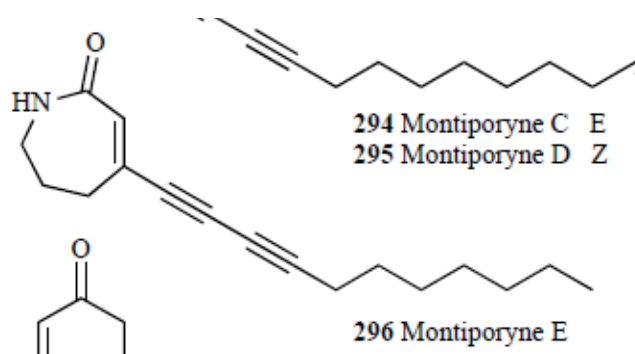


Scheme 11.5 Dimerization of aryl alkynes catalyzed by $[\{\text{RuCl}(\mu\text{-Cl})(\eta^6\text{-arene})\}_2]$ complexes and structure of the π -conjugated polymer (*E*)-6.

Chap 11, Modern Alkyne Chemistry, Trost and Li eds., Wiley, 2015.

Although this example is for aromatic diynes, it does show the ability to generate polymers and the chapter shows many examples of this dimerization reaction catalyzed by transition metal catalysts complexes.

What then is the utility of these polymers? The first potential application is as a medicinal. Several reviews have appeared that illustrate the value of said alkyne monomers and polymers or more accurately oligomers. For example Bioactive acetylenic metabolites by D. Kuklov et. al. *Phytomedicine* 20 (2013) 1145–1159 and Acetylenic Anticancer Agents by A. Siddiq, and V. Dembitsky; *Anti-Cancer Agents in Medicinal Chemistry*, 2008, 8.

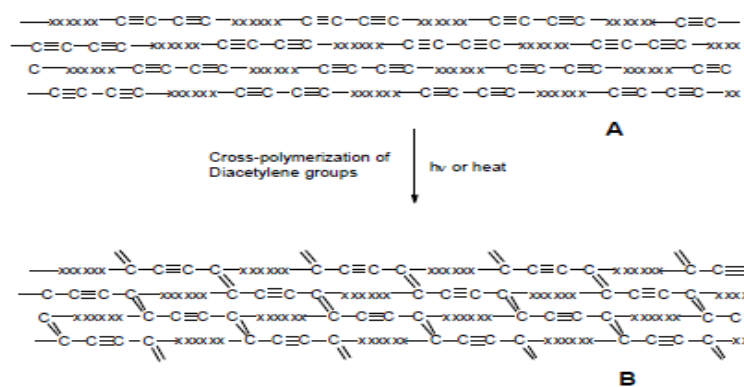


Alkyne structures #296 actually shows a lactam. The medicinal alkynes are mono, di or oligomeric alkynes; therefore the starting monomers I have shown above would be structures worth checking out because as the abstract for Kuklev et. al. article above states:

“This article focuses on anticancer, and other biological activities of acetylenic metabolites obtained from plants and fungi. Acetylenic compounds belong to a class of molecules containing triple bond(s). Naturally occurring acetylenics are of particular interest since many of them display important biological activities and possess anti tumor, antibacterial, antimicrobial, anti fungal, and immuno suppressive properties. They are of great interest to medicine, pharmacology, medicinal chemistry, and the pharmaceutical industries. This review presents structures and describes cytotoxic activities of more than 100 acetylenic metabolites, including fatty alcohols, ketones, and acids, acetylenic cyclohexanoids, spiroketal enol ethers, and carotenoids isolated from fungi and plants.”

However, no pyrrolidone moieties are shown in the myriad of illustrated alkyne structures revealed in the said references. Since the alkynes reviewed are all natural products, it may well be that one built around pyrrolidone might be effective because living entities have never been exposed to said compounds. Medicinal chemical drug discovery can start with a natural product lead but then numerous variations are tried in order to optimize effectiveness (Medicinal Chemistry by G. Patrick, Oxford, 2009 and The Organic Chemistry of Drug Design and Drug Action, Silverman and Holladay, Elsevier, 2014.) Said pyrrolidone acetylenics might be a variation worth pursuing.

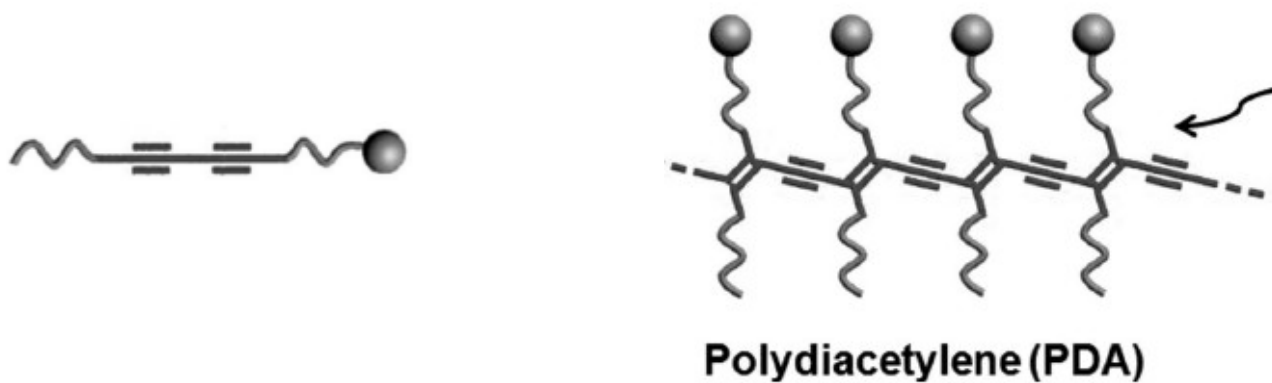
The polydiynes suggested here can react further to cross-link. For example:



Revista de la Sociedad Química de México. Vol. 46. Núm. 1 (2002) 32-37

Polymer Journal, Vol. 26, No. 1, pp 93—97 (1994)

Diacetylene monomers themselves polymerize with UV or heat to form polymers.



Such cross-linked structures have interesting optical properties.

Polydiacetylenes (PDAs)^[10-22] are structurally very unique conjugated polymers. These polymers that possess alternating ene-yne conjugated structures are prepared from self-assembled supramolecular diacetylene (DA) monomers. Owing to the existence of extensively delocalized π -electron networks and conformational restrictions present along the main chain, PDAs have unique optical properties. In particular, PDAs undergo distinct color changes (typically blue-to-red) when their arrayed p-orbitals are distorted under the influence of environmental perturbations (eg., heat, solvent, current, magnetic field, strain force, ions, ligand-receptor interactions).^[23-47]

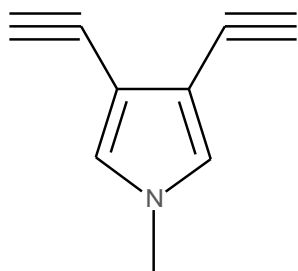
Adv. Funct. Mater. **2014**, *24*, 5186–5193

monomers. The new PAs with appropriate backbone–pendant combinations show various functional properties such as liquid crystallinity, photoconductivity, light emission, ionic susceptibility, photoresistance, chromism, helical chirality, optical nonlinearity, self-assembly, cytocompatibility, and bioactivity. The properties of the PAs are tuned internally and manipulated externally: the former is achieved by changing their molecular structures, especially their functional pendants, while the latter is accomplished by applying thermal, mechanical, electrical, photonic, and chemical stimuli.

Acc. Chem. Res. **2005**, *38*, 745–754

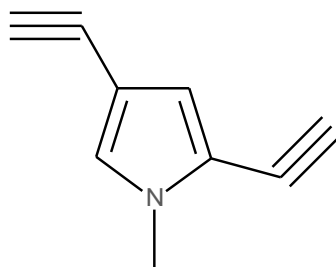
Also take a look at this reference, *Chem. Soc. Rev.*, 2012, **41**, 4610–4630. It covers “Biosensors and chemosensors based on the optical responses of polydiacetylenes.”

An additional type of pyrrolidone containing polymer can be generated from polypyrrole acetylenic derivatives. For example:



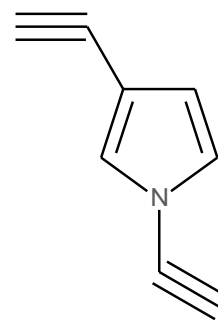
A

3,4-diethynyl-1-methyl-pyrrole



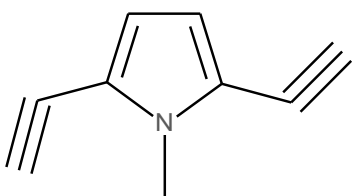
B

2,4-diethynyl-1-methyl-pyrrole



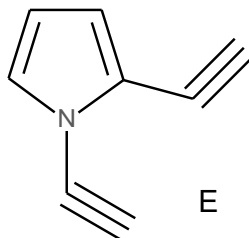
C

1,3-diethynylpyrrole



D

2,5-diethynyl-1-methyl-pyrrole



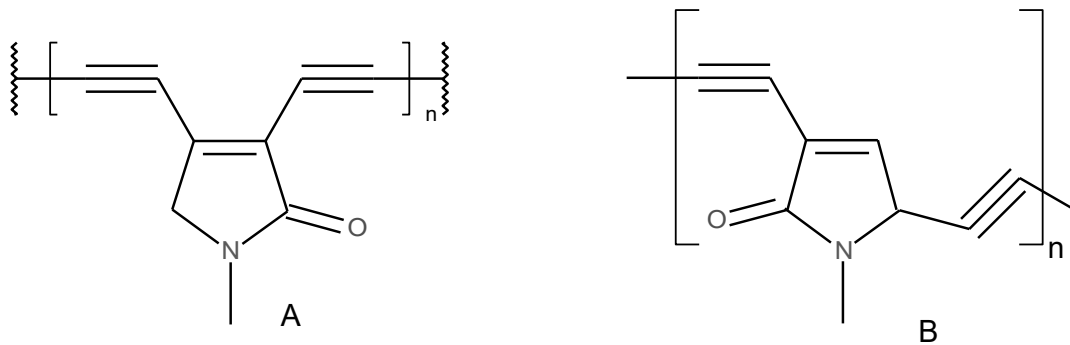
E

1,2-diethynylpyrrole

1. Zh. Org. Khim., 35(10):1530-1533. and 38(7): 1115-1117 and 27(8): 1798
2. Syn. Methods., 48,(3): 295-300.
3. JACS 114(9): 3247-3251.
4. The above are reviewed in **Chemistry of Pyrroles**
by B. A. Trofimov et. al., CRC Press 2014.

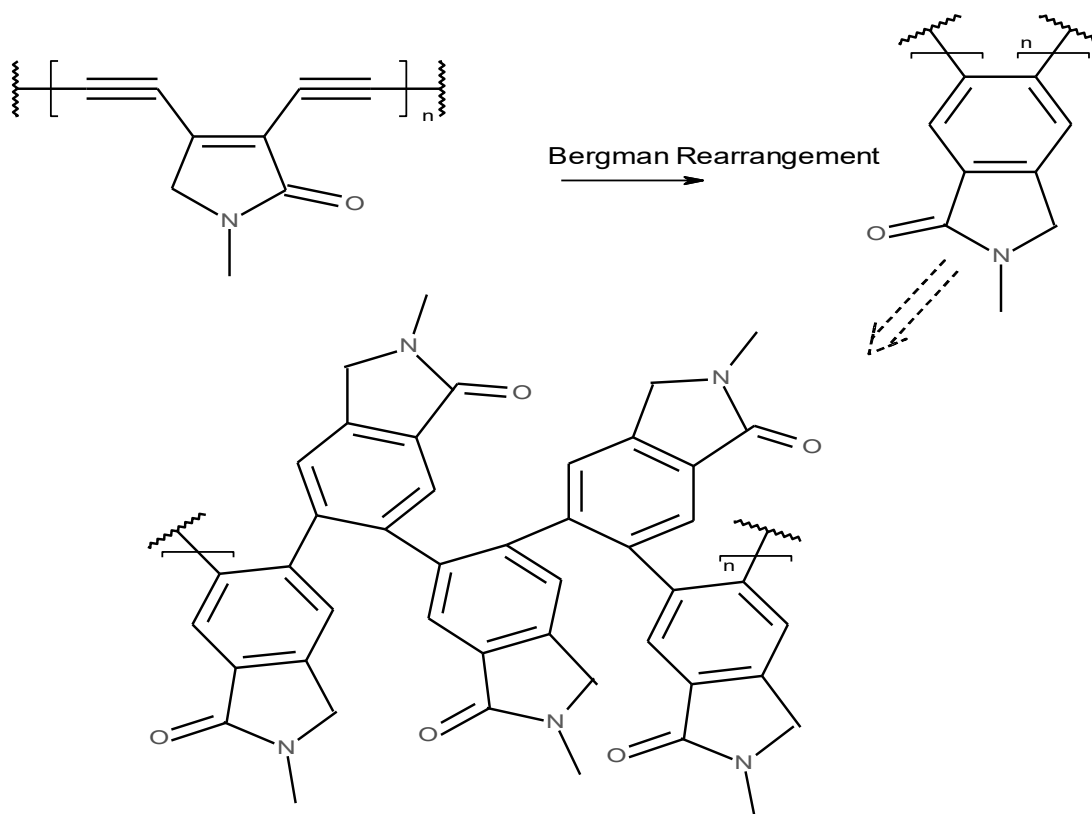
They can after polymerization be oxidized with for example hydrogen peroxide to generate 3-pyrrolin-2-ones(p 508, Pyrroles R. A. Jones Ed. Vol 48 part 1, Wiley, 1990).

For example:

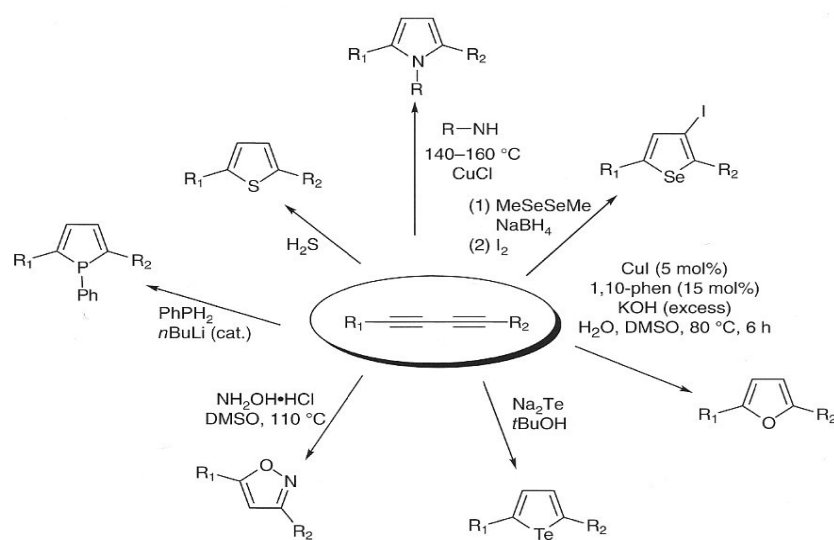


Similar structures for C&E but not for D

“A” polymerized by Glaser-Hay would produce a conjugated polymer that would have very interesting properties. It is also known that when exposed to strong bases, the unsaturation will probably conjugate; therefore, “C, E and possibly D could generate conjugated polymers by a Zipper reaction. Example A above could undergo a Bergman Rearrangement to form a polyphenylene that could be water soluble:



Obviously there are many other coupling reactions; therefore, I recommend for further insight “Modern Alkyne Chemistry” Trost & Li eds., (Wiley, 2015). This book also presents the following examples of reactions of diynes



Scheme 12.17 Synthesis of heterocycles from diynes.

These derivatives can result in the incorporation of these heterocyclics into the polymer backbone, possibly enhancing their conductivity and/or color indicator responses.

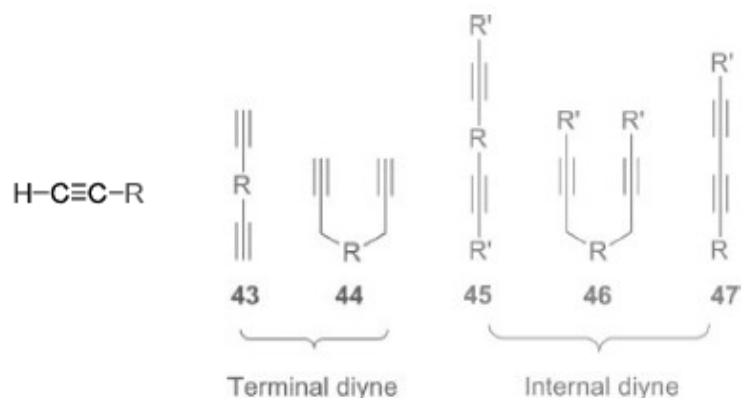
Pyrrolidone can contribute water solubility, interaction of one pyrrolidone with another (witness the high bp for the small NMP molecule) and complexation. Such complexation of target molecules could result in unique indicator PDA polymers for various applications (Biosensors and chemosensors based on the optical response of polydiacetylenes, *Chem. Soc. Rev.*, 2012, **41**, 4610–4630).

The ideas expressed here apply generally to lactams and amides; however, because of the uniqueness of the five membered pyrrolidone, my ideas are expressed highlighting its structure but they are not meant to be limiting.

I found only one reference in the literature concerning alkyne pyrrolidone derivatives (*Macromolecules* 2010, 43, 5538–5543) and I would like to hear from anyone interested in this subject especially if you know of other references?

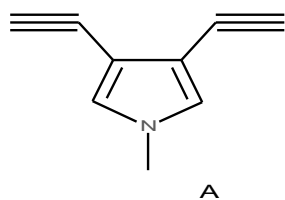
I claim:

1. Acetylenic monomers comprising the following structures,

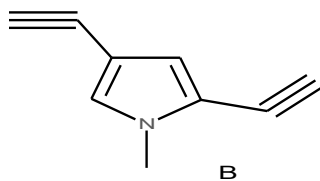


- wherein the R and R' group or groups are mono or disubstituted pyrrolidone rings in which the alkyne moiety is attached at any position on said pyrrolidone rings.
2. The monomers of claim 1 wherein those exhibiting an alkyne with a terminal hydrogen can couple said alkynes by the Glaser-Hay or similar oxidative coupling reactions.
 3. The monomers of claim 1 wherein those exhibiting an alkyne with a terminal hydrogen can be coupled by the click azide reaction to form polymers.
 4. The monomers of claim 1 wherein said monomers can be polymerized by metathesis type reactions.
 5. The monomers of claim 1 wherein said monomers are derived by the base catalyzed reaction of pyrrolidone with propargyl bromide or chloride.
 6. The monomers of claim 1 wherein said monomers are prepared from pyrrolidones derivatised with aldehyde group or groups.
 7. Polymers and copolymers prepared from the monomers of claim 1.

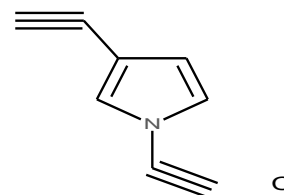
8. Acetylenic monomers comprising the following structures:



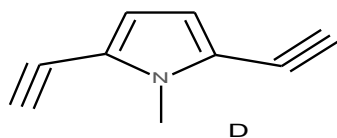
3,4-diethynyl-1-methyl-pyrrole



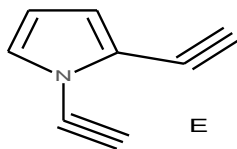
2,4-diethynyl-1-methyl-pyrrole



1,3-diethynylpyrrole



2,5-diethynyl-1-methyl-pyrrole

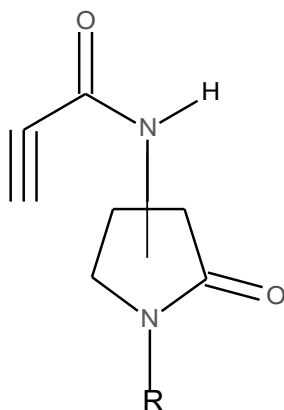


1,2-diethynylpyrrole

9. Polymerization of the monomers of claim 8 by the Glaser-Hay or related reactions.

10. The polymers of claim 8 further reacted with an oxidation reagent to generate 3-pyrrolin-2-ones in said polymer backbone.

11. Acetylenic monomers comprising the following structures:



wherein the R group is chosen from alkyne moieties either directly attached to nitrogen or as a terminal group on an alkyl chain.